

Supplemental material

Community-acquired pneumonia – Use of clinical characteristics of acutely admitted patients for the development of a diagnostic model: A cross-sectional multicentre study

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Table S1: Description of the 70 pre-specified predictors for CAP

Source: The patient interview			
Group	Variable name	Measurement	Consideration/assumption
Demographic information	Age	Continuous, years	Age is a risk factor for CAP [1]. Several studies stratify age groups when investigating pneumonia due to several atypical symptoms and signs and the absence of respiratory symptoms among the elderly. Stratified age groups differ in cut-offs between the ages of ≥ 65 to ≥ 80 years old [2-7].
	Gender	Binary 1=Male 0=Female	The risk of CAP is higher for males [8]. CAP is more severe [7] leading to higher mortality in males [9]. Males' lifestyle factors differ from women resulting in a higher risk of CAP [10].
	Civil status (Living alone)	Binary (Yes/no)	Living alone has a two-fold association with having one or more respiratory tract infections [11].
	Nursing home residence	Binary (Yes/no)	Nursing home residents were found to have several comorbidities [12] and lower physical functioning levels, which might result in a higher risk of CAP [13].
	Employment	Categorical: 1=Working 2=Retired 0=Others (e.g. students, flex job)	Low income and unemployment are associated with readmissions after CAP [14].
Symptoms	Feeling unwell/ Malaise	Binary (Yes/No) Symptoms within 14 days prior to ED admission.	Malaise has been identified as one of the most frequent symptoms for patients infected with <i>Mycoplasma pneumoniae</i> [15].
	Fatigue		Fatigue is associated with pneumonia especially in elderly patients [4].
	Headache		Headache is one of the clinical findings of symptoms of CAP [7, 15]. However, headaches were less common in the older population [7].
	Dizziness		The rationale of the presence of dizziness as a symptom relied on the assumption that several factors such as polypharmacy [16], combined with comorbidities such as cardiovascular diseases [17], symptoms such as confusion, conditions of frailty and malnutrition [18], and lower oxygen saturation [19] could contribute to dizziness.
	Confusion		Confusion e.g. altered mental status or delirium was significantly more frequent in CAP patients [2, 4].
	Dyspnea		Dyspnea was identified as a strong predictor of CAP among febrile patients [20] and one of the main symptoms of pneumonia [2, 21].
	Cough		Cough is a common symptom and one of the most frequent increasing the likelihood of detecting a viral pathogen among CAP patients [15, 22]. Algorithms included cough as a diagnostic predictor [23], and dry cough was a strong predictor in a prediction model for <i>Legionella pneumoniae</i> [24]. Cough was less common in older population [7].
	Secretions		Purulent secretions were a significant symptom and predictor for CAP patients [20, 21].
Sore throat	Some studies identified sore throat as a symptom of CAP [15], and one included the symptom in the prediction rules of pneumonia [5].		

	Cold		Among respiratory diseases, the common cold is one of the most frequent, with symptoms similar to CAP [25].
	Fever feeling		Quantified from reported chills or night sweat or fever measured at home. Included as a rationale of fever.
	Chest pain		Chest pain has been used as a single predictor of CAP [18, 20, 23] or a combined diagnostic predictor [23] and may present as a secondary symptom of coughing or pleuritic involvement [26]. However, chest pain was less common in the older population [7].
	Peripheral edema		The rationale for including peripheral edema as possible predictor is that it is included in the clinical assessment at admission. In case of peripheral edema and respiratory symptoms of dyspnea, chest pain and a history of cardiovascular disease, CAP could be ruled out as a tentative diagnosis replaced with suspicion of cardiovascular disease.
	Nausea		Gastrointestinal symptoms such as nausea, vomiting and diarrhea manifests in 20% of the CAP population [26].
	Vomiting		Gastrointestinal symptoms such as nausea, vomiting and diarrhea manifests in 20% of the CAP population [26].
	Loss of appetite		Loss of appetite could be present in the case of gastrointestinal symptoms [26] and could result from malnutrition [18].
	Abdominal pain		Abdominal pain may be present in the case of gastrointestinal symptoms described above and, therefore, is included in the model [26].
	Diarrhea		Gastrointestinal symptoms such as nausea, vomiting and diarrhea manifests in 20% of the CAP population [26].
	Pain in muscles and joints including back pain		Muscle and joint pain are associated with viral pneumonia as influenza, especially among younger patients and therefore is included in our model [27].
Previous event of CAP	Previous event of CAP	Categorical: 0= Never 1= Once 2= More than once	A previous diagnosis of CAP was reported as having robust evidence as a risk factor for CAP [1]. Furthermore, any hospitalization in the previous five years was reported as a predisposing factor for CAP [8].
Lifestyle factors and aids	Smoke	Categorical: 0=Never been a smoker 1=Current smoker 2=Previous smoker	Smoking has been associated with an increased risk of CAP in several studies [1, 8, 10, 17], and has a strong association with the treatment outcomes of elderly individuals with respiratory tract infections [28].
	Alcohol	Doses per week (a dose=12 grams (1, 5 cl) alcohol). Categories based on the Danish Board of Health recommendations [29]. 0=No alcohol 1=1-7 doses/week maximum doses recommended for women 2=8-14 doses/week maximum dose recommended for men 3= >14 doses	Alcohol has also been associated with increased CAP risk and with treatment outcomes. The risk increases in individuals with higher consumption (>41 g/day) compared to those who consume no alcohol [10, 17, 28].
	Physical activity levels	We categorized physical activity levels based on recommendations from the world health organization for adults with a minimum 150 min/week [30]. 1= Not physically active 2= Less than 2.5hrs/week 3= More than 2.5hrs/week	The risk of CAP decreased in physically active women [10]. In addition, a high level of activity protects against upper respiratory tract infections and reduces the severity and symptoms of the infection [13].
	Activities of daily living	Binary (yes/no) Yes= If the patient had one or more dependencies regarding: bathing, dressing, toileting, transfer, continence and feeding.	Difficulty in maintaining toilet hygiene, preparing meals, and being unable to transfer were associated with an increased risk of respiratory infections [31].

Source: Variables extracted from the patient's medical report			
Comorbidities (diseases)	Neurological	Binary (Yes/no) If the patient was diagnosed with one of these diagnoses.	Cerebrovascular disease/stroke and Parkinson's disease approximately doubled the risk of CAP [17].
	Pulmonary		A history of pneumonia increased the risk of a subsequent episode and patients with chronic respiratory diseases, including chronic obstructive pulmonary disease, bronchitis or asthma, had up to a fourfold increase in the risk of CAP [1, 4, 17].
	Endocrinological		Chronic liver conditions were reported as a risk factor of CAP [8]. Recently, diabetes mellitus has been described as an independent risk factor for sepsis secondary to CAP in very old patients [4] and data from several studies showed an association between diabetes mellitus and moderate risk of CAP [17].
	Renal		Chronic renal disease was reported as an independent risk factor for sepsis secondary to CAP in very old patients [4, 8] and chronic renal disease increased the risk of CAP twofold [17].
	Cardiovascular		Chronic cardiovascular disease increased the risk of CAP up to threefold [4, 17].
	Gastrointestinal		The rationale for including gastrointestinal diseases in the model was that CAP patients have gastrointestinal symptoms that could be related to a differential diagnosis besides CAP.
	Dementia		Dementia approximately doubles the risk of CAP [17].
	Cancer		Cancer was associated with a moderate increase in CAP risk, and a single study reported a fivefold increased risk of CAP for patients with lung cancer [17].
	Rheumatological		A moderate risk of CAP was found in patients with rheumatological diseases [17].
Pharmacological treatments	Polypharmacy	Binary (yes/no) Regular consumption of at least five medications	The increased number of comorbidities of older patients increases the risk of polypharmacy [4, 32]. The prevalence of polypharmacy reached almost 40% among individuals with respiratory tract infections above age 65 years and had a twofold association with treatment outcomes of respiratory tract infections [28]. Furthermore, the prevalence of polypharmacy increased from 45% to 74%, irrespective of antibiotic use if patients were hospitalized with CAP [16].
	Analgesics	Binary (Yes/no) Regular consumption of analgesics	A systematic review reported an association between prescribed opioids and CAP [33].
	Vaccination SARS-CoV-2	Binary (Yes/no) Recent vaccination for SARS-CoV-2	SARS-CoV-2 vaccination was reported during the clinical assessment but was taken out of the model, as the model would be used after the pandemic when vaccination for SARS-CoV-2 rates might decrease. However, the inclusion of this variable did not change the final predictive model.
	Vaccination pneumococcus	Binary (Yes/no) Pneumococcus vaccine (not specified) within 5 years	<i>Streptococcus pneumoniae</i> is one of the most causative pathogens of CAP and the vaccine could be a possible protective predictor for CAP as the risk of CAP increases among those unvaccinated [1, 34, 35].
	Vaccination influenza	Binary (Yes/no) Season influenza vaccine 2020/2021	Influenza vaccine can reduce hospitalization but is questionable if it could have a protective effect in admitted patients [1, 36], therefore, we included this possible predictor to investigate if it could have a protective role in our population.
Severity assessment	CURB-65	Binary ≥ 3 points (Yes/no) Definition: Confusion, urea >7 mmol/L, respiratory rate ≥ 30 bpm, blood pressure (≤ 90 for systolic blood pressure or ≤ 60 for diastolic blood pressure, age > 65 years) Score: one point for each present variable. CURB65 ≥ 3 = severe condition	CURB65 is an assessment tool for the severity of CAP [37] recommended by the guidelines in Europe [38] including in Denmark [39].

	Triage	Based on the 5-level triage system "Danish emergency department triage" (DEPT) [40, 41], we categorized the following: Red/Orange and Green/Blue were pooled due to few patients in the blue and red groups: 1= Red/Orange 2= Yellow 3= Green/Blue	DEPT is a Danish adaption and modification of the "Adaptive Process Triage" (ADAPT) developed in Sweden [42]. DEPT was chosen as it is routinely used in the three included sites. Furthermore, in Denmark, most EDs have implemented formalized triage called "Danish Emergency Process Triage". DEPT shares core similarities with widespread standardized 5-level triage systems [43].
<p>Vital parameters</p> <p>All vital parameters regardless of diastolic blood pressure were based on The National Early Warning Score (NEWS) [44].</p> <p>This score was chosen as it is routinely used in the three EDs included in this study and cut-offs values in predicting CAP are similar from the literature.</p>	Oxygen saturation	Binary < 96 % (Yes/no) The cut-off was based on The National Early Warning Score (NEWS) [44]. However, we did not differentiate between patients with chronic obstructive pulmonary disease.	A similar cut-off of oxygen saturation has been used in investigating predictors for CAP [19].
	Heart rate	Binary < 51 or >90 bpm (Yes/no)	Some studies have investigated and pointed out that a higher heart rate with similar cut-offs as a predictor for CAP [19, 45, 46].
	Blood pressure systolic	Binary <111 or >219 mmHg (Yes/no)	Other cut-offs based on the CURB65-score or lower level of triage (<90mmHg) have been used to predict a high risk of adverse events among inpatients with CAP [47]. This cut-off was also explored in our model without resulting in any difference.
	Blood pressure diastolic	Binary ≤60 mmHg (Yes/no) Based on severity assessment CURB65-score [37]. The NEWS does not include diastolic blood pressure and therefore the value from CURB-65 was chosen.	CURB-65 is routinely used in Denmark as a severity score and is included in the guidelines for antibiotic treatment [39]. As systolic blood pressure has been investigated in prediction rules, we added diastolic blood pressure to our model to explore this variable as a predictor for CAP.
	Respiratory rate (RR)	Binary >20 breaths/min (Yes/no)	There are different cut-offs of RR in the literature [20, 47]. RR> 20/min was defined as a strong prediction of CAP among febrile patients [20].
	Temperature	Binary >38 °C (Yes/no) Measured with ear thermometer [48].	Different cut-offs have been investigated, including the cut-off of >38°C used in this study [49]. Independent of cut-offs, several studies have identified fever as a predictor of CAP [19-21, 23, 45]. However, fever is less common and generally absent in the older population [7].
	Glascow coma score	Binary >15 (Yes/no)	Cognitive impairment [32] has been reported as a strong risk factor for delirium and confusion as a predictor of the severity of CAP [47]. Altered mental status is associated with CAP, especially in the elderly [18].
<p>Blood tests</p> <p>The literature does not describe a clear cut-off for the diagnosis of CAP. We chose a pragmatic approach and applied the cut-offs of serum biomarkers used in the EDs from our institution to reflect reality.</p> <p>Most of the serological biomarkers have been studied for prognostic</p>	Hematocrit	Hematocrit (%), median (IQR) Binary (Yes/no) Cut-off: 40-50 for males and 35-46 for females Yes= outside of the cut-off No= within the cut-off	A hematocrit value of less than 35% was an independent predictor for severity and 2 years of mortality (p = 0.035) [50].
	Hemoglobin	Hemoglobin mmol/L, median (IQR) Binary (Yes/no) Cut-off: 8.3-10.5 for males and 7.3-9.5 for females Yes= outside of the cut-off No= within the cut-off	Hemoglobin correlates with frailty in the elderly and indirectly could be a predictor that should be investigated [51].
	Leukocytes	Leukocytes 10E9/L, median (IQR) Binary (Yes/no) Cut-off: 3.5-8.8 Yes= outside of the cut-off No= within the cut-off	Elevated leukocytes have been reported as a predictor for CAP, especially in pneumonia with negative chest x-ray [52].

<p>purposes. We have included these as potential predictors for CAP to investigate their diagnostic performance combined with signs and symptoms.</p> <p>Binary (Yes/no) measures. Yes= abnormal/ outside of the cut-off No= normal/ within the cut-off</p>	Platelets	<p>Platelets 10E9/L, median (IQR) Binary (Yes/no)</p> <p>Cut-off: 145-350 for males and 165-400 for females Yes= outside of the cut-off No= within the cut-off</p>	<p>Platelet count < 171 × 10⁹/L was included in a prediction model for <i>legionella pneumoniae</i> showing a high diagnostic accuracy [AUC 0.89 (95% CI 0.86–0.93)] [24].</p>
	Neutrophils	<p>Neutrophils 10E9/L, median (IQR) Binary (Yes/no)</p> <p>Cut-off: > 7.5 Yes= >7.5 No= ≤ 7.5</p>	<p>The neutrophil to lymphocyte ratio had a high diagnostic value for CAP patients [53]. Furthermore, higher mortality risk was found for CAP patients and if measured in the early stage of CAP could contribute to the diagnostic and disease severity [54].</p>
	Lymphocytes	<p>Lymphocytes 10E9/L, median (IQR) Binary (Yes/no)</p> <p>Cut-off: 1.00-4.00 Yes= outside of the cut-off No= within the cut-off</p>	<p>The neutrophil to lymphocyte ratio has been studied in prognostic studies and is associated with higher mortality risk in CAP patients and if measured in the early stage of CAP could contribute to the diagnostic and disease severity [54].</p>
	Albumin	<p>Albumin g/L, median (IQR) Binary (Yes/no)</p> <p>Cut-off: 34-45 Yes= outside of the cut-off No= within the cut-off</p>	<p>The ratio of blood urea and albumin has been investigated as a predictive factor for CAP, but poor model performance advocated for further investigation [55]. Furthermore, albumin correlates with frailty in the elderly and indirectly could be a predictor that should be investigated as frailty has been associated with an increased risk of CAP [51]. In addition, serum albumin (<3.4 g/dl) was associated with higher mortality for elderly patients with CAP [18] and was included in a prediction rule for severe adverse events in patients hospitalized with CAP (< 2 g/dL, 2 points; 2–3 g/dL, 1 point) [47].</p>
	Creatinine	<p>Creatinine μmol/L, median (IQR) Binary (Yes/no)</p> <p>Cut-off: 60-105 for males and 45-90 for females Yes= outside of the cut-off No= within the cut-off</p>	<p>Elevated creatinine levels have been reported with almost a sixfold association of poor CAP outcome (OR=5.67; 95%CI: 1.72-18.65) [56]. This result is supported by another study that showed that serum creatinine levels of ≥ 2.8 were a strong predictor of in-hospital mortality in adults with CAP when compared with five serum biomarkers [57].</p>
	Blood urea	<p>Blood urea nitrogen mmol/L, median (IQR) Binary (Yes/no)</p> <p>Cut-off: 3-5-8.1 for males and 3.1-7.9 for females Yes= outside of the cut-off No= within the cut-off</p>	<p>The ratio of blood urea and albumin has been investigated as a predictive factor for CAP, but poor model performance advocated for further investigation [55].</p>
	Sodium	<p>Sodium mmol/L, median (IQR) Binary (Yes/no)</p> <p>Cut-off: 137-145 Yes= outside of the cut-off No= within the cut-off</p>	<p>Hyponatremia < 133 mmol/L was one of the strong predictors in the prediction of CAP caused by <i>legionella pneumoniae</i> [24].</p>
	Prothrombin time-international normalized ratio	<p>Prothrombin (IQR) Binary (Yes/no)</p> <p>Cut-off: <1.2 Yes= ≥ 1.2 No= <1.2</p>	<p>Prothrombin time-international normalized ratio was investigated to distinguish Influenza A (H1N1) from other pneumonia. Prothrombin times were lower in H1N1 compared with non-H1N1 pneumonia patients (p=0.04) [58]. Furthermore, it has been investigated as a factor that could be associated with decreased sensitivity in negative urinary antigen (UAT) tests in CAP caused by pneumococcal. Prothrombin was 50% higher in the UAT-negative patients than in the UAT-positive patients [59]. We chose to include prothrombin in the diagnostic model to explore its significance in or rule out CAP, furthermore, the marker is routinely measured in acutely admitted patients.</p>
	Bilirubin	<p>Bilirubin μmol/L, median (IQR) Binary (Yes/no)</p>	<p>Bilirubin levels were lower in patients with influenza A (H1N1) compared to non-H1N1 pneumonia (p= 0.02)</p>

		Cut-off: <5 or >25 Yes= outside of the cut-off No= within the cut-off	[58]. This marker could add value to a prediction model.
	Glucose	Glucose mmol/L, median (IQR) Binary (Yes/no) Cut-off: > 11.00 Yes= >11.00 No= ≤ 11.00	Patients with CAP frequently present with admission hyperglycemia and have poorer outcomes [60, 61]. Therefore, glucose is included as a potential predictor.
	C- reactive protein (CRP)	C-Reactive Protein, median (IQR) Binary (Yes/no) The cut-off of CRP in our institution is < 5 mg/L at the ED. However, the literature suggests optional cut-offs. Based on the literature and the range of the results from the CRP as continuous variable, we defined the following categories: 1= <20mg/L 2= 20-100 mg/L 3= >100 mg/L	The diagnostic accuracy of CRP in differentiating between bacterial and viral infections of the lower respiratory tract is questionable [62]. However, CRP at different cut-offs increased the performance of prediction models for CAP. It included a cut-off of >20 [20], >30 [63], 50 [23] ≥ 98 [46], and a meta-analysis investigated all three cut-offs of 20, 50, and 100 [64]. CRP levels were found higher when CAP was detected both by a chest x-ray and a chest tomography [52].
Clinical assessment	Stethoscope findings	Binary (Yes/no) Yes for any abnormal stethoscope findings such as crackles and rhonchi.	Several studies investigated associations between abnormal stethoscope findings and the probability of the presence of CAP. They increased the likelihood of CAP [21, 65] and crackles on auscultation had a twofold increase in the prediction of pneumonia [19].
	Abdominal pain on palpation	Binary (Yes/no)	The rationale for including abdominal pain in the clinical assessment was that the literature reported that 20% of symptoms reported by patients with CAP were gastrointestinal symptoms [26].
	Body mass index (BMI).	The BMI was calculated including the high and weight of the patients. The BMI classification was based on "The Centers for diseases control and prevention" [66] and defined with the following categories: 1= Underweight, BMI < 18.5 2= Healthy weight, BMI from 18.5 to <25 3= Overweight, BMI from 25.0 to <30 4= Obesity, BMI from ≥ 30.0	The literature reported the association of several nutritional factors related to CAP and including malnutrition [1, 18], being underweight [8, 17], and BMI was directly associated with an increased risk of CAP among women [10].

Table S2: Characteristics of CAP in the population of patients admitted with an infection (n=954). The values presented of data as continuous, dichotomous or categorical were tested in the model during explorative analysis to identify the best model performance.

Characteristics	Total, n	CAP, n	Not CAP, n	Missings n (%)	OR (95% CI)	p-value
Total of patients	954 (100)	265 (27.8)	689 (72.2)	0 (0.0)		
DEMOGRAPHIC DATA						
Age, median (IQR)	73.0 (59.0; 81.0)	75.0 (63.5; 82.0)	73.0 (57.0; 80.0)	0 (0.0)	1.01 (1.005-1.02)	<0.001
Age ≥75 years	440 (46.1)	133 (50.2)	307 (44.6)	0 (0.0)	1.25 (0.94-1.66)	0.118
Gender male	513 (53.8)	137 (51.7)	376 (54.6)	0 (0.0)	0.89 (0.67-1.18)	0.425
Marital status, Living alone	618 (66.0)	166 (63.8)	452 (66.9)	18 (1.9)	0.87 (0.64-1.18)	0.382
Nursing home resident	66 (7.0)	26 (9.9)	40 (5.9)	13 (1.4)	1.75 (1.05-2.94)	0.317
Occupation				21 (2.2)		
Others	67 (7.2)	17 (6.5)	50 (7.4)		1 (reference)	
Working	202 (21.7)	44 (16.9)	158 (23.5)		0.81 (0.43-1.55)	0.543
Retired	664 (71.2)	200 (76.6)	464 (69.0)		1.26 (0.71-2.25)	0.418
LIFESTYLE FACTORS						
Smoking status				33 (3.5)		
No	323 (35.1)	66 (26.0)	257 (38.5)		1 (reference)	
Current smoker	179 (19.4)	54 (21.3)	125 (18.7)		1.68 (1.10-2.55)	0.015
Previous smoker	419 (45.5)	134 (52.8)	285 (42.7)		1.83 (1.30-2.57)	<0.001
Alcohol status				35 (3.7)		
No alcohol	356 (38.7)	99 (39.1)	257 (38.6)		1 (reference)	
1-7 doses	385 (41.9)	105 (41.5)	280 (42.0)		0.97 (0.70-1.34)	0.870
8-14 doses	105 (11.4)	31 (12.3)	74 (11.1)		1.08 (0.67-1.75)	0.732
> 14 doses	73 (7.9)	18 (7.1)	55 (8.3)		0.84 (0.47-1.51)	0.582
Physically activity				52 (5.4)		
Not physical active	263 (29.2)	74 (29.8)	189 (28.9)		1 (reference)	
Physical activity < 2,5 hr/week	231 (25.6)	64 (25.8)	167 (25.5)		0.97 (0.66-1.45)	0.915
Physical activity ≥ 2,5 hr/week	408 (45.2)	110 (44.4)	298 (45.6)		0.94 (0.66-1.33)	0.735
Body Mass Index, median (IQR)	26.5 (23.2; 30.8)	26.2 (22.9; 29.5)	26.7 (23.3; 31.2)	249 (26.1)	0.97 (0.94-0.99)	0.031
Body Mass Index†				249 (26.1)		
Healthy weight	246 (34.9)	74 (36.1)	172 (34.4)		1 (reference)	
Obese	193 (27.4)	45 (22.0)	148 (29.6)		0.70 (0.45-1.08)	0.114
Overweight	239 (33.9)	74 (36.1)	165 (33.0)		1.04 (0.70-1.53)	0.833
Underweight	27 (3.8)	12 (5.9)	15 (3.0)		1.85 (0.83-4.16)	0.132
ADL dependence*	260 (28.0)	81 (31.2)	179 (26.8)	25 (2.6)	1.23 (0.90-1.69)	0.180
SYMPTOMS						
Feeling unwell	559 (61.2)	173 (67.8)	386 (58.7)	41 (4.3)	1.48 (1.09-2.01)	0.010
Feeling tired	657 (72.6)	190 (75.4)	467 (71.5)	49 (5.1)	1.22 (0.87-1.70)	0.241
Headache	351 (38.3)	99 (38.8)	252 (38.1)	37 (3.9)	1.03 (0.76-1.38)	0.832
Dizziness	346 (37.7)	96 (37.6)	250 (37.8)	37 (3.98)	0.99 (0.73-1.34)	0.973
Confusion	207 (22.6)	58 (22.7)	149 (22.5)	37 (3.89)	1.01 (0.71-1.43)	0.938
Dyspnea	379 (41.4)	171 (67.3)	208 (31.5)	39 (4.1)	4.48 (3.29-6.11)	<0.001
Cough	358 (39.1)	173 (68.1)	185 (28.0)	39 (4.1)	5.49 (4.01-7.52)	<0.001

Expectoration	279 (30.5)	140 (55.1)	139 (21.0)	39 (4.1)	4.61 (3.38-6.28)	<0.001
Sore throat	104 (11.4)	39 (15.4)	65 (9.8)	39 (4.1)	1.66 (1.08-2.54)	0.019
Cold (common cold)	95 (10.4)	45 (17.7)	50 (7.6)	39 (4.1)	2.63 (1.70-4.05)	<0.001
Fever feeling at home	612 (64.2)	169 (63.8)	443 (64.3)	0 (0.0)	0.97 (0.72-1.31)	0.880
Chest pain	168 (18.4)	71 (28.1)	97 (14.7)	40 (4.2)	2.26 (1.60-3.21)	<0.001
Oedema	79 (8.6)	10 (4.0)	69 (10.4)	39 (4.1)	0.35 (1.17-0.69)	0.002
Nausea	304 (33.2)	76 (30.0)	228 (34.4)	38 (3.9)	0.81 (0.59-1.112)	0.211
Vomiting	190 (20.7)	40 (15.8)	150 (22.6)	38 (3.9)	0.64 (0.43-0.94)	0.023
Loss of appetite	524 (57.2)	149 (58.9)	375 (56.6)	38 (3.9)	1.00 (0.82-1.47)	0.523
Gastrointestinal pain	193 (21.1)	40 (15.8)	153 (23.1)	38 (3.9)	0.62 (0.42-0.91)	0.016
Diarrhoea	134 (14.6)	29 (11.5)	105 (15.8)	38 (3.9)	0.68 (0.44-1.06)	0.095
Muscular pain	344 (37.8)	79 (31.3)	265 (40.3)	44 (4.6)	0.67 (0.49-0.92)	0.013
Back pain	132 (14.5)	33 (13.1)	99 (15.0)	44 (4.6)	0.85 (0.55-1.29)	0.455
CLINICAL ASSESSMENT						
Positive stethoscope findings	329 (36.5)	168 (65.4)	161 (25.0)	52 (5.4)	5.67 (4.15-7.75)	<0.001
Abdominal pain by palpation	192 (22.1)	37 (15.0)	155 (25.0)	86 (9.0)	0.52 (0.35-0.78)	0.002
COMORBIDITIES						
Dementia	32 (3.4)	9 (3.4)	23 (3.3)	0 (0.0)	1.01 (0.46-2.22)	0.964
Neurological diseases	172 (18.0)	53 (20.0)	119 (17.3)	0 (0.0)	1.19 (0.83-1.71)	0.326
Respiratory diseases	269 (28.2)	105 (39.6)	164 (23.8)	0 (0.0)	2.10 (1.55-2.84)	<0.001
Endocrinological diseases	296 (31.0)	80 (30.2)	216 (31.3)	0 (0.0)	0.94 (0.69-1.28)	0.728
Nephrological diseases	252 (26.4)	60 (22.6)	192 (27.9)	0 (0.0)	0.75 (0.54-1.05)	0.101
Cardiovascular diseases	390 (40.9)	116 (43.8)	274 (39.8)	0 (0.0)	1.17 (0.88-1.57)	0.259
Gastrointestinal diseases	100 (10.5)	23 (8.7)	77 (11.2)	0 (0.0)	0.75 (0.46-1.23)	0.260
Rheumatological diseases	118 (12.4)	27 (10.2)	91 (13.2)	0 (0.0)	0.74 (0.47-1.17)	0.205
Cancer diseases	85 (8.9)	26 (9.8)	59 (8.6)	0 (0.0)	1.16 (0.71-1.88)	0.544
Prior pneumonia				100 (10.5)		
No	410 (48.0)	79 (33.3)	331 (53.6)		1 (reference)	
Yes, one time	180 (21.1)	50 (21.1)	130 (21.1)		1.61 (1.07-2.42)	0.022
Yes, more than one time	264 (30.9)	108 (45.6)	156 (25.3)		2.90 (2.05-4.10)	<0.001
SEVERITY ASSESSMENT						
CURB65 ≥ 3 **	122 (13.0)	29 (11.3)	93 (13.7)	16 (1.7)	0.80 (0.51-1.25)	0.336
Triage***				59 (6.2)		
Green/Blue	183 (20.4)	37 (14.8)	146 (22.6)		1 (reference)	
Yellow	479 (53.5)	126 (50.4)	353 (54.7)		1.40 (0.93-2.13)	0.105
Red/Orange	233 (26.0)	87 (34.8)	146 (22.6)		2.35 (1.50-3.67)	<0.001
VITAL PARAMETERS						
Respiratory rate, median(IQR)	18.0 (16.0; 22.0)	20.0 (18.0; 24.0)	18.0 (16.0; 20.0)	5 (0.5)	1.10 (1.07-1.13)	<0.001
Respiratory rate >20/min	285 (30.0)	124 (47.0)	161 (23.5)	5 (0.5)	2.88 (2.13-3.88)	<0.001
Oxygen saturation % n/min, median (IQR)	96.0 (94.0; 98.0)	95.0 (93.0; 97.0)	97.0 (95.0; 98.0)	4 (0.4)	0.84 (0.80-0.88)	<0.001
Oxygen saturation < 96 %	393 (41.4)	162 (61.1)	231 (33.7)	4 (0.4)	3.09 (2.30-4.14)	<0.001
Heart rate/min, mean (sd)	90.1 (18.3)	93.2 (18.9)	88.9 (18.0)	1 (0.1)	1.01 (1.005-1.02)	0.001
Heart rate <51 or >90/min	460 (48.3)	148 (55.8)	312 (45.3)	1 (0.1)	1.52 (1.14-2.02)	0.003
Systolic blood pressure mmHg, mean (sd)	132.8 (22.5)	134.2 (21.0)	132.2 (23.1)	3 (0.3)	1.003 (0.99-1.01)	0.215

Systolic blood pressure <111 or >219 mmHg	156 (16.4)	38 (14.4)	118 (17.2)	3 (0.3)	0.81 (0.54-1.21)	0.314
Diastolic blood pressure mmHg, mean (sd)	74.8 (15.3)	74.2 (13.6)	75.0 (15.8)	3 (0.3)	0.99 (0.98-1.006)	0.483
Diastolic blood pressure ≤60 mmHg	163 (17.1)	40 (15.2)	123 (17.9)	3 (0.3)	0.82 (0.55-1.21)	0.329
Temperature, mean (SD)	37.5 (1.0)	37.6 (1.0)	37.4 (0.9)	5 (0.5)	1.22 (1.05-1.40)	0.006
Fever > 38°C	233 (24.6)	77 (29.3)	156 (22.7)	5 (0.5)	1.40 (1.02-1.93)	0.036
Glasgow coma scale <15	31 (3.3)	12 (4.6)	19 (2.8)	5 (0.5)	0.59 (0.28-1.24)	0.168
BLOOD TESTS						
Haematocrit, median (IQR)	38.0 (35.0; 42.0)	38.0 (35.0; 42.0)	39.0 (35.0; 42.0)	260 (27.2)	0.98 (0.95-1.01)	0.465
Haematocrit	268 (38.6)	85 (38.6)	183 (38.6)	260 (27.2)	1.001 (0.72-1.39)	0.994
Haemoglobin mmol/L, median (IQR)	8.0 (7.2; 8.7)	7.9 (7.2; 8.6)	8.0 (7.3; 8.8)	0 (0.0)	0.90 (0.80-1.02)	0.127
Haemoglobin mmol/L	402 (42.1)	118 (44.5)	284 (41.2)	0 (0.0)	1.14 (0.86-1.52)	0.354
Leukocytes 10E9/L, median (IQR)	11.1 (8.3; 14.8)	12.2 (9.5; 15.8)	10.7 (8.0; 14.2)	0 (0.0)	1.05 (1.02-1.07)	<0.001
Leukocytes 10E9/L	670 (70.2)	214 (80.8)	456 (66.2)	0 (0.0)	2.14 (1.52-3.02)	<0.001
Platelets 10E9/L, median (IQR)	240.0 (189.0; 307.8)	260.5 (211.0; 330.8)	232.0 (182.3; 296.0)	10 (1.0)	1.002 (1.001-1.004)	<0.001
Platelets 10E9/L	201 (21.3)	63 (23.9)	138 (20.3)	10 (1.0)	1.23 (0.87-1.72)	0.229
Neutrophils 10E9/L, median (IQR)	8.4 (6.0; 12.2)	9.7 (7.2; 13.0)	8.0 (5.6; 11.6)	10 (1.0)	1.06 (1.03-1.09)	<0.001
Neutrophils 10E9/L	549 (58.2)	187 (71.1)	362 (53.2)	10 (1.0)	2.16 (1.59-2.94)	<0.001
Lymphocytes† 10E9/L, median (IQR)	1.1 (0.7; 1.6)	0.9 (0.6; 1.5)	1.2 (0.8; 1.8)	633 (66.3)	0.98 (0.85-1.12)	0.797
Lymphocytes† 10E9/L	145 (45.2)	53 (55.2)	92 (40.9)	633 (66.3)	1.78 (1.10-2.88)	0.018
Albumin g/L, median (IQR)	39.0 (36.0; 42.0)	39.0 (35.0; 41.0)	39.0 (36.0; 42.0)	7 (0.7)	0.96 (0.93-0.99)	0.029
Albumin g/L	160 (16.9)	39 (14.9)	121 (17.6)	7 (0.7)	0.82 (0.55-1.21)	0.323
Creatinine µmol/L, median (IQR)	84.0 (67.0; 113.0)	81.0 (64.0; 108.0)	86.0 (67.5; 114.0)	0 (0.0)	0.996 (0.993-0.998)	0.003
Creatinine µmol/L	374 (39.2)	106 (40.0)	268 (38.9)	0 (0.0)	1.04 (0.78-1.39)	0.754
Blood urea nitrogen mmol/L, median (IQR)	6.2 (4.4; 8.9)	6.2 (4.5; 8.6)	6.2 (4.4; 9.1)	9 (0.9)	0.99 (0.96-1.02)	0.657
Blood urea nitrogen mmol/L	377 (39.9)	99 (38.1)	278 (40.6)	9 (0.9)	0.90 (0.67-1.20)	0.482
Sodium mmol/L, median (IQR)	137.0 (134.0; 139.0)	137.0 (134.0; 139.0)	137.0 (134.0; 139.0)	0 (0.0)	0.98 (0.95-1.01)	0.394
Sodium mmol/L	432 (45.3)	128 (48.3)	304 (44.1)	0 (0.0)	1.18 (0.89-1.57)	0.245
Prothrombin, median (IQR)	1.1 (1.0; 1.2)	1.1 (1.0; 1.2)	1.1 (1.0; 1.2)	3 (0.3)	1.18 (0.89-1.58)	0.231
Prothrombin	234 (24.6)	65 (24.5)	169 (24.6)	3 (0.3)	0.99 (0.71-1.38)	0.972
Bilirubin µmol/L, median (IQR)	9.0 (6.0; 13.0)	9.0 (6.0; 12.0)	9.0 (6.0; 14.0)	11 (1.1)	0.97 (0.95-0.99)	0.254
Bilirubin µmol/L	152 (16.1)	38 (14.4)	114 (16.8)	11 (1.1)	0.83 (0.55-1.24)	0.369
Glucose mmol/L, median (IQR)	6.7 (5.9; 7.9)	6.9 (6.2; 8.1)	6.6 (5.8; 7.8)	9 (0.9)	1.04 (0.99-1.10)	0.052
Glucose mmol/L	51 (5.4)	19 (7.3)	32 (4.7)	9 (0.9)	1.59 (0.88-2.85)	0.120
C-Reactive Protein mg/L, median (IQR)	95.5 (30.0; 179.3)	125.0 (57.0; 203.5)	82.0 (19.0; 172.0)	0 (0.0)	1.003 (1.001-1.004)	<0.001
C-Reactive Protein mg/L				0 (0.0)		
Low <20mg/L	196 (20.5)	21 (7.9)	175 (25.4)		1 (reference)	
Moderate 21-99 mg/L	291 (30.5)	86 (32.5)	205 (29.8)		3.49 (2.08-5.86)	<0.001
High ≥=100	467 (49.0)	158 (59.6)	309 (44.8)		4.26 (2.60-6.96)	<0.001
VACCINE AND MEDICATIONS						
SARS-CoV-2 †	756 (79.2)	222 (83.8)	534 (77.5)	0 (0.0)	1.49 (1.03-2.17)	0.033
Pneumococcal	530 (55.6)	160 (60.4)	370 (53.7)	0 (0.0)	1.31 (0.98-1.75)	0.063
Influenza	635 (66.6)	191 (72.1)	444 (64.4)	0 (0.0)	1.42 (1.04-1.94)	0.025

Analgesics	404 (42.3)	115 (43.4)	289 (41.9)	0 (0.0)	1.06 (0.79-1.41)	0.684
Polypharmacy****	544 (57.0)	163 (61.5)	381 (55.3)	0 (0.0)	1.29 (0.96-1.72)	0.082

Values are numbers (percentages) unless otherwise specified. *ADL dependence: If the patient had one or more dependencies regarding bathing, dressing, toileting, transfer, continence, and feeding. ** CURB65: confusion, uraemia, respiratory rate, blood pressure, age > 65 years. ***Triage: Danish emergency process triage [40] ****Polypharmacy: regular consumption of at least five medications † variables not included in the multivariate model

Table S3: Characteristics of the 954 patients with suspected infection enrolled in the study. It presents the 70 predictors included in the multivariate analysis and randomization of the training set and validation set.

Characteristics	Total, n	Training set, n	Validation set, n	Missings n (%)	p-value
Total of patients	954 (100)	766 (80.3)	188 (19.7)	0 (0.0)	
DEMOGRAPHIC DATA					
Age, median (IQR)	73.0 (59.0; 81.0)	75.0 (63.5; 82.0)	74.0 (60.0; 82.0)	0 (0.0)	0.54
Age ≥75 years	440 (46.1)	348 (45.4)	92 (48.9)	0 (0.0)	0.39
Gender male	513 (53.8)	408 (53.3)	105 (55.9)	0 (0.0)	0.52
Marital status, Living alone	618 (66.0)	488 (65.0)	130 (70.3)	18 (1.9)	0.17
Nursing home resident	66 (7.0)	55 (7.3)	11 (5.9)	13 (1.4)	0.53
Occupation				21 (2.2)	0.62
Others	67 (7.2)	57 (7.6)	10 (5.5)		
Working	202 (21.7)	162 (21.6)	40 (22.0)		
Retired	664 (71.2)	532 (70.8)	132 (72.5)		
LIFESTYLE FACTORS					
Smoking status				33 (3.5)	0.76
No	323 (35.1)	256 (34.5)	67 (37.4)		
Current smoker	179 (19.4)	145 (19.5)	34 (19.0)		
Previous smoker	419 (45.5)	341 (46.0)	78 (43.6)		
Alcohol status				35 (3.7)	0.60
No alcohol	356 (38.7)	283 (38.2)	73 (40.8)		
1-7 doses	385 (41.9)	315 (42.6)	70 (39.1)		
8-14 doses	105 (11.4)	81 (10.9)	24 (13.4)		
> 14 doses	73 (7.9)	61 (8.2)	12 (6.7)		
Physically activity				52 (5.4)	0.76
Not physical active	263 (29.2)	214 (29.4)	49 (28.2)		
Physical activity < 2,5 hr/week	231 (25.6)	189 (26.0)	42 (24.1)		
Physical activity ≥ 2,5 hr/week	408 (45.2)	325 (44.6)	83 (47.7)		
Body Mass Index†				249 (26.1)	0.74

Healthy weight	246 (34.9)	202 (35.8)	44 (31.2)		
Obese	193 (27.4)	154 (27.3)	39 (27.7)		
Overweight	239 (33.9)	187 (33.2)	52 (36.9)		
Underweight	27 (3.8)	21 (3.7)	6 (4.3)		
ADL dependence*	260 (28.0)	203 (27.1)	57 (31.7)	25 (2.6)	0.22
SYMPTOMS					
Malaise	559 (61.2)	458 (62.0)	101 (58.0)	41 (4.3)	0.34
Feeling tired	657 (72.6)	540 (74.0)	117 (66.9)	49 (5.1)	0.06
Headache	351 (38.3)	287 (38.8)	64 (36.0)	37 (3.9)	0.48
Dizziness	346 (37.7)	287 (38.8)	59 (33.1)	37 (3.98)	0.16
Confusion	207 (22.6)	164 (22.2)	43 (24.2)	37 (3.89)	0.57
Dyspnea	379 (41.4)	309 (42.0)	70 (39.1)	39 (4.1)	0.48
Cough	358 (39.1)	294 (39.9)	64 (35.8)	39 (4.1)	0.30
Fever feeling at home	612 (64.2)	464 (64.5)	118 (62.8)	0 (0.0)	0.66
Expectoration	279 (30.5)	224 (30.4)	55 (30.7)	39 (4.1)	0.94
Sore throat	104 (11.4)	86 (11.7)	18 (10.1)	39 (4.1)	0.54
Cold (common cold)	95 (10.4)	81 (11.0)	14 (7.8)	39 (4.1)	0.21
Chest pain	168 (18.4)	134 (18.2)	34 (19.0)	40 (4.2)	0.81
Oedema	79 (8.6)	61 (8.3)	18 (10.1)	39 (4.1)	0.45
Nausea	304 (33.2)	247 (33.4)	57 (32.2)	38 (3.9)	0.76
Vomiting	190 (20.7)	154 (20.8)	36 (20.3)	38 (3.9)	0.88
Loss of appetite	524 (57.2)	424 (57.4)	100 (56.5)	38 (3.9)	0.83
Gastrointestinal pain	193 (21.1)	145 (19.6)	48 (27.1)	38 (3.9)	0.03
Diarrhoea	134 (14.6)	107 (14.5)	27 (15.3)	38 (3.9)	0.79
Muscular pain	344 (37.8)	289 (39.5)	55 (30.9)	44 (4.6)	0.03
Back pain	132 (14.5)	110 (15.0)	22 (12.4)	44 (4.6)	0.36
CLINICAL ASSESSMENT					
Positive stethoscope findings	329 (36.5)	263 (36.5)	66 (36.5)	52 (5.4)	1.00
Abdominal pain by palpation	192 (22.1)	151 (21.7)	41 (23.7)	86 (9.0)	0.58
COMORBIDITIES					
Dementia	23 (3.0)	9 (4.8)	23 (3.3)	0 (0.0)	0.22
Neurological diseases	137 (17.9)	35 (18.6)	119 (17.3)	0 (0.0)	0.82
Pulmonary diseases	212 (27.7)	57 (30.3)	164 (23.8)	0 (0.0)	0.47
Endocrinological diseases	239 (31.2)	57 (30.3)	216 (31.3)	0 (0.0)	0.81
Nephrological diseases	200 (26.1)	52 (27.7)	192 (27.9)	0 (0.0)	0.67

Cardiovascular diseases	303 (39.6)	87 (46.3)	274 (39.8)	0 (0.0)	0.09
Gastrointestinal diseases	81 (10.6)	19 (10.1)	77 (11.2)	0 (0.0)	0.85
Rheumatological diseases	93 (12.1)	25 (13.3)	91 (13.2)	0 (0.0)	0.67
Cancer diseases	66 (8.6)	19 (10.1)	59 (8.6)	0 (0.0)	0.52
Prior pneumonia				100 (10.5)	0.05
No	343 (50.1)	67 (39.6)	331 (53.6)		
Yes, one time	139 (20.3)	41 (24.3)	130 (21.1)		
Yes, more than one time	203 (29.6)	61 (36.1)	156 (25.3)		
SEVERITY ASSESSMENT					
CURB65 ≥ 3 **	103 (13.6)	19 (10.4)	93 (13.7)	16 (1.7)	0.25
Triage***				59 (6.2)	0.53
Green/Blue	185 (25.6)	48 (27.9)	146 (22.6)		
Yellow	385 (53.3)	94 (54.7)	353 (54.7)		
Red/Orange	153 (21.2)	30 (17.4)	146 (22.6)		
VITAL PARAMETERS					
Respiratory rate >20/min	285 (30.0)	235 (30.8)	50 (26.7)	5 (0.5)	0.27
Oxygen saturation < 96 %	393 (41.4)	324 (42.5)	69 (36.7)	4 (0.4)	0.15
Heart rate <51 or >90/min	460 (48.3)	377 (49.3)	83 (44.1)	1 (0.1)	0.21
Systolic blood pressure <111 or >219 mmHg	156 (16.4)	125 (16.4)	31 (16.6)	3 (0.3)	0.94
Diastolic blood pressure ≤ 60 mmHg	163 (17.1)	131 (17.1)	32 (17.1)	3 (0.3)	0.99
Fever > 38°C	233 (24.6)	190 (24.9)	43 (23.1)	5 (0.5)	0.61
Glascow coma scale <15	31 (3.3)	23 (3.0)	8 (4.3)	5 (0.5)	0.39
BLOOD TESTS					
Haematocrit	268 (38.6)	218 (39.2)	50 (36.2)	260 (27.2)	0.52
Haemoglobin mmol/L	402 (42.1)	329 (43.0)	73 (38.8)	0 (0.0)	0.31
Leukocytes 10E9/L	670 (70.2)	548 (71.5)	122 (64.9)	0 (0.0)	0.07
Platelets 10E9/L	201 (21.3)	168 (22.2)	33 (17.6)	10 (1.0)	0.17
Neutrophils 10E9/L	549 (58.2)	454 (59.9)	95 (51.1)	10 (1.0)	0.03
Albumin g/L	160 (16.9)	130 (17.1)	30 (16.1)	7 (0.7)	0.76
Creatinine μ mol/L	374 (39.2)	303 (39.6)	71 (37.8)	0 (0.0)	0.65
Blood urea nitrogen mmol/L	377 (39.9)	308 (40.5)	69 (37.5)	9 (0.9)	0.46
Sodium mmol/L	432 (45.3)	362 (47.3)	70 (37.2)	0 (0.0)	0.01
Prothrombin	234 (24.6)	186 (24.3)	48 (25.7)	3 (0.3)	0.71
Bilirubin μ mol/L	152 (16.1)	119 (15.7)	33 (17.8)	11 (1.1)	0.48

Glucose mmol/L	51 (5.4)	42 (5.5)	9 (4.8)	9 (0.9)	0.71
C-Reactive Protein mg/L				0 (0.0)	0.07
<20 mg/L	196 (20.5)	151 (19.7)	45 (23.9)		
21-99 mg/L	291 (30.5)	226 (29.5)	65 (34.6)		
≥ 100 mg/L	467 (49.0)	389 (50.8)	78 (41.5)		
VACCINE AND MEDICAMENTATIONS					
Pneumococcal	530 (55.6)	414 (54.0)	116 (61.7)	0 (0.0)	0.06
Influenza	635 (66.6)	512 (66.8)	123 (65.4)	0 (0.0)	0.71
Analgesics	404 (42.3)	336 (43.9)	68 (36.2)	0 (0.0)	0.06
Polypharmacy****	544 (57.0)	443 (57.8)	101 (53.7)	0 (0.0)	0.31

Values are numbers (percentages) unless otherwise specified. *ADL dependence: If the patient had one or more dependencies regarding bathing, dressing, toileting, transfer, continence, and feeding. ** CURB65: confusion, uraemia, respiratory rate, blood pressure, age > 65 years. ***Triage: Danish emergency process triage [40] ****Polypharmacy: regular consumption of at least five medications

Figure S1: Performance of the prediction model presented with the area receiver operating characteristic curve

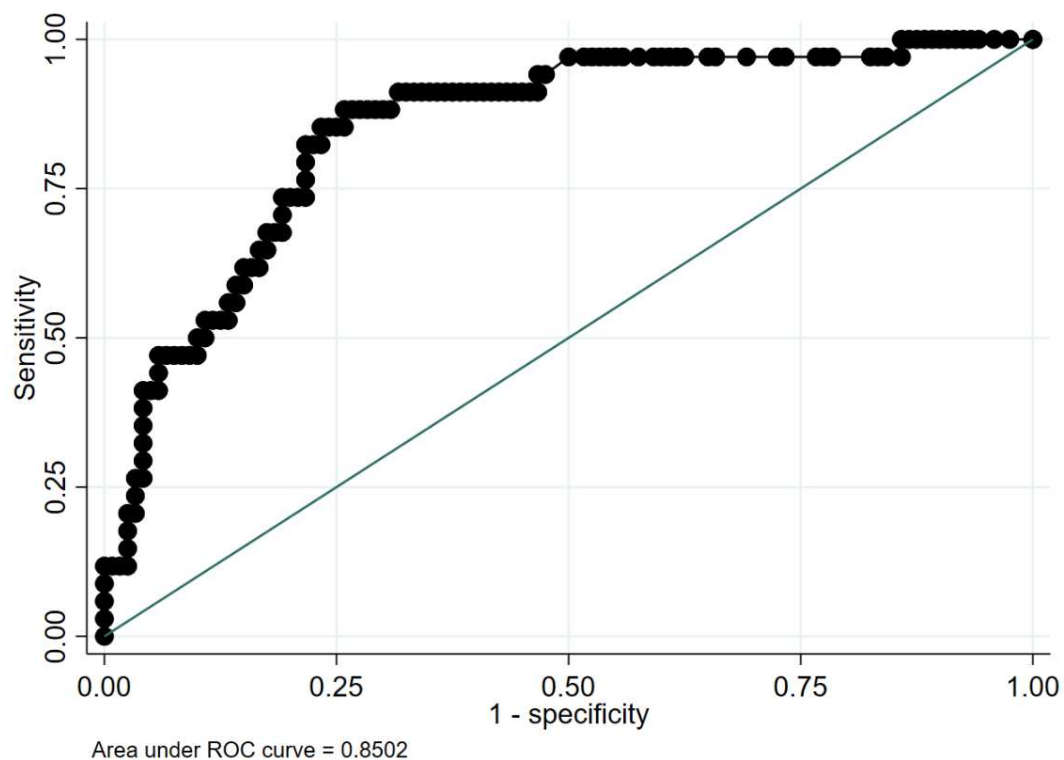
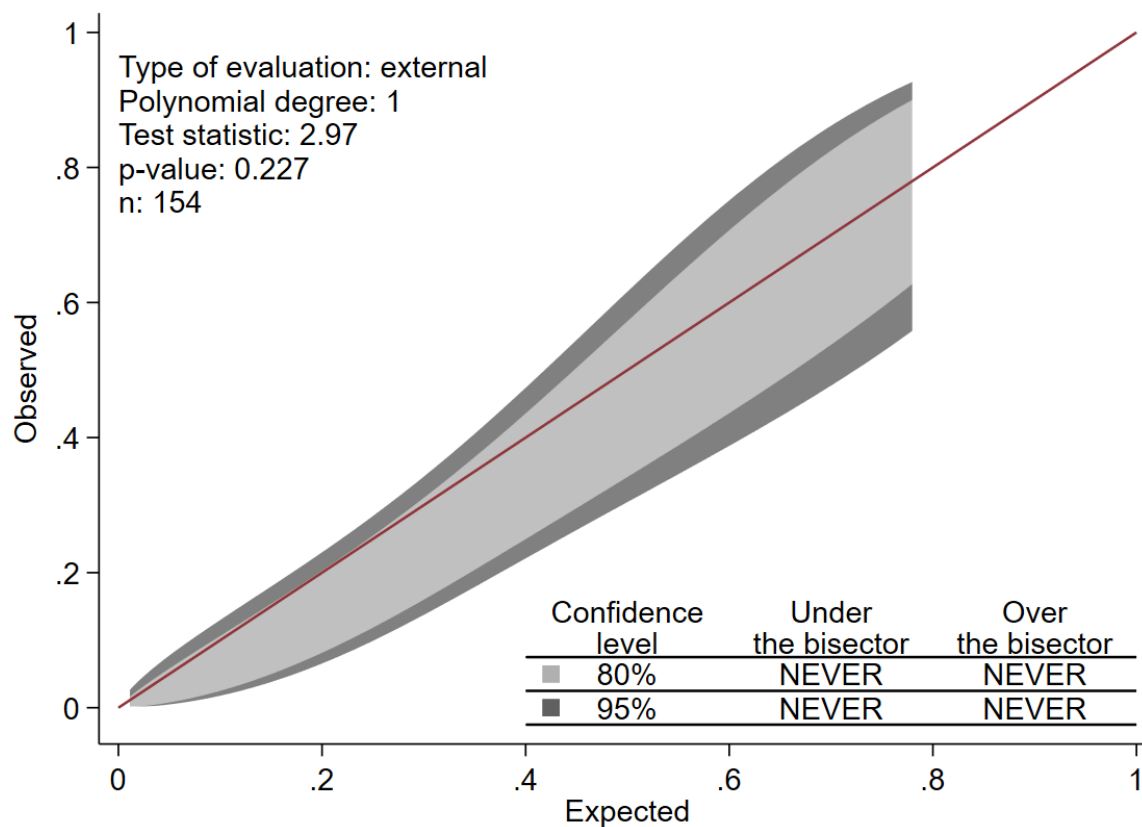


Figure S2: The calibration of the model after recalibration

Formula S1: Based on a lambda result of $\lambda=0.0402856$ and a probability threshold of 0.35, the LASSO calculation with characteristics predictive of CAP as follows:

$$\begin{aligned}
 \text{CAP - score} = & 0.07 \cdot 1_{\text{Unwell=yes}} + 0.35 \cdot 1_{\text{Dyspnea=yes}} + 0.36 \cdot 1_{\text{Expectoration=yes}} + 0.39 \cdot 1_{\text{Cough=yes}} \\
 & + 0.34 \cdot 1_{\text{Cold=yes}} + 0.14 \cdot 1_{\text{Respiratory rate >20/min=yes}} + 0.24 \\
 & \cdot 1_{\text{Oxygen saturation <96%=yes}} + 0.20 \cdot 1_{\text{Chest pain=yes}} + 0.56 \cdot 1_{\text{Stethoscope=yes}} - 0.12 \\
 & \cdot 1_{\text{Previous CAP=no}} + 0.003 \cdot 1_{\text{Leucocytes <3.5 or >8.8 10E9/L=yes}} + 0.08 \\
 & \cdot 1_{\text{Neutrophilocytes >7.5 10E9/L=yes}} - 0.64 \cdot 1_{\text{CRP <20mg/L=yes}} + 0.53 \cdot 1_{\text{Cough=yes}} \cdot 1_{\text{age} \geq 75} \\
 & - 0.05 \cdot 1_{\text{Edema=yes}} \cdot 1_{\text{age} \geq 75} + 0.88 \cdot 1_{\text{Glucose >11 mmol/L=yes}} \cdot 1_{\text{age} \geq 75} + 0.0402856 \\
 & \cdot (0.07 + 0.35 + 0.36 + 0.39 + 0.015 + 0.34 + 0.14 + 0.24 + 0.20 + 0.56 + 0.12 \\
 & + 0.003 + 0.08 + 0.64 + 0.53 + 0.05 + 0.88) - 1.66192 - \log\left(\frac{0.35}{0.65}\right)
 \end{aligned}$$

For best calibration, 0.07 must be subtracted from the score if the score is between 0.08 and 0.47.

Formula S2: A cutoff value greater than 0 indicates the diagnosis CAP according to our model and can be calculated using the following formula:

$$\begin{aligned} \text{CAP - score} = & 0.07 \cdot 1_{\text{Unwell=yes}} + 0.35 \cdot 1_{\text{Dyspnea=yes}} + 0.36 \cdot 1_{\text{Expectoration=yes}} + 0.39 \cdot 1_{\text{Cough=yes}} \\ & + 0.34 \cdot 1_{\text{Cold=yes}} + 0.14 \cdot 1_{\text{Respiratory rate >20/min=yes}} + 0.24 \\ & \cdot 1_{\text{Oxygen saturation <96%=yes}} + 0.20 \cdot 1_{\text{Chest pain=yes}} + 0.56 \cdot 1_{\text{Stethoscope=yes}} - 0.12 \\ & \cdot 1_{\text{Previous CAP=no}} + 0.003 \cdot 1_{\text{Leucocytes <3.5 or >8.8 10E9 /L=yes}} + 0.08 \\ & \cdot 1_{\text{Neutrophilocytes >7.5 10E9 /L=yes}} - 0.64 \cdot 1_{\text{CRP <20mg /L=yes}} + 0.53 \cdot 1_{\text{Cough=yes}} \cdot 1_{\text{age} \geq 75} \\ & - 0.05 \cdot 1_{\text{Edema=yes}} \cdot 1_{\text{age} \geq 75} + 0.88 \cdot 1_{\text{Glucose >11 mmol /L=yes}} \cdot 1_{\text{age} \geq 75} - 0.842742 \end{aligned}$$

For best calibration, 0.07 must be subtracted from the score if the score is between 0.08 and 0.47.

Model specification

Besides the high percentage of missings from lymphocytes (66.3%), lymphocytes contributed to a significantly decreased model performance below 80% and a narrower calibration belt ($p < 0.001$), furthermore lymphocytes were missing for 66.3% of the patients. SARS-CoV-2 vaccine was not included in the final model as the vaccine was related to a specific pandemic and did not change any final predictors or values. The inclusion of the BMI had better prediction performance AUC: 0.86 (CI: 0.79-0.93) and yielded more predictors especially related to lifestyle. The predictors that differed from the final model were: Alcohol (8-14 doses/week) 0.01792, level of physical activity under 2,5 hours/week yielded 0.01067, and obesity appeared with a coefficient of -0.93861. In addition, a symptom of diarrhea (-0.17572), muscular pain (-0.00225), gastrointestinal symptoms (-0.807885), sore throat (0.074709 for patients ≥ 75 years old) and the presence of nephrological diseases (-0.18776 for patients ≥ 75 years old) were predictors of CAP in the model constructed including BMI. From a clinical perspective, we chose to exclude the BMI as the final model would be more useful in an acute setting where reliable information about BMI is not always available. From a statistical perspective, BMI had almost 27% of missings, which would be classified as MAR and possibly selected from the population.

References

1. Almirall, J., et al., *Risk Factors for Community-Acquired Pneumonia in Adults: A Systematic Review of Observational Studies*. *Respiration*, 2017. **94**(3): p. 299-311.
2. Riquelme, R., et al., *Community-acquired pneumonia in the elderly. Clinical and nutritional aspects*. *Am J Respir Crit Care Med*, 1997. **156**(6): p. 1908-14.
3. Janssens, J.P., *Pneumonia in the elderly (geriatric) population*. *Curr Opin Pulm Med*, 2005. **11**(3): p. 226-30.
4. Cillóniz, C., et al., *Community-acquired pneumonia in critically ill very old patients: a growing problem*. *Eur Respir Rev*, 2020. **29**(155).
5. Metlay, J.P., et al., *Influence of age on symptoms at presentation in patients with community-acquired pneumonia*. *Arch Intern Med*, 1997. **157**(13): p. 1453-9.
6. Laporte, L., et al., *Ten-year trends in intensive care admissions for respiratory infections in the elderly*. *Ann Intensive Care*, 2018. **8**(1): p. 84.
7. Ravioli, S., et al., *Age- and sex-related differences in community-acquired pneumonia at presentation to the emergency department: a retrospective cohort study*. *Eur J Emerg Med*, 2022. **29**(5): p. 366-372.
8. Hammond, A., et al., *Predisposing factors to acquisition of acute respiratory tract infections in the community: a systematic review and meta-analysis*. *BMC Infect Dis*, 2021. **21**(1): p. 1254.
9. Barbagelata, E., et al., *Gender differences in community-acquired pneumonia*. *Minerva Med*, 2020. **111**(2): p. 153-165.
10. Baik, I., et al., *A prospective study of age and lifestyle factors in relation to community-acquired pneumonia in US men and women*. *Arch Intern Med*, 2000. **160**(20): p. 3082-8.
11. Heath, G.W., et al., *Exercise and the incidence of upper respiratory tract infections*. *Medicine and science in sports and exercise*, 1991. **23**(2): p. 152-157.
12. Kim, N.E., et al., *Clinical characteristics and outcomes among older nursing home residents hospitalized with pneumonia*. *Arch Gerontol Geriatr*, 2021. **95**: p. 104394.
13. Nieman, D.C., et al., *Upper respiratory tract infection is reduced in physically fit and active adults*. *British journal of sports medicine*, 2011. **45**(12): p. 987-992.
14. Calvillo-King, L., et al., *Impact of social factors on risk of readmission or mortality in pneumonia and heart failure: systematic review*. *Journal of general internal medicine*, 2013. **28**(2): p. 269-282.
15. Clyde, W.A., Jr., *Clinical overview of typical Mycoplasma pneumoniae infections*. *Clin Infect Dis*, 1993. **17 Suppl 1**: p. S32-6.
16. Gamble, J.M., et al., *Medication transitions and polypharmacy in older adults following acute care*. *Ther Clin Risk Manag*, 2014. **10**: p. 189-96.
17. Torres, A., et al., *Risk factors for community-acquired pneumonia in adults in Europe: a literature review*. *Thorax*, 2013. **68**(11): p. 1057-65.
18. Riquelme, R., et al., *Community-acquired pneumonia in the elderly: clinical and nutritional aspects*. *Revista médica de Chile*, 2008. **136**(5): p. 587-593.
19. Moore, M., et al., *Predictors of pneumonia in lower respiratory tract infections: 3C prospective cough complication cohort study*. *Eur Respir J*, 2017. **50**(5).
20. Ding, F., et al., *Development and validation of a simple tool composed of items on dyspnea, respiration rates, and C-reactive protein for pneumonia prediction among acute febrile respiratory illness patients in primary care settings*. *BMC Med*, 2022. **20**(1): p. 360.
21. Nakanishi, M., et al., *Significance of the progression of respiratory symptoms for predicting community-acquired pneumonia in general practice*. *Respirology*, 2010. **15**(6): p. 969-74.

22. Huijskens, E.G.W., et al., *The value of signs and symptoms in differentiating between bacterial, viral and mixed aetiology in patients with community-acquired pneumonia*. J Med Microbiol, 2014. **63**(Pt 3): p. 441-452.
23. Loubet, P., et al., *Community-acquired pneumonia in the emergency department: an algorithm to facilitate diagnosis and guide chest CT scan indication*. Clin Microbiol Infect, 2020. **26**(3): p. 382.e1-382.e7.
24. Beekman, R., et al., *Validating a clinical prediction score for Legionella-related community acquired pneumonia*. BMC Infect Dis, 2022. **22**(1): p. 442.
25. den Engelsen, C., et al., *Infectious diseases and the use of antibiotics in outpatients at the emergency department of the University Hospital of León, Nicaragua*. Int J Infect Dis, 2009. **13**(3): p. 349-54.
26. Mandell, L.A., *Community-acquired pneumonia: An overview*. Postgrad Med, 2015. **127**(6): p. 607-15.
27. Takase, R., et al., *Clinical Manifestations of Patients with Influenza Differ by Age : A Prospective, Multi-centered Study in the Setouchi Marine Area*. Acta Med Okayama, 2021. **75**(5): p. 567-574.
28. Akhtar, A., et al., *Respiratory-tract infections among geriatrics: prevalence and factors associated with the treatment outcomes*. Therapeutic advances in respiratory disease, 2021. **15**: p. 1753466620971141.
29. Sundhedsstyrelsen. *Sundhedsstyrelsens udmeldinger om alkohol*. 2022 [cited 2022 December 06]; Available from: <https://www.sst.dk/da/Viden/Forebyggelse/Alkohol/Alkoholforebyggelse/Sundhedsstyrelsens-udmeldinger-om-alkohol>
30. (WHO), W.H.O. [cited 2022 December 6]; Available from: chrome-extension://efaidnbmnnnibpcajpcglclefindmkaj/<https://apps.who.int/iris/bitstream/handle/10665/337001/9789240014886-eng.pdf>
31. Shang, J., et al., *Risk factors for infection in home health care: Analysis of national Outcome and Assessment Information Set data*. Res Nurs Health, 2020. **43**(4): p. 373-386.
32. Guidet, B., et al., *Caring for the critically ill patients over 80: a narrative review*. Ann Intensive Care, 2018. **8**(1): p. 114.
33. Steffens, C., et al., *The Association Between Prescribed Opioid Receipt and Community-Acquired Pneumonia in Adults: a Systematic Review and Meta-analysis*. J Gen Intern Med, 2020. **35**(11): p. 3315-3322.
34. Walters, J.A., et al., *Pneumococcal vaccines for preventing pneumonia in chronic obstructive pulmonary disease*. Cochrane Database Syst Rev, 2017. **1**(1): p. Cd001390.
35. Kraicer-Melamed, H., S. O'Donnell, and C. Quach, *The effectiveness of pneumococcal polysaccharide vaccine 23 (PPV23) in the general population of 50 years of age and older: A systematic review and meta-analysis*. Vaccine, 2016. **34**(13): p. 1540-1550.
36. Liang, C.Y., et al., *Effectiveness of influenza vaccination in the elderly: a population-based case-crossover study*. BMJ Open, 2022. **12**(2): p. e050594.
37. Chalmers, J.D., et al., *Severity assessment tools for predicting mortality in hospitalised patients with community-acquired pneumonia. Systematic review and meta-analysis*. Thorax, 2010. **65**(10): p. 878-83.
38. Lim, W.S., et al., *BTS guidelines for the management of community acquired pneumonia in adults: update 2009*. Thorax, 2009. **64 Suppl 3**: p. iii1-55.
39. Rosenvinge, F.S. *Antibiotikavejledning for Region Syddanmark*. 06.10.2021 [cited 2022 22 september]; Available from: <https://ekstern.infonet.regionsyddanmark.dk/Files/Dokument547684.htm>.
40. Plesner, L.L., et al., *The formation and design of the TRIAGE study-baseline data on 6005 consecutive patients admitted to hospital from the emergency department*. Scandinavian journal of trauma, resuscitation and emergency medicine, 2015. **23**(1): p. 1-9.

41. *User Manuel Danish Emergency Process Triage.*
42. Nordberg, M., S. Lethvall, and M. Castrén, *The validity of the triage system ADAPT.* Scandinavian journal of trauma, resuscitation and emergency medicine, 2010. **18**: p. 1-1.
43. Farrohknia, N., et al., *Emergency department triage scales and their components: a systematic review of the scientific evidence.* Scand J Trauma Resusc Emerg Med, 2011. **19**: p. 42.
44. Jones, M., *NEWSDIG: The National Early Warning Score Development and Implementation Group.* Clin Med (Lond), 2012. **12**(6): p. 501-3.
45. Htun, T.P., et al., *Clinical features for diagnosis of pneumonia among adults in primary care setting: A systematic and meta-review.* Sci Rep, 2019. **9**(1): p. 7600.
46. Gong, L., et al., *Clinical profile analysis and nomogram for predicting in-hospital mortality among elderly severe community-acquired pneumonia patients with comorbid cardiovascular disease: a retrospective cohort study.* BMC Pulm Med, 2022. **22**(1): p. 312.
47. Sakakibara, T., et al., *A prediction rule for severe adverse events in all inpatients with community-acquired pneumonia: a multicenter observational study.* BMC pulmonary medicine, 2022. **22**(1): p. 34.
48. Mogensen, C.B., et al., *Ear measurement of temperature is only useful for screening for fever in an adult emergency department.* BMC Emerg Med, 2018. **18**(1): p. 51.
49. Mackowiak, P.A., F.A. Chervenak, and A. Grünebaum, *Defining Fever.* Open Forum Infect Dis, 2021. **8**(6): p. ofab161.
50. Waterer, G.W., L.A. Kessler, and R.G. Wunderink, *Medium-term survival after hospitalization with community-acquired pneumonia.* Am J Respir Crit Care Med, 2004. **169**(8): p. 910-4.
51. Zhao, L.H., J. Chen, and R.X. Zhu, *The relationship between frailty and community-acquired pneumonia in older patients.* Aging Clin Exp Res, 2023. **35**(2): p. 349-355.
52. Kitazawa, T., et al., *Characteristics of pneumonia with negative chest radiography in cases confirmed by computed tomography.* J Community Hosp Intern Med Perspect, 2020. **10**(1): p. 19-24.
53. Huang, Y., et al., *Diagnostic value of blood parameters for community-acquired pneumonia.* Int Immunopharmacol, 2018. **64**: p. 10-15.
54. Alzoubi, O. and A. Khanfar, *Association between neutrophil to lymphocyte ratio and mortality among community acquired pneumonia patients: a meta-analysis.* Monaldi Arch Chest Dis, 2021. **92**(3).
55. Milas, G.P., V. Issaris, and V. Papavasileiou, *Blood urea nitrogen to albumin ratio as a predictive factor for pneumonia: A meta-analysis.* Respir Med Res, 2022. **81**: p. 100886.
56. Kassaw, G., et al., *Outcomes and Predictors of Severe Community-acquired Pneumonia Among Adults Admitted to the University of Gondar Comprehensive Specialized Hospital: A Prospective Follow-up Study.* Infect Drug Resist, 2023. **16**: p. 619-635.
57. Adnan, M., et al., *Prognostic value of five serum markers predicting in-hospital mortality among adults with community acquired pneumonia.* J Infect Dev Ctries, 2022. **16**(1): p. 166-172.
58. Rendón-Ramírez, E.J., et al., *TGF- β Blood Levels Distinguish Between Influenza A (H1N1)pdm09 Virus Sepsis and Sepsis due to Other Forms of Community-Acquired Pneumonia.* Viral Immunol, 2015. **28**(5): p. 248-54.
59. Watanabe, H., et al., *Clinical factors associated with negative urinary antigen tests implemented for the diagnosis of community-acquired pneumococcal pneumonia in adult patients.* Med Princ Pract, 2015. **24**(2): p. 189-94.
60. Zeng, W., et al., *Association of admission blood glucose level and clinical outcomes in elderly community-acquired pneumonia patients with or without diabetes.* Clin Respir J, 2022. **16**(8): p. 562-571.
61. Barmanray, R.D., et al., *In-hospital hyperglycemia but not diabetes mellitus alone is associated with increased in-hospital mortality in community-acquired pneumonia (CAP): a systematic review and meta-analysis of observational studies prior to COVID-19.* BMJ Open Diabetes Res Care, 2022. **10**(4).

62. van der Meer, V., et al., *Diagnostic value of C reactive protein in infections of the lower respiratory tract: systematic review*. *Bmj*, 2005. **331**(7507): p. 26.
63. van Vugt, S.F., et al., *Use of serum C reactive protein and procalcitonin concentrations in addition to symptoms and signs to predict pneumonia in patients presenting to primary care with acute cough: diagnostic study*. *Bmj*, 2013. **346**: p. f2450.
64. Ebell, M.H., et al., *Accuracy of Biomarkers for the Diagnosis of Adult Community-acquired Pneumonia: A Meta-analysis*. *Acad Emerg Med*, 2020. **27**(3): p. 195-206.
65. Ebell, M.H., et al., *Accuracy of Signs and Symptoms for the Diagnosis of Community-acquired Pneumonia: A Meta-analysis*. *Acad Emerg Med*, 2020. **27**(7): p. 541-553.
66. Division of Nutrition, P.A., and Obesity, National Center for Chronic Disease Prevention and Health Promotion. 3 June 2022 [cited 2023 2 March]; Available from: <https://www.cdc.gov/obesity/basics/adult-defining.html>.