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Early prediction of hospital admission for emergency department patients, a comparison between patients younger or older than 70-years.

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Lucke et al. Early prediction of hospital admission for emergency department patients, a comparison between patients younger or older than 70-years.

TITLEPAGE

Title

Early prediction of hospital admission for emergency department patients, a comparison between patients younger or older than 70-years.

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Lucke et al. Early prediction of hospital admission for emergency department patients, a comparison between patients younger or older than 70-years

ABSTRACT

Objective: The aim of this study was to develop models that predict hospital admission of emergency department patients in patients younger and older than 70 and compare their performance.

Method: Prediction models were derived in a retrospective observational study of all patients ≥18 years-old visiting the emergency department (ED) of a university hospital during the first 6 months of 2012. Patients were stratified into two age groups (<70 years-old, ≥ 70years-old). Multivariable logistic regression analysis was used to identify predictors of hospital admission among factors available immediately after patient arrival to the ED. Validation of the prediction models was performed on patients presenting to the ED during the second-half of the year 2012.

Results: 10,807 patients were included in the derivation and 10,480 in the validation cohorts. Strongest independent predictors of hospital admission among the 8,728 patients <70 years-old were age, sex, triage category, mode of arrival, performance of blood tests, chief complaint, ED revisit, type of specialist, phlebotomised blood sample, and all vital signs. Area-under-the-curve (AUC) of the validation cohort for those <70 years-old was 0.86 (95%CI 0.85-0.87). Among the 2,079 patients ≥70 years the same factors were predictive except for gender, type of specialist and heart rate; the AUC was 0.77 (95%CI 0.75-0.79). The prediction models could identify a group of 10% patients with the highest risk in whom hospital admission was predicted at ED triage with a positive predictive value (PPV) of 71% (95%CI 68-74%) in younger and PPV 87% (95%CI 81-92%) in older patients.

Conclusion:

Demographic and clinical factors readily available early in the ED visit can be useful in identifying patients who are likely to be admitted to hospital. While the model for the younger patients had a higher AUC, the model for older patients had a higher PPV in identifying the patients at highest risk for admission. Of note, heart rate was not a useful predictor in the older patients.

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Lucke et al. Early prediction of hospital admission for emergency department patients, a comparison between patients younger or older than 70-years

What this paper adds	
What is already known on this subject	**What this study adds**
• Patients presenting to the emergency department (ED) are at risk for hospital admission, functional decline and mortality, with older patients having even higher risks. • Clinical decision making tools for older patients in the ED have not been found to be effective. • It is unknown whether independent predictors may vary between age groups, which may influence the design of future tools.	• The models created in this study indicate that predictors of hospital admission from the ED are similar for younger and older patients, but differ in their prognostic capabilities. The overall prognostic ability of the models was greater for the patients under 70, but the model for older patients is better at identifying the a group of patients very likely to be admitted. • These results constitute preparatory work towards creating a screening instrument that could adequately predict hospital admission, particularly for older adults.

Lucke et al. Early prediction of hospital admission for emergency department patients, a comparison between patients younger or older than 70-years

INTRODUCTION

Older adults presenting to emergency departments (EDs) for medical care frequently are admitted to the hospital[1-4]. Despite a high probability of admission, they are at risk of having prolonged length of stay in the ED, which increases the chance of in-hospital adverse events[5]. If ED physicians had an accurate decision-making tool they could use early during the ED visit to predict which older patients have the highest probability of being admitted using routinely available demographic and clinical factors available at triage, ED length of stay might be reduced. Interventions to expedite the admission of older patients might also improve health-related and ED flow and function outcomes. Such a tool however, is not yet available[6]. It also is not yet known if demographic and clinical factors predictive of hospital admission are the same for both older and younger ED patients, and if decision-making tools comprised of these factors perform equally well for both age groups.

Independent predictors of hospital admission of ED patients have been identified[7] previously, yet mainly reflect disease severity. The Modified Early Warning Score (MEWS)[8] is frequently used to quantify disease severity and can predict probability of hospital admission,[9] disposition[10] and mortality[11] of ED patients. However, physiology, polypharmacy and multiple comorbidities of older patients affect measured vital signs and delay recognition of serious disease; when relying solely on vital signs a proportion of severely ill older patients requiring admission will not be identified[12]. Given the discrepancy in the utility of hospital admission prediction models using vital signs and disease severity when they are applied to different age groups, tools helping to predict need for admission based on other clinical characteristics also might not be equally useful for older and younger ED adult patients. If this is the case, different prediction rules should be derived and used based on patient age.

The goal of this study was therefore to derive prediction models separately for older and younger adults which identify need for hospital admission, using routinely demographic and clinical data available at ED triage. We further aimed to assess how well these prediction models performed for these two age groups. The ultimate aim for this prediction model was for its eventual application in identifying early which patients would be admitted from the ED, potentially improving efficiency of care pathways and reducing ED length of stay.

METHOD

Study design and setting

This investigation involved deriving and validating a hospital admission prediction rule for adult ED patients. Data were obtained retrospectively from the ED of the Leiden University Medical Center (LUMC), which is a tertiary care hospital with an annual census of approximately 30.000 ED visits. LUMC has an Acute Medical Unit (13 beds) designed to accept admissions from the ED. The Medical Ethics Committee waived the need for informed consent because data were collected as part of past clinical care and de-identified after extraction from the patient files.

Selection of participants

Inclusion criteria

We included all ED visits by adults ≥ 18 years-old to LUMC between January 1, 2012 and December 31, 2012. ED patients who presented between January 1 – June 30 were included in the derivation cohort, while those presenting July 1 – December 31 were included in the validation cohort.

Exclusion criteria

Patients who arrived to the ED undergoing cardiopulmonary resuscitation or classified as Manchester Triage System[13] (MTS) category 'red' (needing immediate care) were excluded because their likelihood of hospital admission was so great that a prediction tool would not be needed for this population. Patients who died in the ED and those who left without being evaluated also were excluded. In addition, patients with ED visits due to logistical reasons were excluded, such as those attending for a planned re-evaluation because they could not wait until the next available out-patient clinic appointment, visits to the ED because of lack of availability of time in the out-patient clinic, laboratory checks for logistical reasons and patients who were sent away from the ED to visit their GP (Figure 1). For this, a pre-defined list of objective criteria, based on expert opinion, was used. Patient files were checked by a single researcher (JAL) to assess exclusion criteria.

Study protocol and measurements

Data were automatically harvested from the electronic patient files (Chipsoft-EZIS®, version 5.2, 2006-2014, Amsterdam, The Netherlands) using an application designed by the LUMC department of Information Technology. One investigator (JAL) checked the data for validity and corrected typing errors. This was performed by reference to medical records in case of outliers. Furthermore using sampling JAL checked patient records to assess if study data was adequately withdrawn from the patients files. The data were not extracted manually and not subject to interpretation. Therefore, a measure of inter-rater variability is not applicable. Because the aim of this investigation was to develop a tool, using data readily available at triage, the following data were collected: age, sex, Manchester Triage System (MTS) triage category, chief complaint, mode of arrival to ED, type of specialist, ED visits within prior 30 days, indication for phlebotomised blood sample testing and vital signs. These variables were chosen by the study authors based on clinical judgement, frequently used variables in similar research[14 15] [16], their availability upon patient arrival to the ED and inclusion in the ED electronic medical records. A detailed description of the collection of all variables can be found in Supplemental Material.

Outcomes

The primary endpoint of this study was hospital admission, defined as either admission to the LUMC or transfer to another hospital for admission. This outcome was downloaded directly from the patient files.

Data Analysis

Patients were divided into two age groups for analysis, <70 years and ≥70 years-old, in line with the age cut-off used in government initiated interventions in The Netherlands[17]. Data were summarized as number and percentages or means and standard deviation for normally distributed variables, or as medians with interquartile ranges for non-normally distributed variables, as appropriate. Missing measurements of vital signs were handled as a separate category and analysed alongside categories of measured values, for example oxygen saturation has 4 categories: <90%, 91-94%, ≥95% and missing, where the reference category is ≥95% . Student's t-tests assuming independence were used to compare groups for normally distributed variables and Mann-Whitney-U tests for non-normally distributed variables. Chi-square tests were used for categorical variables. Univariable binary logistic regression was used to assess possible predictors of hospital admission using demographic and clinical characteristics extracted from the medical records. Age (< 70 years-old or ≥ 70-years-old) as an effect modifier of the relationship between variables in the model and the outcome of hospital admission was tested in the univariable analyses. Multivariable binary logistic regression was used to create an optimal model. Odds Ratios (ORs) and corresponding 95% confidence intervals (CIs) were estimated. Risks associated with age were expressed per 10 year age groups. The general rule of thumb that at least 10 events per predictor variable are needed to prevent over-fitting of the model was used. Because the database contained more than 3000 hospital admissions all potential predictor variables could be incorporated in the model[18].

An optimal model was created for each age group, using backward elimination with Akaike's Information Criterion to eliminate predictors from the model, with a cut-off point of $p<0.05$. This made the model as small as possible whilst still containing all clinically relevant parameters. Goodness of fit was tested using the Hosmer-Lemeshow test, this was performed ten times in a random subsample of 1000 patients.

This method standardized the power of the Hosmer-Lemeshow test to prevent overpowering caused by the large number of study subjects[19].

Receiver operator characteristics curves were drafted and area under the curve (AUC) estimated to measure the discriminative performance of the models. Temporal validation of the models were performed using data collected from the second-half of 2016. Calibration of the models in the validation cohort was assessed using calibration plots.

The distribution of risk of admission per age group was calculated for the validation cohort using the following equation: $\frac{1}{1+e^{(\text{intercept}+\text{linear predictor})}}$. The individual risk of each patient was calculated and ranked. The 10% of the ED patient population, per age group, with the highest chance of hospital was designated 'high risk'. This was deemed a clinically relevant and feasible cut-off point for risk of admission, for which sensitivity, specificity, positive predictive value, negative predictive value were calculated.

As a sensitivity analysis, the alternative clinically relevant vital sign cut-off values were assessed as predictors in the models and their discriminative performance and calibration were re-assessed. In a second sensitivity analysis, we created a multivariable model using the whole year 2012 (without dividing the year into successive six-month blocks of time) and randomly selected a training and test cohort to assess for introduction of bias due to the temporal validation.

Statistical significance was set at the alpha=0.05 level for all analyses. All statistical analyses were performed using IBM SPSS Statistics package (version 23, New York, USA).

Lucke et al. Early prediction of hospital admission for emergency department patients, a comparison between patients younger or older than 70-years

RESULTS

Characteristics of study subjects

In 2012, there were 27,862 visits to the LUMC ED, of which 21,287 were included in this analysis (Figure 1). The 6575 excluded patients were due to ED use for logistical reasons or arrival during CPR (n=1486), patients aged ≤18 years (n=4802) or patients with red triage or who deceased (n=287).

Baseline characteristics of the study population stratified by age group are shown in Table 1. The distribution of demographics and clinical characteristics by age group were similar within the derivation and validation cohorts.

Table 1. Baseline characteristics of study population.

	Derivation			Validation		
	<70 years	**≥70 years**		**<70 years**	**≥70 years**	
Baseline features	n=8728	n=2079	**P value**	n=8411	n=2069	**P value**
Age, median IQR	44.8 (28.8-57.4)	78.1 (73.9-83.6)		44.8 (28.4-58.0)	77.9 (73.9-83.0)	
Male, *n (%)*	4762 (54.6)	995 (47.9)	<0.001	4597 (54.7)	1044 (50.5)	0.001
Triage category, *n (%)*			<0.001			<0.001
<10 minutes	1921 (22.0)	657 (31.6)		1893 (22.5)	683 (33.0)	
<1 hour	3567 (40.9)	943 (45.4)		3557 (42.3)	966 (46.7)	
<2 hour	3205 (36.7)	472 (22.7)		2921 (34.7)	410 (19.8)	
<4 hours	35 (0.4)	7 (0.3)		40 (0.5)	10 (0.5)	
Arrival mode, *n (%)*			<0.001			<0.001
Self-referral	4258 (48.8)	467 (22.5)		3794 (45.1)	404 (19.5)	
Ambulance/other institution	1316 (15.1)	596 (28.7)		1659 (19.7)	833 (40.3)	
Referred by GP/specialist	3154 (36.1)	1016 (48.9)		2958 (35.2)	832 (40.2)	
Type of specialist			<0.001			<0.001
Medicine	3809 (43.6)	1251 (60.2)		3732 (44.4)	1245 (60.2)	
Surgery	4919 (56.4)	828 (39.8)		4679 (55.6)	824 (39.8)	
Revisit to the ED, *n (%)*			0.082			0.071
Visit <30 days	922 (10.6)	247 (11.9)		873 (10.4)	243 (11.7)	
Chief complaint[1]			<0.001			<0.001
Minor trauma	3656 (42.2)	621 (30.1)		3301 (39.6)	641 (31.2)	
Major trauma	183 (2.1)	32 (1.5)		208 (2.5)	28 (1.4)	
Chest pain	980 (11.3)	302 (14.6)		992 (11.9)	329 (16.0)	
Dyspnea	426 (4.9)	221 (10.7)		394 (4.7)	179 (8.7)	
Syncope	219 (2.5)	118 (5.7)		241 (2.9)	100 (4.9)	
Psychiatric complaints	219 (2.5)	34 (1.6)		230 (2.8)	26 (1.3)	
Malaise	1032 (11.9)	377 (18.3)		1034 (12.4)	403 (19.6)	
Abdominal pain	935 (10.7)	183 (8.9)		922 (11.1)	183 (8.9)	
Other	1018 (11.7)	177 (8.6)		1019 (12.2)	164 (8.0)	
Vital signs						
Systolic BP, mmHg[2]	136 (21.4)	145 (27.3)	<0.001	135 (21.5)	145 (28.1)	<0.001
0_2 saturation, % [3] *median, IQR*	98 (98-100)	98 (96-100)	<0.001	99 (97-100)	98 (96-99)	<0.001
Temperature, °C[4]	37.0 (0.8)	36.9 (1.0)	<0.001	37.0 (0.8)	36.9 (0.9)	<0.001

Respiratory rate, /min[5]	17.6 (4.6)	18.7 (5.5)	0.007	17.6 (4.8)	18.6 (5.4)	<0.001
Heart rate, /min[6]	86 (20)	84 (20)	<0.001	86 (21)	84 (21)	<0.001
Testing, *n (%)*			<0.001			<0.001
Phlebotomised blood sample	4714 (54.0)	1606 (77.2)		4583 (54.5)	1599(77.3)	

a) Values are mean, standard deviation unless noted otherwise.
b) Abbreviations: SD: standard deviation. n:number, IQR: interquartile range, GP: general practitioner, min: minute
c) Vital parameters measured are: 0_2: oxygen saturation, measured in percentage oxygenated haemoglobin. Systolic BP: Systolic blood pressure, measured in millimetres of mercury. Temperature measured in degrees Celsius. Heart rate and respiratory rate are measured as times per minute.
d) Number of measured values per age group.
<70 years: 1:n=17009, 2:n=9924, 3:n=10018, 4:n=9953, 5:n=5807, 6:n=10371
≥70 years: 1:n=4118, 2:n=3232, 3:n=3208, 4:n=2890, 5:n=2302, 6:n=3292
e) P values are measured by t-test for scale values and chi-square for categorical values. Mann-Whitney U test for non-parametric variables.

In the derivation cohort, 2,014 (23.1%) younger patients and 898 (43.2%) older patients were admitted to the hospital. In the validation cohort, 2,030 (24.1%) younger patients and 919 (44.4%) older patients were admitted. Baseline characteristics between patients in the derivation cohort admitted to hospital and those discharged are shown in Table 2.

Table 2. Baseline characteristics of study population, the derivation cohort stratified around hospital admission.

	<70 years			**≥70 years**		
	Discharged	**Admitted**		**Discharged**	**Admitted**	
Baseline features	n=6714	n=2014	**P value**	n=1181	n=898	**P value**
Age, median IQR	41.9 (26.8-55.6)	52.4 (40.0-62.0)	<0.001	78.1 (73.7-83.4)	78.1 (74.2-83.7)	0.280
Male, *n (%)*	3625 (54.0)	1137 (56.5)	0.052	529 (44.8)	466 (51.9)	0.001
Triage category, *n (%)*			<0.001			<0.001
<10 minutes	1066 (15.9)	855 (42.5)		270 (22.9)	387 (43.1)	
<1 hour	2609 (38.9)	958 (47.6)		530 (44.9)	413 (46.0)	
<2 hour	3007 (44.8)	198 (9.8)		374 (31.7)	98 (10.9)	
<4 hours	32 (0.5)	3 (0.1)		7 (0.6)	0 (0)	
Arrival mode, *n (%)*			<0.001			<0.001
Self-referral	3648 (54.3)	610 (30.3)		303 (25.7)	164 (18.3)	
Ambulance/other institution	782 (11.6)	534 (26.5)		287 (24.3)	309 (34.4)	
Referred by GP/specialist	2284 (34.0)	870 (43.2)		591 (50.0)	425 (47.3)	
Type of specialist			<0.001			<0.001
Medicine	2430 (36.2)	1379 (68.5)		605 (51.2)	646 (71.9)	
Surgery	4284 (63.8)	635 (31.5)		576 (48.8)	252 (28.1)	
Revisit to the ED, *n (%)*			<0.001			
Visit <30 days	595 (8.9)	327 (16.2)		118 (10.0)	129 (14.4)	0.002
Chief complaint[1]			<0.001			<0.001
Minor trauma	3370 (50.6)	286 (14.3)		456 (39.0)	165 (18.4)	
Major trauma	103 (1.5)	80 (4.0)		11 (0.9)	21 (2.3)	
Chest pain	764 (11.5)	216 (10.8)		215 (18.4)	87 (9.7)	
Dyspnea	238 (3.6)	188 (9.4)		93 (7.9)	128 (14.3)	
Syncope	141 (2.1)	78 (3.9)		64 (5.5)	54 (6.0)	
Psychiatric complaints	127 (1.9)	92 (4.6)		13 (1.1)	21 (2.3)	
Malaise	526 (7.9)	506 (25.3)		136 (11.6)	241 (26.9)	
Abdominal pain	592 (8.9)	343 (17.1)		81 (6.9)	102 (11.4)	
Other	804 (12.1)	214 (10.7)		101 (8.6)	76 (8.5)	
Vital signs						

Systolic BP, mmHg[2]	138 (20)	135 (23)	<0.001	148 (27)	142 (27)	<0.001
0_2 saturation, % [3] *median, IQR*	99 (98-100)	99 (97-100)	<0.001	98 (96-100)	98 (95-99)	<0.001
Temperature, °C[4]	36.9 (0.7)	37.2 (1.1)	<0.001	36.8 (0.6)	37.1 (1.2)	<0.001
Respiratory rate, /min[5]	16.9 (3.9)	18.6 (5.4)	<0.001	17.5 (4.3)	19.7 (6.1)	<0.001
Heart rate, /min[6]	83 (19)	91 (22)	<0.001	82 (21)	86 (20.7)	0.002
Performed test, *n (%)*			<0.001			<0.001
Phlebotomised blood sample	2868 (42.7)	1846 (91.7)		747 (63.3)	859 (95.7)	

a) Values are mean, standard deviation unless noted otherwise.
b) Abbreviations: SD: standard deviation. n:number, IQR: interquartile range, GP: general practitioner, min: minute
c) Vital parameters measured are: 0_2: oxygen saturation, measured in percentage oxygenated haemoglobin. Systolic BP: Systolic blood pressure, measured in millimetres of mercury. Temperature measured in degrees Celsius. Heart rate and respiratory rate are measured as times per minute.
d) Number of measured values per age group.
<70 years: 1:n=8668, 2:n=5006, 3:n=5000, 4:n=4795, 5:n=2895, 6:n=5178,
≥70 years: 1:n=2065, 2:n=1589, 3:n=1582, 4:n=1434, 5:n=1154, 6:n=1614
e) P values are measured by t-test for scale values and chi-square for categorical values. Mann-Whitney U test for non-parametric variables.

Differences in baseline characteristics between the derivation and validation cohorts, stratified by age, can be found in Supplemental Table 1.

Relationship of patient demographic and clinical factors to hospital admission

The univariable analyses examining the relationship between patient demographic and clinical characteristics and hospital admission stratified by the two age groups are provided in Supplemental Table 2. The factors associated with hospital admission were the same for both age groups (for example; urgent triage category, phlebotomised blood sample, fever) although the strength of the relationships differed for some factors between age groups. The variables in the final model for the younger patients are age, sex, triage category, arrival mode, chief complaint, ED revisit, type of specialist, phlebotomised blood sample, oxygen saturation, systolic BP, temperature, heart rate and respiratory rate. The variables in the final model for the older patients are triage category, arrival mode, chief complaint, type of specialist, phlebotomised blood sample, oxygen saturation, systolic BP, temperature and respiratory rate.

As shown in the results for the multivariable models by age groups (Table 3), urgent triage category, hospital arrival by ambulance, indication for taking a phlebotomised blood sample, presenting complaint of "malaise", or a non-surgical problem, a systolic blood pressure below 100mmHg, oxygen saturation below 95%, fever or tachypnea >30 breaths/min were associated with greater odds of hospital admission for both age groups. Chest pain, loss of consciousness and dyspnea as a presenting complaint, as well as no measured blood pressure were associated with a significantly decreased odds of being admitted among older patients while in younger patients chest pain decreased the probability of hospital admission. In the sensitivity analyses, similar results were found for the relationship between patient demographic and clinical factors and hospital admission when a single model instead of separate models for the two age groups were used (Supplemental Table 3) and when a randomly selected training and test cohort were used for these comparisons (Supplemental Table 4).

Table 3: Final multivariable models of hospitalization of patients at the Emergency Department.

	< 70 years			≥70 years		
Predictor	**OR**	**95% CI**		**OR**	**95% CI**	
Age/10	1.25	1.19	1.30			
Sex						
Male	1.25	1.11	1.42			
Female	ref	ref	ref			
Triage category						
>1 hour	ref	ref	ref	ref	ref	ref
< 1 hour	2.22	1.85	2.67	1.72	1.27	2.33
< 10 min	3.64	2.93	4.52	3.15	2.19	4.53
Arrival mode						
Self- referral	ref	ref	ref	ref	ref	ref
Referred	1.21	1.05	1.40	1.09	0.82	1.44
Ambulance	1.94	1.63	2.32	1.40	1.03	1.90
Chief Complaint						
Minor trauma	ref	ref	ref	ref	ref	ref
Major trauma	1.31	0.89	1.94	0.90	0.39	2.08
Chest pain	0.28	0.21	0.36	0.19	0.13	0.29
Dyspnea	0.79	0.58	1.07	0.44	0.28	0.68
Syncope	0.74	0.51	1.06	0.52	0.32	0.83
Psychiatric	1.48	1.03	2.13	1.29	0.59	2.84
Malaise	1.31	1.03	1.66	1.27	0.90	1.78
Abdominal pain	1.34	1.07	1.68	1.11	0.74	1.66
Other	1.13	0.89	1.43	1.23	0.80	1.88
Type of specialist						
Medicine	1.17	0.99	1.37			
Surgery	ref	ref	ref			
Revisit to the ED	1.57	1.32	1.88	1.94	1.41	2.67
Phlebomotised blood sample	4.79	3.83	5.99	7.46	4.94	11.28
Oxygen saturation						
≤ 90%	1.80	0.93	3.48	4.26	1.77	10.25
91-94%	1.78	1.26	2.51	1.62	1.04	2.52
≥ 95%	ref	ref	ref	ref	ref	ref
Missing	1.11	0.81	1.52	1.14	0.67	1.92
Systolic BP						
≤100	1.96	1.33	2.88	1.67	0.91	3.06
101-199	ref	ref	ref	ref	ref	ref
>200	1.32	0.70	2.47	0.74	0.41	1.32
Missing	0.57	0.40	0.82	0.52	0.30	0.89
Temperature						
≤35.0	1.86	0.89	3.87	0.96	0.36	2.56
35.1-38.4	ref	ref	ref	ref	ref	ref
≥38.5	3.34	2.41	4.61	3.43	1.82	6.47
Missing	0.85	0.70	1.02	0.93	0.69	1.25

Lucke et al. Early prediction of hospital admission for emergency department patients, a comparison between patients younger or older than 70-years

Heart rate						
<50	0.67	0.36	1.26			
51 - 100	ref	ref	ref			
101 -110	1.62	1.29	2.03			
111-129	1.57	1.22	2.02			
>130	2.57	1.76	3.74			
Missing	1.07	0.69	1.68			
Respiratory rate						
<8	0.75	0.15	3.74	2.37	0.15	36.95
9-14	ref	ref	ref	ref	ref	ref
15-20	0.94	0.76	1.15	1.04	0.74	1.45
21-29	1.29	0.99	1.69	1.74	1.16	2.62
>30	3.98	1.99	7.95	4.41	1.86	10.43
Missing	1.05	0.85	1.29	0.99	0.69	1.42
Intercept	-4.572			-2.623		
AUC (95% CI)	0.85 (0.84-0.86)			0.81 (0.79-0.82)		
GoF-value	0.289			0.559		
Temporal validation AUC (95%CI)	0.86 (0.85-0.87)			0.77 (0.75-0.79)		

a) Abbreviations: n: number, OR: odds ratio, 95%CI: 95% confidence interval. GoF= Hosmer-Lemeshow Goodness of Fit χ^2 test. AUC: Area Under The Curve

b) Age in years divided by ten.

c) Vital parameters measured are oxygen saturation, measured in percentage oxygenated haemoglobin. Systolic BP: Systolic blood pressure, measured in millimetres of mercury. Temperature measured in degrees Celsius. Heart rate and respiratory rate are measured as times per minute.

d) P-value values are derived from multiple logistic regression analysis.

e) Individual chance of hospital admission <70 years $= 1/(1 + \exp\left(-\left(-4.572 + \left(0.220 * \frac{\text{age}}{10}\right) + 0.225 * \text{male} + 0.798 * \text{triage} < 1\text{ hour} + 1.292 * \text{triage} < 10\text{ min} + 0.194 * \text{self} - \text{referral} + 0.664 * \text{ambulance} + 0.273 * \text{major trauma} + -1.282 * \text{chestpain} + -0.238 * \text{breathlessness} + -0.305 * \text{syncope} + 0.391 * \text{psychiatric} + 0.269 * \text{malaise} + 0.294 * \text{abdominal pain} + 0.122 * \text{other complaint} + 0.155 * \text{medicine} + 0.453 * \text{revisit} + 1.567 * \text{blood drawn} + 0.585 * \text{sat} \leq 90\% + 0.576 * \text{sat}91 - 94\% + 0.103 * \text{missing sat} + 0.674 * \text{BP} \leq 100 + 0.277 * \text{BP} \geq 200 + -0.558 * \text{BP missing} + 0.619 * \text{temp} \leq 35 + 1.205 * \text{temp} \geq 38.5 + -0.165 * \text{temp missing} + -0.395 * \text{heartrate} \leq 50 + 0.481 * \text{heartrate } 101 - 110 + 0.450 * \text{heartrate } 111 - 129 + 0.943 * \text{heartrate} \geq 130 + 0.071 * \text{heartrate missing} + -0.290 * \text{resp rate} \leq 8 + -0.064 * \text{resp rate } 15 - 20 + 0.256 * \text{resp rate } 21 - 29 + 1.380 * \text{resp rate} \geq 30 + 0.047 * \text{resp rate missing}\right)\right))$

f) Individual chance of hospital admission ≥70 years $=1/(1 + \exp(-(-2.623 + 0.541 * \text{triage} < 1\text{ hour} + 1.148 * \text{triage} < 10\text{ min} + 0.086 * \text{self} - \text{referral} + 0.337 * \text{ambulance} + -0.103 * \text{major trauma} + -1.640 * \text{chestpain} + -0.829 * \text{breathlessness} + -0.659 * \text{syncope} + 0.258 * \text{psychiatric} + 0.236 * \text{malaise} + 0.102 * \text{abdominal pain} + 0.208 * \text{other complaint} + 0.663 * \text{revisit} + 2.010 * \text{blood drawn} + 1.449 * \text{sat} \leq 90\% + 0.483 * \text{sat}91 - 94\% + 0.128 * \text{missing sat} + 0.511 * \text{BP} \leq 100 + -0.300 * \text{BP} \geq 200 + -0.655 * \text{BP missing} + - 0.037 * \text{temp} \leq 35 + 1.232 * \text{temp} \geq 38.5 + -0.071 * \text{temp missing} + 0.861 * \text{resp rate} \leq 8 + 0.037 * \text{resp rate } 15 - 20 + 0.555 * \text{resp rate } 21 - 29 + 1483 * \text{resp rate} \geq 30 + -0.014 * \text{resp rate missing})))$

The AUC of the prediction model for the derivation cohort for hospital admission among patients <70 years-old was 0.85 (95%CI 0.84-0.86), which was higher than the AUC of the prediction model for ≥70 years-old (0.81 (95% CI 0.79-0.82). In the temporal validation cohort, the AUC for younger patients was 0.86 (95%CI 0.85-0.87), which also was higher than the model for older patients, which was 0.77 (95%CI 0.75-0.79).

The calibration plots in Figure 2 show the observed hospital admission rate in relation to the predicted chance of hospital admission in the validation group. The Hosmer-Lemeshow Goodness of Fit-test in both groups was p>0.05, suggesting that predicted probabilities are in line with the observed and that the model fit the data well. In a sensitivity analysis using different cut-off points for vital signs in younger and older patients, there were no differences in the performance of either model.

As shown in Figure 3, there were more younger adult patients with a lower predicted chance of hospital admission in the validation cohort than for the older adult group. The predicted chance of hospital admission was also more equally distributed among the older patients. Table 4 depicts the test performance parameters of the models in predicting hospital admission by age group. Specificity, PPV and LR+ were higher in older patients. The prediction model shows superior predictive applicability than for example triage category alone.

Lucke et al. Early prediction of hospital admission for emergency department patients, a comparison between patients younger or older than 70-years.

Table 4: Predictive applicability of prediction model in validation cohort

	Sens (95%CI)	Spec (95% CI)	PPV(95% CI)	NPV(95% CI)	LR+(95% CI)	LR-(95% CI)
10% of population with highest risk of hospital admission						
<70 years	0.30 (0.28-0.32)	0.96 (0.96-0.97)	0.71 (0.68-0.74)	0.81 (0.80-0.82)	7.85 (6.81-9.04)	0.73 (0.71-0.75)
≥70 years	0.19 (0.17-0.22)	0.98 (0.96-0.98)	0.87 (0.81-0.91)	0.60 (0.58-0.62)	8.23 (5.54-12.2)	0.82 (0.80-0.85)
Triage category - <10 min						
<70 years	0.42 (0.40-0.44)	0.84 (0.83-0.85)	0.45 (0.43-0.47)	0.82 (0.81-0.83)	2.58 (2.39-2.78)	0.69 (0.68-0.72)
≥70 years	0.46 (0.42-0.49)	0.77 (0.75-0.80)	0.61 (0.58-0.65)	0.64 (0.61-0.67)	1.99 (1.76-2.27)	0.70 (0.66-0.75)

a) Abbreviations: 95%CI: 95% confidence interval, sens: sensitivity, spec: specificity, PPV: positive predictive value, NPV: negative predictive value, LR+: positive likelihood ratio, LR-: negative likelihood ratio, AUC: area under the curve

DISCUSSION

In this investigation, we found that routinely collected demographic and clinical patient data at ED triage can be used to predict hospital admission among ED patients. However, although the predictors of hospital admission are the same regardless of age groups, the strength of the relationships between patient demographic and clinical factors and hospital admission as well as the performance of the predictive models differ by age groups (<70 year-old vs. ≥70 years-old). Overall predictive performance of the model was better for younger patients, although positive predictive value was higher among older patients.

Our findings are in concordance with prior studies[7 9 14 20] [10]. Most of these variables, like triage category[13], chief complaint and abnormal vital signs[9], reflect illness severity at ED presentation. Sun *et al.*[14] derived a prediction model for hospital admission in over 300.00 ED patients in Singapore. It was validated using split-validation and the model used age, race, arrival mode, triage category, preceding hospital admission or ED visit and chronic conditions as predictors. The AUC of this model was 0.85, which is comparable to our findings. Cameron et al. created a similar prediction model in over 300.000 adult ED patients in Scotland. This prediction model used age, early warning score, triage category, referral and arrival mode and preceding hospital admission within one year and found an AUC of 0.88. A model by Meisel et al. in the United States to predict hospital admission in the pre-hospital phase used age and chief complaint as predictors and found an AUC of 0.80[20]. For all these studies, the investigators observed that age was an important factor in predicting hospital admission, however they did not compare the predictive properties of disease severity between the younger and older patients. A prediction model for hospitalization for ED patients in 4,873 patients ≥75 years-old by LaMantia et al[21] , included injury severity, heart rate, diastolic blood pressure and patient chief complaint as predictors had an AUC of 0.73 (95%CI 0.69-0.76), with a sensitivity of 33%, specificity 88% and LR of 2.75. Our model performed better, possibly due to inclusion of more demographic and clinical characteristics. Also sample size, differences in care system and selection of patients could have influenced the performance of the models. Physiology, polypharmacy and multi-morbidity affects the measured vital signs of older patients, and some studies indicate that when relying solely on vital signs a proportion of severely ill older patients will be missed [12]. To address this concern, we assessed whether the predictors of hospital admission are different for older as compared to younger adult ED patients. In our model for older patients, age was not a predictor. One explanation for this observation may be that by limiting the age range to those 70 years-old and older to assess the predictive value of age there was limited contrast in this population and hence a lack of power to detect differences by age. As an alternative explanation, among older patients disease severity and geriatric factors (eg. pre-existing functional or cognitive impairment) are more important than calendar age. As shown in Table 2 there is no difference between median age for patients hospitalized or discharged in the older age group. For these reasons models that combine predictors of disease severity and geriatric factors may perform even better than ours, but such models do not exist yet.

In contrast to the prediction rule derived by Meisel et al. 'chest pain' as chief complaint was associated with a lower probability of hospital admission in our models for both older and younger patients. This observation could be explained by the care system in the region where the study was performed that patients with ST-elevation myocardial infarction bypass this ED and go to the heart-catheterisation laboratory immediately[22]. Older patients with dyspnea and syncope also had a decreased chance of hospital admission, which we explain by the fact that those patients with severe dyspnea or who have not regained consciousness after syncope are triaged 'red' and were excluded from the study.

Although it was one of the important predictors of hospital admission in our models, there were missing values for vital signs in our study database. We believe that these values are missing because the triage nurse probably deemed vital signs registration unnecessary if the patient was not perceived ill. Using missing measurements of vital signs, such as the absence of measured blood pressure, as valuable information in this study, seemed to be a marker of being less ill (Table 3). Using the combination of predictors in this study into a prediction model successfully identified the 10% of the ED patient population with the highest risk of hospital admission, for both younger and older patients.

The prediction model for older patients had a lower AUC but higher PPV for this population. When predicting chance of hospital admission, one would want a high positive predictive value. When designing an intervention based on such a prediction model, the patients with the highest risk should be targeted to prevent unnecessary and costly admissions. A low number of false-positives is therefore desirable.

Lucke et al. Early prediction of hospital admission for emergency department patients, a comparison between patients younger or older than 70-years

Using the prediction model created in this study identifies the 10% of the ED patient population with the highest probability of hospital admission with a PPV of 71% in the young and 81% in the old.

The PPV for hospital admission was higher in older than in younger patients, likely due to the higher a priori chance of hospital admission for older patients (derivation cohort: 23.1% admission rate in younger patients vs. 43.2% for older patients, validation cohort 24.1% admission rate in younger patients, 44.4% in older patients). In addition, the LR+ was slightly better for older patients, which increases its clinical utility. Thus, this tool could trigger early awareness of the high chance of hospital admission, which could affect the clinical decision-making, preparation for admission, enhancement of ED work flow and shortened length of ED stay. The overall discriminative performance of the model and odds ratios of the individual predictors were significantly higher for younger patients. This observation could be explained by three different mechanisms. First, the relationship between vital signs and disease severity is likely to be different between younger and older patients. It is well known that with aging the physiology of the body changes, with less homeostatic, respiratory and cardiovascular reserve. In combination with polypharmacy (eg. beta-blockers), severely ill older patients show less prominent vital sign abnormalities. For example, in this study heart rate was an independent predictor for younger but not older patients. This finding was also shown in two recent studies in which normal vital signs proved to be less specific for the absence of severe illness for older adults[23] [24]. This phenomenon is not captured using standard MEWS-cut off points and could explain a part of the difference in discriminative power between models observed in this study.

Second, older patients with multiple comorbidities are often in a delicate equilibrium in which they can still function with relative independence and health. However, relative minor trauma or disease can disturb this equilibrium and result in severe illness and need for hospitalization[25]. The absence of comorbidities in our model and other or currently existing models, could also explain the difference in the discriminative performance between the models for younger and older patients [10 11].

Finally, older patients are sometimes hospitalized for their increased vulnerability rather than disease severity. For example, a patient with a small social network and low functional capabilities with the same minor trauma as a younger person, would more easily be hospitalized. It has recently been shown that tools that exclusively use frailty to predict adverse outcomes in older patients, lack specificity and predictive capability[6]. The fact that overall discriminative performance of our model for the older group was lower could be explained by the lack of information about conditions more prevalent among older patients such as impaired cognitive function and functional status.

We therefore hypothesize that the combination of two dimensions: 'disease severity' and 'geriatric phenotypes' such as multi-morbidity and social, cognitive and physical function of the acutely presenting older patient, will result in an optimal model for prediction of adverse events and hospitalization.

Strengths of this study are the large number of patients and events. These features enable better estimates of test performance parameters of the models. The clear and clinically relevant endpoint also is one of the strengths, as it is without bias whether a patient was admitted or not. The present study had several limitations. First, this was a retrospective study which limits the ability to examine possible predictors which might have been obtained prospectively. There is also risk for information bias, although this was minimized by automatically harvesting data from the electronic patient files. Possible variables were selected based upon earlier research, clinical judgement and availability in the ED records. The second threat was missing measurements of vital signs, for which we conceived a solution. The fact that a parameter was not measured in a specific patient was considered to contain information with respect to the indication to perform such a measurement and as such analysed alongside measured values rather than imputed. Third, there were no data available on geriatric phenotypes such as multi-morbidity and social, cognitive and physical function, also the comorbidities in young patients are lacking. Whilst these factors could have an important impact on hospitalization, it was possible to create a robust model with high specificity. Fourth, we used temporal validation to validate the model. Temporal factors could affect who was admitted, for example time of year and changes in admission over time. However, as a sensitivity analysis we performed the same study with a randomly selected split-cohort and found similar results.

Finally, the admission rate in the current single centre study may be different in other care systems which influences its clinical applicability and PPVs of prediction models. While the prediction models has been created according to the recommendations by Stiell. et al[26] and has been internally validated using temporal data, it was not prospectively validated, evaluated in another patient population, implemented and disseminated or analysed for cost-effectiveness because it is still in the early stages of development.

In summary, the composition of prediction models for hospital admission are similar for ED patients younger and older than 70 years-old, although the AUC is higher in the model for younger patients and the model for older patients showed a higher PPV and LR+. This retrospective study could help identify determinants of admission in older ED patients. Further research should investigate the combination of disease severity with frailty to improve prediction of hospital admission. We are currently performing a multicentre, prospective follow up study (www.apop.eu)[27] in which we will derive, validate and implement a prediction model according to internationally acknowledged recommendations[26] to optimize care for this vulnerable patient group.

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DISCLOSURES

The authors declare no conflict of interest.

AUTHOR CONTRIBUTION STATEMENT

SPM, GJB, CH, AJF and BG designed the study. SPM and GJB obtained funding. JAL and JDG collected the data from the electronic patient files and JAL checked them for validity. AJMC provided statistical advice. JAL and FC performed the statistical analysis and drafted the paper. BG and SPM advised during the drafting process. All authors contributed to its revision and gave approval of the final version of the article.

COMPLIANCE WITH ETHICAL STANDARDS

The Medical Ethics Committee waived the need for informed consent as data were collected as part of past clinical care and handled anonymously.

Lucke et al. Early prediction of hospital admission for emergency department patients, a comparison between patients younger or older than 70-years

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Lucke et al. Early prediction of hospital admission for emergency department patients, a comparison between patients younger or older than 70-years.

LEGENDS OF FIGURES

Figure 1: Flowchart of participant selection.

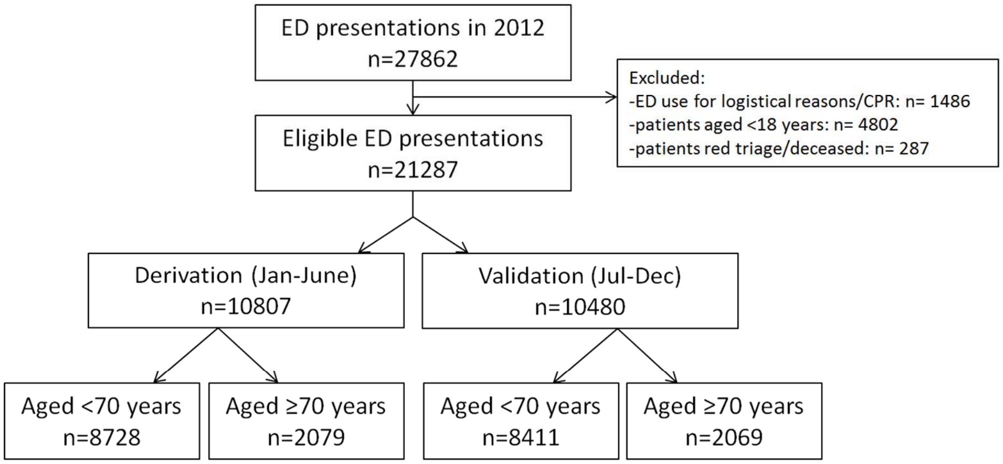
ED: Emergency department. CPR: cardiopulmonary resuscitation. Red triage: most urgent triage category, needing immediate care, often in trauma room. ED use for logistical reasons means a pre-planned re-evaluation, laboratory check or patient who had left without being seen. Individual visits were included, there can be multiple visits of one patient in this study.

Figure 2: Calibration plot of expected and observed chance of admission for patients aged <70 and ≥ 70 years – validation cohort.

Patients are divided into ten equal groups to compare expected and observed chance of admission per group. Ideally the dots would be aligned across the grey striped line. ● Indicates decile of patient group.

Figure 3: Distribution of chance of admission predicted by our model for patients aged <70 and ≥70 years – validation cohort.

The x-axes is a scale of individually predicted chance of hospital admission, ranging from 0-100%. On the y-axes is the percentage of patients in the study with that individual risk.



ED: Emergency department. CPR: cardiopulmonary resuscitation. Red triage: most urgent triage category, needing immediate care, often in trauma room. ED use for logistical reasons means a pre-planned re-evaluation, laboratory check or patient who had left without being seen. Individual visits were included, there can be multiple visits of one patient in this study.

388x179mm (96 x 96 DPI)

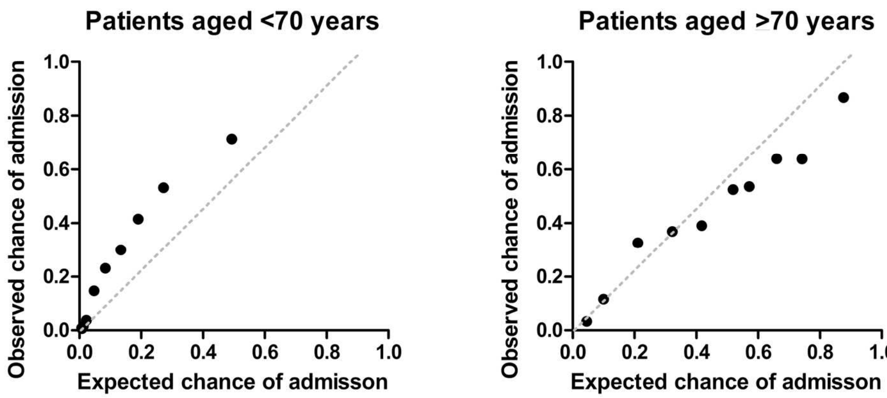


Figure 2: Calibration plot of expected and observed chance of admission for patients aged <70 and ≥ 70 years – validation cohort.

Patients are divided into ten equal groups to compare expected and observed chance of admission per group. Ideally the dots would be aligned across the grey striped line. ● Indicates decile of patient group.

84x39mm (600 x 600 DPI)

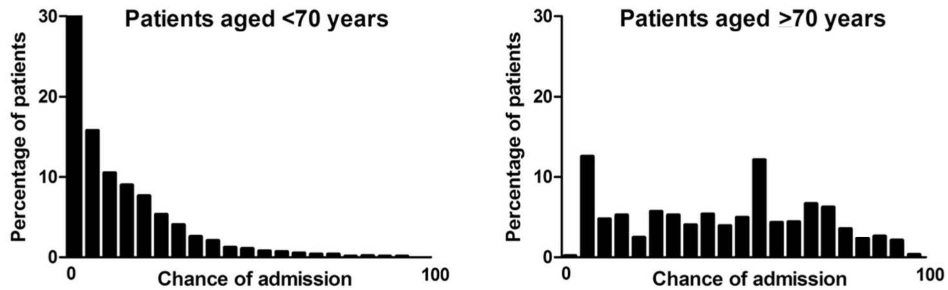


Figure 3: Distribution of chance of admission predicted by our model for patients aged <70 and ≥70 years – validation cohort.

The x-axes is a scale of individually predicted chance of hospital admission, ranging from 0-100%. On the y-axes is the percentage of patients in the study with that individual risk.

99x41mm (300 x 300 DPI)

Appendix 1: Description of collection and categorizing of variables.

DATA COLLECTION

Age and sex

Age and sex of the patient are checked with the identity card of the patient.

Triage category and chief complaint

All patients are triaged upon ED arrival by an ED-nurse according to the Manchester Triage System (MTS)[1]. The MTS consists of 52 presenting complaints to determine the patients acuity. Per presenting complaint, key questions further specify the patients acuity. Finally, questions and measurements using the ABCDE assessment are used to determine the definitive triage category. The most urgent category (red), needing immediate care, were excluded. In order of urgency the next categories are: orange (care <10 minutes), yellow (care <1 hour), green (care <2 hours), blue (care < 4 hours). For example, the presenting complaint fever would become yellow, but if the patient has an oxygen saturation less than 90% it would become orange or even red. The chief complaint was assessed using one of 52 categories available in the MTS and grouped into nine categories for analysis (appendix 2).

Mode of arrival

Patients were divided into three groups of arrival: self-referral, referred by a physician (general practitioner or medical specialist), or ambulance. When a patient was referred by a doctor, but travelled to the ED by ambulance this was categorized as 'Ambulance'. Transfers to our ED from other hospitals were also in this category.

Type of specialist

Type of specialist that the patient was assigned to was categorized into surgical (for example: surgery, orthopedics, urology) or medical (for example: internal medicine, neurology, cardiology, pulmonology).

Revisit within 30 days

From the electronic patient files data was derived as to whether the patient visited our ED within 30 days prior to the included visit. The variable 'revisit within 30 days' indicates that the index visit is their second visit within 30 days prior to the index visit.

Drawing of blood

The nurse caring for the patient draws blood according to protocol and the chief complaint, in consultation with the responsible physician. The decision to draw blood is made as soon as possible after the arrival of the patient, often within minutes. If no laboratory results were noted in the electronic patient file from the day of the ED visit, this was categorized as 'no phlebotomised blood sample'.

Vital signs

The nurse caring for the patient measures vital signs according to protocol and chief complaint, in consultation with the responsible physician. Oxygen saturation, blood pressure, respiratory rate and heart rate were measured using a medical monitor (IntelliVue MP50®, Amsterdam, The Netherlands) and manually registered into the patient file. Temperature was measured using a tympanic thermometer (Genius 2®, Mansfield, U.S.) and manually registered. The categories for vital parameters were selected according to the Modified Early Warning Score (MEWS)[2], with categories containing less than 1% of patients being merged. Missing vital signs were not imputed, but analyzed alongside registered data because a valid measurement also indicates necessity. Besides the indication for a measurement, we assessed whether the vital sign was considered too high or too low according to MEWS.

References:

1. Azeredo TR, Guedes HM, Rebelo de Almeida RA, et al. Efficacy of the Manchester Triage System: a systematic review. International emergency nursing 2015;**23**(2):47-52 doi: 10.1016/j.ienj.2014.06.001[published Online First: Epub Date]|.

2. Subbe CP, Kruger M, Rutherford P, et al. Validation of a modified Early Warning Score in medical admissions. QJM : monthly journal of the Association of Physicians 2001;**94**(10):521-6

Appendix 2: Categories of presenting complaints

CATEGORIES OF PRESENTING COMPLAINTS

9 groups of presenting complaints.

1. Minor trauma injuries
2. Major trauma injuries
3. Chest pain
4. Dyspnea
5. Syncope
6. Mental Health Problems
7. Malaise
8. Abdominal Pain
9. Others

52 possible flowcharts of Manchester Triage System re-categorized in 9 groups of presenting complaints:

1. Abdominal pain in adults	Abdominal pain (8)
2. Abdominal pain in children	Irrelevant
3. Abscesses and local infections	Minor trauma injuries (1)
4. Allergy	Others (9)
5. Apparently drunk	Others (9)
6. Assault	Minor Trauma Injuries (1)
7. Asthma	Dyspnea (4)
8. Back pain	Others (9)
9. Behaving strangely	Mental Health Problems (6)
10. Bites and stings	Minor trauma injuries (1)
11. Burns and scalds	Minor trauma injuries (1)
12. Chest pain	Chest Pain (3)
13. Collapsed adult	Loss of consciousness (5)
14. Crying baby	Irrelevant

15. Dental problems	Minor Trauma Injuries (1)
16. Diabetes	Others (9)
17. Diarrhea and vomiting	Abdominal pain (8)
18. Ear problems	Others (9)
19. Exposure to chemicals	Minor Trauma Injuries (1)
20. Facial problems	Minor Trauma Injuries (1)
21. Falls	Minor Trauma Injuries (1)
22. Fits	Loss of consciousness (5)
23. Foreign body	Minor Trauma Injuries (1)
24. GI bleeding	Abdominal pain (8)
25. Headache	Others (9)
26. Head injury	Minor trauma Injuries (1)
27. Irritable child	Irrelevant
28. Limb problems	Minor Trauma Injuries (1)
29. Limping child	Irrelevant
30. Major trauma	Major Trauma Injuries (2)
31. Mental illness	Mental Health Problems (6)
32. Neck pain	Others (9)
33. Overdose and poisoning	Mental Health Problems (6)
34. Palpitations	Chest pain (3)
35. Pregnancy	Others (9)
36. Psychiatric Illness	Mental Health Problems (6)
37. PV bleeding	Others (9)
38. Rashes	Others (9)
39. Self-harm	Mental Health Problems (6)
40. Sexually acquired infection	Others (9)
41. Shortness of breath in adults	Dyspnea (4)
42. Shortness of breath in children	Irrelevant
43. Sore throat	Others (9)

44. Testicular pain	Others (9)
45. Torso injury	Minor Trauma Injuries (1)
46. Unwell adult	Malaise (7)
47. Unwell child	Irrelevant
48. Urinary problems	Others (9)
49. Worried parent	Others (9)
50. Wounds	Minor Trauma Injuries (1)
51. Major incidents-primary	Major Trauma injuries (2)
52. Major incidents secondary	Major Trauma injuries (2)

Supplemental table 1. Comparing baseline characteristics for age groups between derivation and validation cohorts

Baseline features	Derivation <70 years n=8728	Validation <70 years n=8411	P value	Derivation >70 years n=2079	Validation >70 years n=2069	P value
Age, median IQR	44.8 (28.8-57.4)	44.8 (28.4-58.0)	0.870	78.1 (73.9-83.6)	78.9 (73.9-83.0)	0.178
Male, *n (%)*	4762 (54.6)	4597 (54.7)	0.901	995 (47.9)	1044 (50.5)	0.094
Triage category, *n (%)*			0.049			0.130
<10 minutes	1921 (22.0)	1893 (22.5)		657 (31.6)	683 (33.0)	
<1 hour	3567 (40.9)	3557 (42.3)		943 (45.4)	966 (46.7)	
<2 hour	3205 (36.7)	2921 (34.7)		472 (22.7)	410 (19.8)	
<4 hours	35 (0.4)	40 (0.5)		7 (0.3)	10 (0.5)	
Arrival mode, *n (%)*			<0.001			<0.001
Self-referral	4258 (48.8)	3794 (45.1)		467 (22.5)	404 (19.5)	
Ambulance/other institution	1316 (15.1)	1659 (19.7)		596 (28.7)	833 (40.3)	
Referred by GP/specialist	3154 (36.1)	2958 (35.2)		1016 (48.9)	832 (40.2)	
Type of specialist			0.336			1.0
Medicine	3809 (43.6)	3732 (44.4)		1251 (60.2)	1245 (60.2)	
Surgery	4919 (56.4)	4679 (55.6)		828 (39.8)	824 (39.8)	
Revisit to the ED, *n (%)*						
Visit <30 days	922 (10.6)	873 (10.4)	0.693	247 (11.9)	243 (11.7)	0.892
Chief complaint[1]			0.040			0.263
Minor trauma	3656 (42.2)	3301 (39.6)		621 (30.1)	641 (31.2)	
Major trauma	183 (2.1)	208 (2.5)		32 (1.5)	28 (1.4)	
Chest pain	980 (11.3)	992 (11.9)		302 (14.6)	329 (16.0)	
Dyspnea	426 (4.9)	394 (4.7)		221 (10.7)	179 (8.7)	
Syncope	219 (2.5)	241 (2.9)		118 (5.7)	100 (4.9)	
Psychiatric complaints	219 (2.5)	230 (2.8)		34 (1.6)	26 (1.3)	
Malaise	1032 (11.9)	1034 (12.4)		377 (18.3)	403 (19.6)	
Abdominal pain	935 (10.7)	922 (11.1)		183 (8.9)	183 (8.9)	
Other	1018 (11.7)	1019 (12.2)		177 (8.6)	164 (8.0)	
Vital signs						
Systolic BP, mmHg[2]	136 (21.4)	135 (21.5)	0.021	145 (27)	145 (28)	0.566
O_2 saturation, %[3] *median, IQR*	98 (98-100)	99 (97-100)	<0.001	98 (96-100)	98 (96-99)	0.100
Temperature, °C[4]	37.0 (0.8)	37.0 (0.8)	0.065	36.9 (1.0)	36.9 (0.9)	0.913
Respiratory rate, /min[5]	17.6 (4.6)	17.6 (4.8)	0.875	18.7 (5.5)	18.6 (5.4)	0.666
Heart rate, /min[6]	86 (20)	86 (21)	0.783	84 (20)	84 (21)	0.982
Performed test, *n (%)*						
Phlebotomised blood sample	4714 (54.0)	4583 (54.5)	0.530	1606 (77.2)	1599 (77.3)	0.979

a) Values are mean, standard deviation unless noted otherwise.
b) Abbreviations: SD: standard deviation. n:number, IQR: interquartile range, GP: general practitioner, min: minute
c) Vital parameters measured are: O_2: oxygen saturation, measured in percentage oxygenated haemoglobin. Systolic BP: Systolic blood pressure, measured in millimetres of mercury. Temperature measured in degrees Celsius. Heart rate and respiratory rate are measured as times per minute.
d) Number of measured values per age group.
<70 years: 1:n=17009, 2:n=9924, 3:n=10018, 4:n=9953, 5:n=5807, 6:n=10371
>70 years: 1:n=4118, 2:n=3232, 3:n=3208, 4:n=2890, 5:n=2302, 6:n=3292
e) P values are measured by t-test for scale values and chi-square for categorical values. Mann-Whitney U test for non-parametric variables.

Supplemental table 2: Univariable association of predictors of hospitalization of patients aged younger and older than 70 years at the emergency department – derivation cohort

Predictor	**< 70 years n=8728**				**≥ 70 years n=2079**				**P for interaction**
	n (%)	**OR**	**95%CI**		**n (%)**	**OR**	**95% CI**		
Age/10		1.42	1.37	1.47		1.06	0.93	1.22	
Sex									0.071
Male	4762 (54.6)	1.11	1.00	1.22	995 (47.9)	1.33	1.12	1.58	
Female	3966 (45.4)	ref	ref	ref	1084 (52.1)	ref	ref	ref	
Triage category									<0.001
>1 hour	3240 (37.1)	ref	ref	ref	479 (23.0)	ref	ref	ref	
< 1 hour	3567 (40.9)	5.55	4.73	6.52	943 (45.4)	3.03	2.34	3.92	
< 10 min	1921 (22.0)	12.13	10.24	14.36	657 (31.6)	5.57	4.25	7.31	
Arrival mode									<0.001
Self- referral	4258 (48.8)	ref	ref	ref	467 (22.4)	ref	ref	ref	
Referred	3154 (36.1)	2.28	2.03	2.56	1016 (48.9)	1.33	1.06	1.67	
Ambulance	1316 (15.1)	4.08	3.55	4.70	596 (28.7)	1.99	1.55	2.55	
Chief Complaint									<0.001
Minor trauma	3656 (42.2)	ref	ref	ref	321 (30.1)	ref	ref	ref	
Major trauma	183 (2.1)	9.15	6.67	12.55	32 (1.5)	5.28	2.49	11.18	
Chest pain	980 (11.3)	3.33	2.75	4.04	302 (14.6)	1.12	0.82	1.52	
Dyspnea	426 (4.9)	9.31	7.42	11.67	221 (10.7)	3.80	2.76	5.24	
Syncope	219 (2.5)	6.52	4.82	8.81	119 (5.7)	2.33	1.56	3.49	
Psychiatric	219 (2.5)	8.54	6.36	11.46	34 (1.6)	4.46	2.19	9.12	
Malaise	1032 (11.9)	11.34	9.55	13.46	377 (18.3)	4.90	3.72	6.45	
Abdominal pain	935 (10.8)	6.83	5.70	8.17	183 (8.9)	3.48	2.47	4.90	
Other	1018 (11.7)	3.14	2.59	3.80	177 (8.6)	2.08	1.47	2.94	
Type of specialist									<0.001
Medicine	3809 (43.6)	3.83	3.44	4.26	1251 (60.2)	2.44	2.03	2.94	
Surgery	4919 (56.4)	ref	ref	ref	828 (39.8)	ref	ref	ref	
Revisit to the ED	922 (10.6)	1.99	1.72	2.31	247 (11.9)	1.51	1.16	1.97	0.074
Phlebotomised blood sample	4714 (54.0)	14.74	12.49	17.38	1606 (77.2)	12.80	9.09	18.02	0.467
Oxygen saturation									0.005
≤ 90%	57 (0.7)	4.19	2.39	7.35	53 (2.5)	6.93	3.11	15.45	
91-94%	188 (2.2)	2.91	2.16	3.92	126 (6.1)	2.19	1.48	3.22	
≥ 95%	4755 (54.5)	ref	ref	ref	1403 (67.5)	ref	ref	ref	
Missing	3728 (42.7)	0.13	0.12	0.15	497 (23.9)	0.21	0.17	0.28	
Systolic BP									0.007
≤100	146 (1.7)	2.96	2.11	4.15	61 (2.9)	2.27	1.30	3.97	
101-199	4813 (55.1)	ref	ref	ref	1468 (70.6)	ref	ref	ref	
>200	47 (0.5)	1.76	0.99	3.13	60 (2.9)	0.89	0.53	1.49	
Missing	3722 (42.6)	0.11	0.09	0.13	490 (23.6)	0.17	0.13	0.22	
Temperature									0.004
≤35.0	36 (0.4)	2.68	1.39	5.19	22 (1.1)	1.83	0.76	4.39	
35.1-38.4	4471 (51.2)	ref	ref	ref	1307 (62.9)	ref	ref	ref	
≥38.5	288 (3.3)	7.51	5.65	9.99	105 (5.1)	7.40	4.10	13.36	
Missing	3933 (45.1)	0.21	0.18	0.24	645 (31.0)	0.33	0.26	0.40	
Heart rate									
≤50	63 (0.7)	0.80	0.46	1.40	31 (1.5)	1.87	0.89	3.93	

51 - 100	4098 (47.0)	ref	ref	ref	1308 (62.9)	ref	ref	ref	
101 -110	456 (5.2)	1.85	1.52	2.25	115 (5.5)	1.72	1.16	2.55	
111-129	395 (4.5)	2.51	2.04	3.09	95 (4.6)	1.76	1.15	2.71	
≥130	166 (1.9)	3.05	2.22	4.18	65 (3.1)	1.06	0.64	1.74	
Missing	3550 (40.7)	0.12	0.10	0.14	465 (22.4)	0.18	0.13	0.23	
Respiratory rate									0.048
≤8	8 (0.1)	1.12	0.26	4.70	3 (0.1)	2.16	0.19	24.12	
9-14	726 (8.3)	ref	ref	ref	237 (11.4)	ref	ref	ref	
15-20	1566 (17.9)	1.09	0.91	1.31	584 (28.1)	1.04	0.77	1.40	
21-29	517 (5.9)	1.78	1.42	2.24	273 (13.1)	1.96	1.37	2.79	
≥30	78 (0.9)	8.50	4.67	15.45	57 (2.7)	6.61	3.00	14.56	
Missing	5833 (66.8)	0.32	0.27	0.38	925 (44.5)	0.45	0.33	0.60	

a) Abbreviations: n: number, OR: odds ratio, 95%CI: 95% confidence interval. AUC: Area Under The Curve
b) Age in years divided by ten.
c) Vital parameters measured are: oxygen saturation, measured in percentage oxygenated hemoglobin. Systolic BP: Systolic blood pressure, measured in millimeters of mercury. Temperature measured in degrees Celsius. Heart rate and respiratory rate are measured as times per minute.
d) P-for interaction

Supplemental table 3: Complete multivariable model of hospitalization of patients at the Emergency Department – derivation cohort.

	< 70 years				≥ 70 years			
Predictor	**OR**	**95% CI**		**P-value**	**OR**	**95% CI**		**P value**
Age/10	1.25	1.19	1.30	<0.001	1.11	0.94	1.31	0.226
Sex								
Male	1.25	1.11	1.42	<0.001	1.01	0.82	1.25	0.918
Female	ref	ref	ref	ref	ref	ref	ref	ref
Triage category								
>1 hour	ref	ref	ref	ref	ref	ref	ref	ref
< 1 hour	2.22	1.85	2.67	<0.001	1.70	1.26	2.31	0.001
< 10 min	3.64	2.93	4.52	<0.001	3.09	2.14	4.45	<0.001
Arrival mode								
Self- referral	ref	ref	ref	ref	ref	ref	ref	ref
Referred	1.21	1.05	1.40	0.007	1.09	0.82	1.45	0.541
Ambulance	1.94	1.63	2.32	<0.001	1.40	1.03	1.91	0.030
Chief Complaint								
Minor trauma	ref	ref	ref	ref	ref	ref	ref	ref
Major trauma	1.31	0.89	1.94	0.171	0.94	0.40	2.18	0.881
Chest pain	0.28	0.21	0.36	<0.001	0.19	0.12	0.30	<0.001
Dyspnea	0.79	0.58	1.07	0.128	0.41	0.25	0.67	<0.001
Syncope	0.74	0.51	1.06	0.099	0.48	0.29	0.79	0.004
Psychiatric	1.48	1.03	2.13	0.036	1.19	0.53	2.69	0.668
Malaise	1.31	1.03	1.66	0.026	1.22	0.83	1.79	0.316
Abdominal pain	1.34	1.07	1.68	0.012	1.12	0.74	1.69	0.600
Other	1.13	0.89	1.43	0.317	1.24	0.80	1.94	0.342
Type of specialist								
Medicine	1.17	0.99	1.37	0.062	1.10	0.81	1.49	0.526
Surgery	ref	ref	ref	ref	ref	ref	ref	ref
Revisit to the ED	1.57	1.32	1.88	<0.001	1.95	1.41	2.69	<0.001
Phlebotomised blood sample	4.79	3.83	5.99	<0.001	7.25	4.76	11.05	<0.001
Oxygen saturation								
≤ 90%	1.80	0.93	3.48	0.083	4.42	1.83	10.68	0.001
91-94%	1.78	1.26	2.51	0.001	1.58	1.02	2.47	0.042
≥ 95%	ref	ref	ref	ref	ref	ref	ref	ref
Missing	1.11	0.81	1.52	0.522	1.25	0.68	2.29	0.475
Systolic BP								
≤100	1.96	1.33	2.88	0.001	1.70	0.92	3.13	0.091
101-199	ref	ref	ref	ref	ref	ref	ref	ref
>200	1.32	0.70	2.47	0.386	0.71	0.39	1.28	0.259
Missing	0.57	0.40	0.82	0.002	0.59	0.31	1.11	0.103
Temperature								
≤35.0	1.86	0.89	3.87	0.099	0.91	0.34	2.41	0.844
35.1-38.4	ref	ref	ref	ref	ref	ref	ref	ref
≥38.5	3.34	2.41	4.61	<0.001	3.36	1.78	6.36	<0.001
Missing	0.85	0.70	1.02	0.083	0.94	0.70	1.27	0.691
Heart rate								
≤50	0.67	0.36	1.26	0.214	2.07	0.90	4.76	0.086
51 - 100	ref	ref	ref	ref	ref	ref	ref	ref
101 -110	1.62	1.29	2.03	<0.001	1.35	0.86	2.11	0.196
111-129	1.57	1.22	2.02	<0.001	1.20	0.73	1.98	0.471
≥130	2.57	1.76	3.74	<0.001	0.76	0.41	1.39	0.369
Missing	1.07	0.69	1.68	0.753	0.81	0.39	1.70	0.577

Respiratory rate								
≤8	0.75	0.15	3.74	0.724	2.62	0.17	39.95	0.488
9-14	ref	ref	ref	ref	ref	ref	ref	ref
15-20	0.94	0.76	1.15	0.546	1.06	0.75	1.49	0.745
21-29	1.29	0.99	1.69	0.060	1.79	1.18	2.71	0.006
≥30	3.98	1.99	7.95	<0.001	4.48	1.87	10.73	0.001
Missing	1.05	0.85	1.29	0.659	1.02	0.70	1.47	0.930
Intercept	-4.572				-3.521			
AUC (95% CI)	0.853 (0.844-0.861)				0.808 (0.790-0.826)			
GoF-value	0.289				0.455			

e) Abbreviations: n: number, OR: odds ratio, 95%CI: 95% confidence interval. GoF= Hosmer-Lemeshow Goodness of Fit χ^2 test. AUC: Area Under The Curve
f) Age in years divided by ten.
g) Vital parameters measured are: oxygen saturation, measured in percentage oxygenated hemoglobin. Systolic BP: Systolic blood pressure, measured in millimeters of mercury. Temperature measured in degrees Celsius. Heart rate and respiratory rate are measured as times per minute.
h) P-value values are derived from multiple logistic regression analysis.

Supplemental table 4: Multivariable model of hospitalization of patients at the Emergency Department - training and test cohort

	< 70 years					≥ 70 years				
Predictor	**beta**	**OR**	**95% CI**		**P-value**	**beta**	**OR**	**95% CI**		**P-value**
Age/10	0.228	1.26	1.20	1.31	<0.001	0.259	1.30	1.10	1.53	0.002
Sex										
Male	0.280	1.32	1.17	1.50	<0.001					
Female	ref	ref	ref	ref	ref					
Triage category										
>1 hour	ref	ref	ref	ref	ref	ref	ref	ref	ref	ref
< 1 hour	0.772	2.16	1.79	2.62	<0.001	0.752	3.77	2.60	5.46	<0.001
< 10 min	1.302	3.68	2.95	4.59	<0.001	1.327	2.12	1.54	2.92	<0.001
Arrival mode										
Self- referral	ref	ref	ref	ref	ref	ref	ref	ref	ref	ref
Referred	0.207	1.93	1.62	2.29	<0.001	0.250	1.28	0.96	1.72	0.095
Ambulance	0.656	1.23	1.06	1.43	0.006	0.543	1.72	1.27	2.33	<0.001
Main Complaint										
Minor trauma	ref	ref	ref	ref	ref	ref	ref	ref	ref	ref
Major trauma	0.137	1.15	0.78	1.69	0.486	-0.115	0.89	0.39	2.03	0.785
Chest pain	-1.534	0.22	0.16	0.28	<0.001	-1.220	0.30	0.20	0.44	<0.001
Dyspnea	-0.576	0.56	0.41	0.77	<0.001	-0.210	0.81	0.53	1.25	0.343
Collaps	-0.332	0.72	0.51	1.02	0.065	-0.755	0.47	0.29	0.77	0.003
Psychiatric	0.284	1.33	0.93	1.91	0.123	0.083	1.09	0.50	2.35	0.833
Malaise	0.134	1.14	0.90	1.46	0.276	0.308	1.36	0.96	1.93	0.081
Abdominal pain	0.111	1.12	0.89	1.41	0.351	-0.141	0.87	0.58	1.31	0.503
Other	-0.046	0.96	0.75	1.23	0.717	0.033	1.03	0.66	1.61	0.884
Type of specialist										
Medicine	0.344	1.41	1.20	1.67	<0.001					
Surgery	ref	ref	ref	ref	ref					
Revisit to the ED	0.561	1.75	1.46	2.10	<0.001	0.498	1.65	1.18	2.29	0.003
Phlebotomised blood sample	1.642	5.17	4.10	6.51	<0.001	1.893	6.64	4.33	10.19	<0.001
Oxygen sturation										
≤ 90%	0.655	1.93	1.00	3.72	0.051	1.482	4.40	1.55	12.48	0.005
91-94%	0.387	1.47	1.05	2.07	0.025	0.216	1.24	0.83	1.86	0.294
≥ 95%	ref	ref	ref	ref	ref	ref	ref	ref	ref	ref
Missing	0.090	1.09	0.78	1.53	0.600	0.032	1.03	0.58	1.85	0.914
Systolic BP										
≤100	0.802	2.23	1.52	3.27	<0.001					
101-199	ref	ref	ref	ref	ref					
>200	0.243	1.28	0.67	2.43	0.462					
Missing	-0.453	0.64	0.46	0.89	0.008					
Temperature										
≤35.0	0.225	1.25	0.58	2.72	0.571	-0.017	0.98	0.38	2.52	0.971
35.1-38.4	ref	ref	ref	ref	ref	ref	ref	ref	ref	ref
≥38.5	1.356	3.88	2.79	5.40	<0.001	1.688	5.41	2.61	11.23	<0.001
Missing	-0.041	0.96	0.80	1.16	0.668	-0.228	0.80	0.59	1.08	0.137
Heart rate										
≤50	0.095	1.10	0.64	1.89	0.729	0.713	2.04	0.90	4.63	0.088
51 - 100	ref	ref	ref	ref	ref	ref	ref	ref	ref	ref
101 -110	0.458	1.58	1.26	1.99	<0.001	-0.030	0.97	0.64	1.47	0.888
111-129	0.417	1.52	1.17	1.97	0.002	0.105	1.11	0.69	1.79	0.667
≥130	0.620	1.86	1.27	2.72	0.001	-0.740	0.48	0.26	0.89	0.02

Missing	-0.106	0.90	0.58	1.40	0.638	-0.324	0.72	0.38	1.39	0.328
Respiratory rate										
≤8	-0.840	0.43	0.09	1.98	0.280	21.663	∞	0	∞	0.999
9-14	ref	ref	ref	ref	ref	ref	ref	ref	ref	ref
15-20	-0.026	0.97	0.80	1.20	0.802	0.189	1.21	0.87	1.68	0.261
21-29	0.352	1.42	1.09	1.86	0.010	0.630	1.88	1.26	2.79	0.002
≥30	1.220	3.39	1.79	6.41	<0.001	1.073	2.93	1.38	6.20	0.005
Missing	-0.007	0.99	0.81	1.22	0.949	-0.054	0.95	0.67	1.34	0.761
Intercept	-4.687					-5.021				
Training cohort AUC (95% CI)	0.86 (0.85-0.87)					0.80 (0.78-0.82)				
GoF-value	0.387					0.373				
Test cohort AUC (95%CI)	0.85 (0.84-0.86)					0.78 (0.76-0.80)				

a) Abbreviations: n: number, OR: odds ratio, 95%CI: 95% confidence interval. GoF= Hosmer-Lemeshow Goodness of Fit χ^2 test. AUC: Area Under The Curve
b) Age in years divided by ten.
c) Vital parameters measured are:oxygen saturation, measured in percentage oxygenated hemoglobin. Systolic BP: Systolic blood pressure, measured in millimeters of mercury. Temperature measured in degrees Celsius. Heart rate and respiratory rate are measured as times per minute.
d) P-value values are derived from multiple logistic regression analysis.

REBUTTAL

MS ID#: emermed-2016-205846.R6

MS TITLE: Early prediction of hospital admission for emergency department patients, a comparison between patients younger or older than 70-years.

Authors: Lucke, Jacinta; de Gelder, Jelle; Clarijs, Fleur; Heringhaus, Christian; de Craen, Anton; Fogteloo, Anne; Blauw, Gerard Jan; de Groot, Bas; Mooijaart, Simon

May 2017

Editor:
Comments to the Author:
Thank you for your recent revision. Our remaining concern is about the exclusion for "unjustified ED visits."

Question 1:
First, we are very concerned that readers might not find the term "unjustified ED visits" acceptable and in conflict with permitting laypeople to decide their healthcare needs and priorities. This term needs to be removed from the paper. It is not necessary to label these visits but rather fully describe them, which leads to our second point.
Answer 1:
We will adjust this term, and change it to ‘ED visits due to logistical reasons’
Adjustment:
‘unjustified ED visits’ changes into ‘ED visits due to logistical reasons’ throughout the manuscript.

Question 2: In your most recent reply to reviewers you state that the list included patients with: planned re-evaluation (e.g patients with a wound or abdominal pain that could not wait for the next available appointment in de out-patient clinic), visits to the ED because of lack of availability of time in the out-patient clinic, laboratory checks for logistical reasons, patients who were sent away from the ED to visit their GP etc (because a visit to the GP is approximately 350 euro’s less expensive in the current Dutch health care system).
This list should be included in your Methods. Most of these seem reasonable exclusions in that the patients were either scheduled to be seen, the ED was presumably the only site to get labs, or they were not seen because they were sent to GP clinics. H*owever, there is one group of patients who were seen by the ED but came because of lack of availability of time in the outpatient clinic. Why would these patients be excluded?* In some cases, patients will present to an outpatient clinic and be sick enough to require admission. Please explain why you chose to exclude these patients and also how you were able to retrospectively identify them in your cohort. You should also tell us how many such patients there were - if only a few, this would not affect your results much, but if its the majority, this could have had an impact on your results.

Answer 2:
These patients were excluded because the ED is sometimes used as an alternative pathway to get patients into the outpatient clinic. For example, a patient calls from home to his/her medical specialist because of a non-urgent problem but there are no places on their scheduled consultation hour. The specialist sends the patient to the ED, and because the patient is in the ED, the scheduling of the consultation hour is re-arranged and a place in the outpatient clinic is created. These patients do not require ED care, but rather use a backdoor into the outpatient clinic. This is registered in the file of the patient in the free text of the ‘reason for ED visit’ section, therefore we were able to identify this retrospectively. As you can imagine, this can be undesirable course of action as a patient is registered in the ED but does not receive care there, however it was a common practice during the inclusion period.
In the same group we categorized patients with eye or ENT problems that were registered in the ED but were not treated in the ED. Because the eye and ENT specialists prefer to see the patients in the outpatient clinic (where they have additional material and personnel), these patients are not treated in the ED but go to the outpatient clinic immediately. However they are registered in the computer system as ED visitors, therefore for the this retrospective study we had to exclude them. A total of 415 patients were excluded for this reason, 1.5% of all registered ED visits in that year.

Adjustment:

We will provide additional explanation about this exclusion in the method section. We feel that the exclusion of these patients is justified as they do not require ED care and are not a true part of the ED patient population. If they would be included this would only introduce bias as they contain many missing data (because they were not treated in the ED, their charts are empty and only contain the referral to the outpatient clinic) and do not have similar chances of hospital admission compared to patient who visit the ED due to an acute situation.

We hope this explanation is satisfactory and we can proceed to swift publication of this manuscript.

Kind regards on behalf of the authors,

Jacinta Lucke