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Nonspecific Symptoms Lack Diagnostic Accuracy for Infection in Older Emergency Department Patients

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Abstract

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Author contributions: JMC and KBS conceived the study and designed the trial. JMC obtained research funding. JMC, RL, and LTS performed the determinations of infections status. DMK performed the data analysis. JMC primarily drafted the manuscript. DMK, LTS, CC, CWB, DJP, and KH contributed substantially to data interpretation and revisions of the manuscript. JMC takes responsibility for the paper as a whole.

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Objectives: To determine if nonspecific symptoms and fever affect the posttest probability of acute bacterial infection in older emergency department (ED) patients.

Design: Preplanned, secondary analysis of a prospective observational study

Setting: Tertiary care, academic ED.

Participants: 424 ED patients 65 years old, including all chief complaints.

Measurements: We identified presence of altered mental status, malaise/lethargy, and fever as reported by the patient, as documented in the chart, or both. Bacterial infection was adjudicated by agreement among 2 of three expert reviewers. Odds ratios were calculated using univariable logistic regression. Positive and negative likelihood ratios (PLR, NLR) were used to determine each symptom's effect on posttest probability of infection.

Results: Of 424 subjects, 77 (18%) had bacterial infection. Accounting for different reporting methods, presence of altered mental status (PLR range 1.40–2.53) or malaise/lethargy (PLR range 1.25–1.34) only slightly increased posttest probability of infection. Their absence did not assist with ruling out infection (NLR >0.50 for both). Fever 38°C either before or during the ED visit had moderate to large increases in probability of infection (PLR 5.15–18.10) with initial fever in the ED perfectly predictive, but absence of fever did not rule out infection (NLR 0.79–0.92). Results were similar when analyzing lower respiratory, gastrointestinal, and urinary tract infections individually. 47% of older adults diagnosed with UTI did not complain of UTI symptoms.

Conclusions: The presence of either altered mental status or malaise/lethargy does not substantially increase the probability of bacterial infection in older ED adults and should not be used alone to indicate infection in this population. Fever 38°C is associated with increased probability of infection.

Keywords

Infection; emergency department; diagnosis; delirium

INTRODUCTION

Background:

Bacterial infection accounts for three million annual visits by older adults to United States emergency departments (EDs).¹ Accurate infection diagnosis is complicated by the absence of typical symptoms found in younger adults, lack of accurate diagnostic criteria, absence of timely culture results, chronic microorganism colonization, and comorbidities.^{2–5} Both over-diagnosis and under-diagnosis can occur.^{2,6} Over-diagnosis may result in increased costs, inappropriate antibiotic use, missed alternative diagnoses, and preventable admissions.^{5,7–9} Under-diagnosis can result in failure to adequately treat bacterial infections.^{5,10}

In prior work, we demonstrated that commonly accepted criteria for antibiotic initiation, the Loeb criteria and Centers for Disease Control guidelines, do not accurately identify the presence of bacterial infection in older ED patients.² Prior authors have noted an association between infection and nonspecific symptoms such as altered mental status/confusion and

malaise/lethargy as well as fever in older adults.^{6,11–15} Clinicians often use the presence of these nonspecific symptoms to diagnose infection even in the absence of classic signs and symptoms.¹⁶ Further complicating accurate diagnosis is the high prevalence of nonspecific symptoms in the older ED population.^{17–19} Given the failure of specific criteria, an examination of the current practice and use of nonspecific symptoms to drive ED infection diagnosis is required.

Although demonstrating an association, prior studies have not shown whether non-specific symptoms can accurately diagnose infection. Likelihood ratios, which estimate the change in post-test probability of disease given a test result, are the preferred method.²⁰ Our primary objective was to determine if patient complaint or clinician's documentation of altered mental status, malaise/lethargy, or fever affect the posttest probability of acute bacterial infection in older adult ED patients.

METHODS

Study design and setting:

This was a preplanned secondary analysis of a study designed to identify agreement between criterion standard expert physician reviewers, treating physicians, and current diagnostic criteria for diagnosis of bacterial infection in older ED adults.² The primary study from 10/2011 through 04/2013 was a prospective, observational cohort study of older adults presenting to the ED of an urban, tertiary care center with 60,000 annual visits. Institutional review board approval was obtained. STROBE and STARD guidelines were followed.²¹

Selection of Participants:

All ED patients aged ≥ 65 years were potentially eligible. Exclusion criteria included incarceration, trauma team evaluation, suicidal or homicidal ideation, prior enrollment, non-English speaking, or patient otherwise unable to complete the survey. The electronic medical record was reviewed by study personnel in real-time to identify and consent a convenience sample of eligible patients during daytime, evening, and weekend shifts 4–6 hours per day.

Interventions:

A patient survey was administered by trained research staff collecting data on demographics, symptoms, and patient report of altered mental status/confusion, malaise/lethargy, and/or fever within the prior 24 hours. For patients with altered mental status, an accompanying adult could answer. The Confusion Assessment Method-ICU (CAM-ICU) was administered to all patients.²²

Chart review collected chief complaint, medical history, test results, exam findings, vital signs, and physician-documented altered mental status/confusion, malaise/lethargy, weakness, and/or fatigue.²³ Abstractors used a code book, were unaware of study hypotheses, and underwent a two-hour training session.

There is a lack of a gold standard for infections in older adults whether using diagnostic criteria, specific tests, or inpatient physician diagnosis.^{2,5,24–28} As a result, we used agreement among expert case reviewers as the criterion standard for infection.^{2,24,29–31} Two

expert physicians, one board-certified in infectious disease (RL) and one in emergency medicine and internal medicine with geriatrics expertise (JMC) identified presence of bacterial infections as a 4 or 5 on a 5-point Likert scale. They reviewed all records surrounding the episode of care through a minimum of five succeeding days including the patient survey; ED records; laboratory, microbiology, and imaging results; inpatient progress notes, H&Ps, consults, and discharge summaries; and any outpatient notes. They did not use specific criteria or a checklist. In cases of disagreement, a third expert board-certified in emergency medicine and graduate of a geriatrics fellowship (LTS) performed a review. Adjudicators were blinded to others' determinations.

Measurements:

Altered mental status/confusion was identified three ways: a positive CAM-ICU, the patient's or accompanying family member's affirmative response to "Confusion or altered mental status" in the prior 24 hours; and ED documentation of "confusion" or "altered mental status." This approach was chosen as CAM-ICU is rarely performed in EDs, ED physicians act off of their perception of altered mental status, and patient report can differ from both of these. We examined each measure individually and also created an aggregate variable if any of these three were positive.

Malaise/lethargy was documented as present by a positive patient or family member response to a patient survey question regarding new presence of "malaise/lethargy/fatigue" or ED documentation of "malaise," "lethargy," "fatigue," or "generalized weakness." An aggregate variable was also created if either were positive.

Fever was defined by patient report of fever $\geq 38.0^{\circ}\text{C}$ in the 24 prior hours prior or temperature $\geq 38.0^{\circ}\text{C}$ during the ED stay. We also examined a cutoff of 37.2°C ³² and created aggregate fever variables for each cutoff.

Outcomes:

Bacterial infection was considered present if identified by at least two expert reviewers and could include: lower respiratory (excluding isolated bronchitis or chronic obstructive pulmonary disease exacerbations), urinary tract (UTI) (cystitis, pyelonephritis, or prostatitis), skin/soft tissue (cellulitis, cutaneous abscess, surgical wound infection, deep skin infection, diabetic foot infection, or decubitus ulcer), neurologic (bacterial meningitis), orthopedic (osteomyelitis or septic arthritis), gastrointestinal (appendicitis, diverticulitis, hepatobiliary infection, colitis, intra-abdominal abscess, or other intra-abdominal), or isolated bacteremia.

Analysis:

We calculated descriptive statistics and test characteristics including sensitivity, specificity, positive likelihood ratio (PLR) and negative likelihood ratio (NLR) with 95% CIs. We identified the unadjusted relationship between each characteristic and infection using univariable logistic regression. We used SAS v9.4 (SAS Institute, Inc., Cary, NC) and STATA v12 (STATA Corp, College Station, TX). For interpretation of likelihood ratios, a PLR of 1–2 was considered to have no effect on post-test probability (0–15%), 2–5 slight

increase (15–30%), 5–10 moderate increase (30–45%), and >10 large increase (>45%). An NLR of 0.5–1 was considered to have no effect on posttest probability (–0.0 to –0.15%), 0.2–0.5 slight decrease (–15 to –30%), 0.1–0.2 moderate decrease (–30 to –45%), and <0.1 a large decrease (>–45%).²⁰

The primary analysis was conducted with presence of any infection as the outcome variable. We also performed sensitivity analyses excluding skin and soft tissue infections from the diagnosis of true bacterial infection and another using a more restrictive diagnosis of UTI which included both presence of urinary symptoms and positive urine culture.² We performed secondary analyses specific to diagnosis of lower respiratory, gastrointestinal, and urinary tract infections. For these analyses we compared those with the specific infection type to those without infection, excluding those with other types of infection.

RESULTS

Characteristics of study subjects:

The primary study included 424 subjects.² Table 1 provides patient characteristics overall and stratified by presence of infection. Criterion standard reviewers identified infection in 77 (18%) patients: 18 (4.2%) lower respiratory, 19 (4.5%) UTI, 22 (5.2%) gastrointestinal, 15 (3.5%) skin/soft tissue, and 3 (3.8%) other infections. They agreed on presence of infection in 95% of cases (kappa = 0.82).

Main results:

Table 2 reports unadjusted odds ratios and test characteristics for nonspecific symptoms in predicting infection. Altered mental status was associated with increased odds of infection (OR 2.73) only when documented on the ED chart. It had sensitivity <20% regardless of how recorded and specificity 87% to 97%. PLR and NLR values demonstrate that its presence had no effect to slight effect to increase or decrease the posttest probability of bacterial infection.

When reported by the patient, malaise/lethargy was associated with a significant increase in the odds (OR=1.75) of infection but not when reported in only the ED chart or when either was reported. It had sensitivity 23–61% and specificity 51–82% depending on how recorded. PLR and NLR values demonstrate that presence of malaise/lethargy had no effect to slight effect to increase or decrease the posttest probability of bacterial infection.

Patients with ED-measured or patient-reported temperatures $\geq 38.0^{\circ}\text{C}$ had greater odds of infection than those without. Fever $\geq 38.0^{\circ}\text{C}$, was highly specific for infection. Patient report of fever $\geq 38.0^{\circ}\text{C}$ had a PLR of 5.15 and any ED fever $\geq 38.0^{\circ}\text{C}$ a PLR of 18.1 indicating moderate and large increases in posttest probability respectively. Using a cutoff of 37.2°C for fever resulted in PLRs which only slightly increased posttest probability of disease, while NLRs remained >0.75 . The sensitivity analyses found no significant changes to the results reported in Table 2.

Table 3 reports unadjusted odds ratios and test characteristics for nonspecific symptoms in predicting presence of lower respiratory infections. The odds ratios were not significant and

the PLRs and NLRs of altered mental status and lethargy/fatigue had no effect on posttest probability of disease. The PLRs of fever $\geq 38.0^{\circ}\text{C}$ had a large increase and that of $\geq 37.2^{\circ}\text{C}$ a moderate increase in posttest probability. NLRs were all >0.50 . Among symptoms of respiratory infection, sensitivity was 61% or less for all and NLRs had only slight effect on decreasing posttest probability of disease.

For UTI (Table 4), the PLR for ED chart review report of altered mental status was 5.69 (95% CI 2.3–14) indicating moderate effect on increased posttest probability of UTI. Malaise/lethargy had PLRs <5 for UTI. Only 47% (9 of 19) of patients diagnosed with a UTI had at least one specific UTI symptom. Several symptoms did moderately increase the posttest probability of UTI with PLRs >5.0 . Gastrointestinal infection results (Table 5) were similar, fever and abdominal pain had PLRs >5.0 . Confidence intervals for specific infection types were generally wide, reflecting the smaller number of individual infections.

Sample size was powered for the primary study.² It was adequate for this analysis as it allowed sufficient precision in the CIs about the estimates of test performance with sensitivity point estimates' 95% CIs less than $\pm 10\%$ and specificity's $\pm 5\%$.

DISCUSSION

The potentially infected older adult presents a substantial diagnostic challenge to emergency physicians.^{2,33} Presentation of infection is frequently atypical in older adults as compared to younger adults including up to 1/3 with pneumonia and 2/3 with UTI.^{13,34} Diagnostic criteria fail to accurately identify infection in this population.² As a substitute, ED clinicians frequently diagnose infection based solely on the presence of nonspecific signs and symptoms such as altered mental status, or malaise/lethargy.^{4,6,13,35} However, the accuracy of such an approach has undergone minimal investigation. This has important implications in the use of antibiotics in the older ED population. Antibiotics are often empirically administered in response solely to nonspecific symptoms. If these symptoms are not associated with posttest probability of infection, use of antibiotics in this setting should be questioned.

Most authors have identified the frequency of nonspecific symptoms and/or the increased odds of infection in patients with a nonspecific symptom.^{3,11–13} The more relevant question is what effect the presence of these symptoms has on either infection diagnosis. The most relevant measure of diagnostic accuracy is the likelihood ratio which quantifies the change in posttest probability of disease given either a positive or negative finding.²⁰

Altered mental status is frequently present in older ED adults with infections such as bacteremia (OR 2.6), UTI (7–18% prevalence), and lower respiratory infection (12–30% prevalence).^{11–14,36} It was present in 6–18% of those with infection in our study. Altered mental status had poor sensitivity but high specificity for infection. The high specificity is likely due to the non-specific population selected for the study as many older adults present to the ED with conditions clearly not associated with altered mental status. Despite this high specificity, based on LRs, altered mental status is neither able to assist with ruling-in nor ruling-out infection. This is consistent with other studies that have shown that delirium is

often present in both infected and non-infected older ED patients. Kennedy et al found that although 35% of ED patients with delirium had an infection, 21% of those without delirium also had an infection.³⁷ Ducharme et al found that there was no difference in presence of positive urine culture in older ED patients with confusion, weakness, or fever versus those without such symptoms.⁴ The frequent occurrence of altered mental status in older ED patients limits this symptom's accuracy for the diagnosis of infection.

Malaise/lethargy was common in this study with a slightly higher rate in those with infection, as has been previously described.^{11,12} Malaise/lethargy did increase the odds of infection when reported by the patient but not when charted by the ED or in aggregate. Both sensitivity and specificity were poor, likely due to the high frequency of this symptom through the entire older ED population. As a result, malaise/lethargy was also not able to assist with making the diagnosis of infection.

Prior authors have noted that a fever $\geq 38.0^{\circ}\text{C}$ is strongly associated with bacterial infection in older adults, but has poor sensitivity.^{15,16,38} Fever is present in 12–25% of older ED adults with lower respiratory infection and 20% with UTI.^{13,14} A fever of $\geq 38.0^{\circ}\text{C}$ had poor sensitivity and NLRs, consistent with these past studies. However, fever $\geq 38.0^{\circ}\text{C}$ was highly specific and substantially increased the posttest probability of disease.

Several authors have suggested using a 37.2°C temperature cutoff in older adults to increase sensitivity.³² Although there was some increase in sensitivity and improvement in NLR, the NLR still did not adequately decrease posttest probability of infection. Using this lower cutoff also resulted in lower PLRs making it unhelpful in ruling-in infection.

Non-specific symptoms and fever performed similarly when examining lower respiratory infection as they were not associated with or helpful in ruling-in or ruling-out lower respiratory infection. The atypical presentation of lower respiratory infection in older ED adults is shown in that only cough reported in the ED chart had a sufficiently high PLR to assist in diagnosis. The absence of specific symptoms did not assist in ruling out lower respiratory infection. For gastrointestinal infection, abdominal pain and ever increased posttest probability of disease. However, the sub-population studied excluded subjects with other infections which likely artificially elevated the PLR for fever.

Patients with UTI frequently have nonspecific chief complaints including altered mental status and constitutional complaints.⁶ In our study, only when altered mental status was documented in the ED chart was there a moderate increase in posttest probability (PLR 5.69). Presence of malaise/lethargy did not assist with diagnosis. Certain UTI symptoms were associated with increased probability of disease, but absence of specific symptoms was not adequate to rule out UTI.

These findings illuminate a current controversy in UTI diagnosis. National guidelines call for not diagnosing UTI or initiating antibiotics in cases of asymptomatic bacteriuria (ASB).^{7,39,40} Avoiding antibiotics in ASB has been included in the Choosing Wisely campaign and there have been calls to adopt this policy not only in outpatient but also in acute care settings.^{41–43} However, although ASB has been studied in multiple settings including nursing homes and the community,³⁹ this approach has not been validated in the ED where

patients present for an acute event or change in status. In our data and prior studies, ED and inpatient physicians often diagnose UTI in older adults in absence of urinary symptoms.^{13,44} Although current dogma indicates that these patients had ASB rather than UTI, that may be incorrect as in multiple studies of bacteremic UTI, one half or less of older adults had urinary symptoms.^{27,28,45,46} In this study, two experts, frequently felt that patients had acute UTI even in the absence of symptoms. These findings indicate a need to further explore the relationship between ED presentation, acute UTI, and ASB in the ED population as distinct from the community or nursing home and that conclusions drawn from studies in those settings should not necessarily be applied to the acute care setting.

There are several potential study limitations including that this was a single academic center study. As there is no specific gold standard for identifying the presence of altered mental status or lethargy/fatigue, we considered both patient report and physician report to reflect clinical practice.^{47,48} As a result, in some cases only certain measures were found to be significant. However, the direction of results was generally consistent.⁴⁹ We also only looked at variables in isolation. It may be that combinations of nonspecific symptoms could reveal patterns consistent with infection. Caregiver report may have overestimated patient symptom severity which could worsen specificity.⁵⁰

The expert reviewers considered the presence of the symptoms under study in their determination of presence of infection. This could lead to incorporation bias but represents the only practicable way to determine if infection is present in the absence of gold standard diagnostic tests. The direction of such bias would be to improve performance of the symptoms for predicting infection. However, both altered mental status and malaise/lethargy still performed poorly.

Using agreement among experts as the criterion standard was necessary as there is not a gold standard test.⁴² This approach has been successfully used in inpatients for skin/soft tissue infection and UTI, among other conditions.^{24,29–31} Experts in this study had access to all elements of the records plus patient survey results. As a result, they were able to consider all relevant factors. The high rate of agreement for presence of infection supports the choice of this method.

The study was not powered to answer questions regarding individual infections with the result that many CIs in Table 3 are quite wide. In general, results for individual infections should be taken as exploratory. Finally, the population studied was that of all ED patients, not only those with suspected infection. It is possible that a more focused patient population could return different results. However, based on current dogma, the presence of nonspecific symptoms often drives a diagnosis of infection in older adults. Studying only those with clear complaint of infection would likely miss many with infections.

In conclusion, the presence of either altered mental status or malaise/lethargy does not substantially increase the probability of bacterial infection being present in older ED adults. These non-specific symptoms should not be used alone to indicate infection in this patient population. Fever $\geq 38^{\circ}\text{C}$ is associated with moderate to large increases in probability of

bacterial infection. Results were generally similar for lower respiratory tract, gastrointestinal and urinary tract infections specifically.

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Impact statement: We certify that this work is novel. The potential impact of this research on clinical care is to decrease the over-diagnosis of infection in older adult in the ED, limiting antibiotic overuse, facilitating searches for alternative diagnoses, and improving care for older adults in the ED.

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Table 1:

Characteristics of 424 older adult emergency department patients stratified by presence of infection

Characteristic	Overall (n=424) Count (%) / Mean (SD)	Infection present (n=77) Count (%) / Mean (SD)	No Infection present (n=347) Count (%) / Mean (SD)
Demographics			
Age (years)	74 (7.4)	74 (7.6)	74.6 (7.4)
Female gender	244 (58%)	44 (57%)	200 (58%)
Race: Asian	3 (0.7%)	1 (1.3%)	2 (0.6%)
Black	71 (17%)	7 (9%)	64 (19%)
White	344 (81%)	68 (88%)	276 (80%)
Other	6 (1.4%)	1 (1.3%)	4 (1.2%)
Hispanic Ethnicity	7 (1.6%)	1 (1.3%)	6 (1.8%)
Charlson Comorbidity Index	2.3 (2.3)	2.5 (2.4)	2.3 (2.3)
Antibiotics ordered in ED	78 (18%)	43 (56%)	35 (10%)
Vital Signs			
Initial heart rate (beats per minute)	84 (20)	85 (16)	83 (20)
Initial systolic blood pressure (mmHg)	138 (28)	133 (30)	139 (28)
Initial respiratory rate (breaths per minute)	18 (4)	19 (7.7)	17 (3.1)
Final ED disposition			
Discharge	173 (41%)	13 (17%)	160 (46%)
Admit to intensive care unit	4 (0.9%)	3 (3.9%)	1 (0.3%)
Admit to inpatient unit	245 (58%)	60 (78%)	185 (53%)
Left against medical advice	1 (0.2%)	1 (1.3%)	0 (0%)
Expired	0 (0%)	0 (0%)	0 (0%)
Altered mental status/confusion			
CAM-ICU positive for delirium	16 (3.8%)	5 (6.5%)	11 (3.2%)
Patient report: Confusion or altered mental status	42 (10%)	10 (13%)	32 (9.2%)
ED chart: Confusion or altered mental status	25 (5.9%)	9 (12%)	16 (4.6%)
Aggregate altered mental status: CAM-ICU positive, patient report, or ED chart report	59 (14%)	14 (18%)	45 (13%)
Malaise, lethargy, fatigue			
Patient report: Malaise, lethargy, or fatigue	183 (43%)	42 (55%)	141 (41%)
ED chart: Malaise, lethargy, or fatigue	79 (19%)	18 (23%)	61 (18%)
Aggregate variable: Either patient report or ED chart report	217 (51%)	47 (61%)	170 (49%)
Fever (cutoff 38.0°C)			
Patient report: Fever 38.0°C in the prior 24 hours	30 (7.1%)	16 (21%)	14 (4.0%)
Initial ED temperature 38.0°C	6 (1.4%)	6 (7.8%)	0 (0%)
Any ED temperature 38.0°C	10 (2.4%)	8 (11%)	2 (0.6%)
Aggregate variable: Patient report or any ED temperature 38.0°C	35 (8.2%)	19 (25%)	16 (4.6%)
Fever (cutoff 37.2°C)			

Characteristic	Overall (n=424)	Infection present (n=77)	No Infection present (n=347)
	Count (%) / Mean (SD)	Count (%) / Mean (SD)	Count (%) / Mean (SD)
Initial ED temperature 37.2°C	31 (7.3%)	14 (18%)	17 (4.9%)
Any ED temperature 37.2°C	46 (11%)	17 (22%)	29 (8.3%)
Aggregate variable: Patient report of fever 38.0°C or any ED temperature 37.2°C	63 (15%)	25 (32%)	38 (11%)

ED=emergency department, bpm=beats per minute, mmHg=millimeters of mercury, CAM-ICU = confusion assessment method-ICU

Table 2:

Unadjusted odds ratios and test characteristics for the presence of symptoms in bacterial infection among older ED patients

Characteristic/symptom	OR	(95% CI)	p value	Sensitivity	Specificity	PLR	NLR
Altered mental status							
Delirium positive CAM-ICU	2.14	(0.72–6.38)	0.168	6.7% (2.2–15)	97% (94–98)	2.07 (0.74–5.79)	0.96 (0.90–1.03)
Patient report: Confusion or altered mental status	1.46	0.67–3.13	0.319	13% (6.4–23)	91% (87–94)	1.41 (0.72–2.74)	0.96 (0.87–1.05)
ED chart: Confusion or altered mental status	2.73	(1.16–6.43)	0.022	12% (5.5–21)	95% (93–97)	2.53 (1.16–5.51)	0.93 (0.85–1.01)
Aggregate variable: CAM-ICU positive, patient report or ED chart confusion or altered mental status	1.49	(0.77–2.88)	0.234	18% (10–29)	87% (83–90)	1.4 (0.81–2.42)	0.94 (0.84–1.05)
Malaise/lethargy							
Patient report: Malaise, lethargy, or fatigue	1.75	(1.07–2.88)	0.027	54% (43–66)	59% (54–65)	1.34 (1.06–1.71)	0.77 (0.59–0.99)
ED chart: Malaise, lethargy, or fatigue	1.42	(0.78–2.58)	0.244	23% (14–34)	82% (78–86)	1.33 (0.83–2.11)	0.93 (0.82–1.06)
Aggregate variable: Patient report or ED charted malaise, lethargy, or fatigue	1.63	(0.98–2.70)	0.057	61% (49–72)	51% (46–56)	1.25 (1.01–1.53)	0.76 (0.57–1.03)
Fever (cutoff 38.0°C)							
Patient report: Fever 38.0°C in the prior 24 hours	6.24	(2.90–13.44)	<0.001	21% (12–32)	96% (93–98)	5.15 (2.63–10.10)	0.83 (0.73–0.93)
Initial ED temperature 38.0°C	1.00	perfectly predictive		7.9% (2.9–16)	100% (99–100)	NA	0.92 (0.86–0.98)
Any ED temperature 38.0°C	20.11	(4.18–96.81)	<0.001	10% (4.6–20)	99% (98–100)	18.1 (3.92–83.60)	0.90 (0.83–0.97)
Aggregate variable: Patient report or any ED temperature 38.0°C	6.77	(3.29–13.94)	<0.001	25% (16–36)	95% (93–97)	5.35 (2.89–9.92)	0.79 (0.69–0.90)
Fever (cutoff 37.2°C)							
Initial ED temperature 37.2°C	4.31	(2.02–9.20)	<0.001	18% (10–29)	95 (92–97)	3.71 (1.91–7.20)	0.86 (0.77–0.96)
Any ED temperature 37.2°C	3.11	(1.61–6.01)	<0.001	22% (13–33)	92% (88–94)	2.64 (1.53–4.56)	0.85 (0.75–0.96)
Aggregate variable: Patient report of fever 38.0°C or any ED temperature 37.2°C	3.90	(2.18–7.01)	<0.001	32% (22–44)	89% (85–92)	2.96 (1.9–4.6)	0.76 (0.65–0.89)

OR=odds ratio, CI=confidence interval, PLR=positive likelihood ratio, NLR=negative likelihood ratio, ED=emergency department

Table 3:

Unadjusted odds ratios and test characteristics for the presence of symptoms in lower respiratory infection among 365 older ED patients *

Characteristic/symptom	OR (95% CI)	p value	Sensitivity	Specificity	PLR	NLR
Altered mental status						
Delirium positive CAM-ICU	2.01 (0.24–16.57)	0.518	6.2% (0.16–30)	97% (94–98)	1.94 (0.27–14.1)	0.97(0.85–1.11)
Patient report: Confusion or altered mental status	1.23 (0.27–5.59)	0.788	11% (1.4–35)	91% (87–94)	1.20 (0.31–4.64)	0.98(0.83–1.16)
ED chart: Confusion or altered mental status	1.21 (0.15–9.69)	0.855	5.6% (0.14–27)	95% (93–98)	1.20 (0.17–8.56)	0.99(0.88–1.11)
Aggregate variable: CAM-ICU positive, patient report or ED chart confusion or altered mental status	1.34 (0.37–4.82)	0.652	17% (3.6–41)	87% (83–90)	1.29 (0.44–3.74)	0.96(0.78–1.18)
Malaise/lethargy						
Patient report: Malaise, lethargy, or fatigue	0.93 (0.35–2.46)	0.883	39% (17–64)	59% (54–65)	0.96 (0.53–1.73)	1.03(0.70–1.50)
ED chart: Malaise, lethargy, or fatigue	1.80 (0.62–5.23)	0.282	28% (9.7–54)	82% (78–86)	1.58 (0.72–3.43)	0.88(0.66–1.17)
Aggregate variable: Patient report or ED charted malaise, lethargy, or fatigue	1.30 (0.50–3.38)	0.588	56% (31–78)	51% (46–56)	1.13 (0.74–1.74)	0.87(0.52–1.48)
Fever (cutoff 38.0°C)						
Patient report: Fever 38.0°C in the prior 24 hours	23.78 (8.18–69.17)	<0.001	50% (26–74)	96% (93–98)	12.40 (6.21–24.70)	0.52(0.33–0.83)
Initial ED temperature 38.0°C	perfectly predictive		17% (3.6–41)	100% (99–100)		0.83(0.68–1.02)
Any ED temperature 38.0°C	48.85 (8.24–289)	<0.001	22% (6.4–48)	98% (97–100)	14.9 (4.60–48.20)	0.79(0.62–1.01)
Aggregate variable: Patient report or any ED temperature 38.0°C	20.69 (7.23–59.20)	<0.001	50% (26–74)	95% (93–97)	10.8 (5.58–21.10)	0.52(0.33–0.83)
Fever (cutoff 37.2°C)						
Initial ED temperature 37.2°C	7.47 (2.38–23.36)	0.001	28% (9.7–53)	95% (92–97)	5.67 (2.36–13.60)	0.76(0.57–1.01)
Any ED temperature 37.2°C	5.48 (1.92–15.68)	0.002	33% (13–59)	92% (88–94)	3.99 (1.90–8.36)	0.73(0.52–1.01)
Aggregate variable: Patient report or any ED temperature 37.2°C	10.16 (3.78–27.32)	<0.001	56% (31–78)	89% (85–92)	5.07 (3.04–8.45)	0.50(0.30–0.84)
Respiratory symptoms						
ED rapid breathing	3.51 (1.30–9.48)	0.014	39% (17–64)	85% (80–88)	2.54 (1.35–4.77)	0.72(0.50–1.05)
ED cough	17.18 (6.19–47.69)	<0.001	61% (36–83)	92% (88–94)	7.29 (4.39–12.10)	0.42(0.24–0.76)
ED sputum	5.12 (1.32–19.92)	0.02	17% (3.6–41)	96% (94–98)	4.44 (1.39–14.20)	0.87(0.70–1.07)
Patient report: rapid breathing	2.71 (1.04–7.11)	0.042	44% (22–69)	77% (72–82)	1.95 (1.12–3.39)	0.72(0.47–1.09)
Patient report: cough	4.98 (1.90–13.10)	0.001	50% (26–74)	83% (79–87)	2.99 (1.78–5.02)	0.60(0.38–0.96)
Patient report: sputum	4.75 (1.68–13.51)	0.003	33% (13–59)	91% (87–93)	3.51 (1.69–7.27)	0.74(0.53–1.02)

* Subjects analyzed include those with the specific infection type versus no infection. Those with other infection types are excluded.

OR=odds ratio; CI=confidence interval; PLR=positive likelihood ratio; NLR=negative likelihood ratio

Table 4:

Unadjusted odds ratios and test characteristics for the presence of symptoms in urinary tract infection among 366 older ED patients *

	OR (95% CI)	p	Sensitivity	Specificity	PLR	NLR
Altered mental status						
Delirium positive CAM-ICU	1.67 (0.20–13.67)	0.632	5.3% (0.13–26)	97% (94–98)	1.64 (0.22–12)	0.98 (0.88–1.11)
Patient report: Confusion or altered mental status	4.54 (1.62–12.77)	0.004	32% (13–57)	91% (87–94)	3.42 (1.63–7.17)	0.75 (0.55–1.02)
ED chart: Confusion or altered mental status	7.37 (2.36–22.98)	0.001	26% (9.2–51)	95% (93–97)	5.69 (2.33–13.90)	0.77 (0.59–1.01)
Aggregate variable: CAM-ICU positive, patient report or ED chart confusion or altered mental status	3.91 (1.46–10.46)	0.007	37% (16–62)	87% (83–90)	2.84 (1.48–5.44)	0.72 (0.51–1.03)
Malaise, lethargy, fatigue						
Patient report: Malaise, lethargy, or fatigue	5.48 (1.78–16.85)	0.003	79% (54–94)	59% (54–65)	1.94 (1.49–2.53)	0.36 (0.15–0.85)
ED chart: Malaise, lethargy, or fatigue	2.16 (0.79–5.90)	0.134	32% (13–57)	82% (78–86)	1.79 (0.89–3.61)	0.83 (0.61–1.13)
Aggregate variable: Patient report or ED charted malaise, lethargy, or fatigue	8.85 (2.01–38.88)	0.004	90% (67–99)	51% (46–56)	1.83 (1.51–2.20)	0.21 (0.06–0.77)
Fever (cutoff 38.0°C)						
Patient report: Fever 38.0°C in the prior 24 hours	4.45 (1.16–17.10)	0.029	16% (3.4–40)	96% (93–98)	3.91 (1.23–12.50)	0.88 (0.72–1.07)
Initial ED temperature 38.0°C	perfectly predictive		5.6% (0.14–27)	100% (99–100)	perfectly predictive	0.94(0.84–1.06)
Any ED temperature 38.0°C	10.05 (0.87–116.49)	0.065	5.6% (0.14–27)	99% (98–100)	9.56 (0.91–101)	0.95 (0.85–1.06)
Aggregate variable: Patient report or any ED temperature 38.0°C	5.51 (1.64–18.53)	0.006	21% (6–46)	95% (93–97)	4.57 (1.69–12.30)	0.83 (0.66–1.05)
Fever (cutoff 37.2°C)						
Initial ED temperature 37.2°C	5.18 (1.55–17.29)	0.008	21% (6.0–46)	95% (92–97)	4.30 (1.6–11.50)	0.83 (0.66–1.05)
Any ED temperature 37.2°C	3.91 (1.32–11.64)	0.014	26% (9.2–51)	92% (88–94)	3.15 (1.37–7.22)	0.80 (0.61–1.05)
Aggregate variable: Patient report or any ED temperature 37.2°C	4.74 (1.76–12.78)	0.002	37% (16–62)	89% (85–92)	3.36 (1.74–6.51)	0.71 (0.50–1.00)
Urinary tract symptoms						
Urgency	2.04 (0.65–6.47)	0.223	21% (6.0–46%)	88% (84–92)	1.83 (0.73–4.57)	0.90 (0.71–1.14)
Frequency	1.55 (0.49–4.85)	0.454	21% (6.0–46)	85% (81–89)	1.43 (0.58–3.55)	0.93 (0.73–1.17)
Suprapubic pain	4.07 (1.36–12.12)	0.012	26% (9.2–51)	92% (88–95)	3.26 (1.42–7.49)	0.80 (0.61–1.05)
Gross hematuria	2.70 (0.31–23.12)	0.365	5.3% (0.13–26)	98% (96–99)	2.61 (0.34–20.1)	0.97 (0.87–1.08)
Low back pain	0.77 (0.22–2.72)	0.684	16% (3.4–40)	80% (76–84)	0.81 (0.28–2.33)	1.05 (0.86–1.28)
Incontinence	9.51 (3.38–26.79)	<0.001	37% (16–62)	94% (91–96)	6.37 (3.08–13.20)	0.67 (0.48–0.95)
Foley catheter in place	6.37 (0.63–64.32)	0.117	5.3% (0.13–26)	99% (98–100)	6.09 (0.66–55.80)	0.96 (0.86–1.06)
ED chart suprapubic pain	6.67 (1.25–35.51)	1.25	10% (1.3–33)	98% (96–99)	6.07 (1.31–28.10)	0.91 (0.78–1.06)
ED chart hematuria	perfect predictor					

	OR (95% CI)	p	Sensitivity	Specificity	PLR	NLR
ED chart low back pain	perfect predictor					
Any patient reported symptom	1.63 (0.65–4.14)	0.296	47% (24–71)	65% (59–70)	1.3 (0.82–2.19)	0.82 (0.53–1.26)

* Subjects analyzed include those with the specific infection type versus no infection. Those with other infection types are excluded.

OR=odds ratio; CI=confidence interval; PLR=positive likelihood ratio; NLR=negative likelihood ratio

Table 5:

Unadjusted odds ratios and test characteristics for the presence of symptoms in gastrointestinal infection among 368 older ED patients *

Characteristic/symptom	OR (95% CI)	p value	Sensitivity	Specificity	PLR	NLR
Altered mental status						
Delirium positive CAM-ICU	1.43 (0.17–11.63)	0.736	4.5% (0.1–22.8)	97% (94–98)	1.42 (0.19–10.5)	0.99(0.90–1.08)
Patient report: Confusion or altered mental status	perfect predictor	—	0% (0.0–15.4)	91% (87–94)	—	1.10 (1.07–1.14)
ED chart: Confusion or altered mental status	0.98 (0.12–7.77)	0.986	4.6% (0.11–23)	95% (93–97)	0.98 (0.14–7.08)	1.00 (0.91–1.10)
Aggregate variable: CAM-ICU positive, patient report or ED chart confusion or altered mental status	0.32 (0.04–2.43)	0.271	4.6% (0.11–23)	87% (83–90)	0.35 (0.05–2.42)	1.1 (0.99–0.51)
Malaise/lethargy						
Patient report: Malaise, lethargy, or fatigue	3.13 (1.24–7.87)	0.015	68% (45–86)	59% (54–65)	1.68 (1.23–2.29)	0.54 (0.29–0.99)
ED chart: Malaise, lethargy, or fatigue	1.04 (0.34–3.18)	0.948	18% (5.2–40)	82 (78–86)	1.03 (0.41–2.58)	0.99 (0.81–1.22)
Aggregate variable: Patient report or ED charted malaise, lethargy, or fatigue	2.23 (0.89–5.61)	0.088	68% (45–86)	51% (46–56)	1.39 (1.03–1.89)	0.62 (0.34–1.16)
Fever (cutoff 38.0°C)						
Patient report: Fever 38.0°C in the prior 24 hours	1.13 (0.14–9.03)	0.906	4.5% (0.11–23)	96% (93–98)	1.13 (0.15–8.18)	0.99 (0.91–1.09)
Initial ED temperature 38.0°C	perfect predictor	—	4.5% (0.11–23)	100% (99–100)	—	0.96 (0.87–1.05)
Any ED temperature 38.0°C	17.1 (2.29–127.77)	0.006	9.1% (1.1–29)	99% (98–100)	15.6 (2.3–106)	0.91 (0.80–1.04)
Aggregate variable: Patient report or any ED temperature 38.0°C	3.27 (0.87–12.19)	0.078	14% (2.9–35)	95% (93–97)	2.96 (0.93–9.39)	0.90 (0.77–1.07)
Fever (cutoff 37.2°C)						
Initial ED temperature 37.2°C	3.06 (0.82–11.38)	0.094	14% (2.9–35)	95% (92–97)	2.78 (0.88–8.78)	0.91 (0.88–8.78)
Any ED temperature 37.2°C	2.43 (0.77–7.68)	0.128	18% (5.2–40)	92% (88–94)	2.18 (0.84–5.64)	0.89 (0.73–1.09)
Aggregate variable: Patient report or any ED temperature 37.2°C	1.81 (0.58–5.62)	0.307	18% (5.2–40)	89% (85–92)	1.66 (0.65–4.23)	0.92 (0.75–1.12)
Gastrointestinal symptoms						
ED abdominal pain	19.30 (7.16–52.05)	<0.001	73% (50–89)	88% (84–91)	5.99 (4.09–8.78)	0.31 (0.16–0.62)
Patient report: abdominal pain	9.09 (3.64–22.769)	<0.001	64% (41–83)	84% (80–88)	3.94 (2.65–5.86)	0.43 (0.25–0.76)
Patient report: diarrhea	1.87 (0.52–6.73)	0.337	14% (2.9–35)	92% (89–95)	1.75 (0.58–5.33)	0.94 (0.79–1.11)

* Subjects analyzed include those with the specific infection type versus no infection. Those with other infection types are excluded.

OR=odds ratio; CI=confidence interval; PLR=positive likelihood ratio; NLR=negative likelihood ratio