Author’s response to reviews

Title: Prevalence and factors associated with one-year mortality of infectious diseases among elderly emergency department patients in a middle-income country

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Author’s response to reviews:

Reviewer reports:

Richard Wolfe (Reviewer 1):

1. In both the abstract and the paper, as a conclusion you note that 1/3rd of elderly ED patients died within 1 year. Do you mean elderly emergency patients with infection or do you mean those patients who were admitted? A little more precision is needed as this could also mean that all elderly patients who presented to your ED for all causes, died within 1 year. This final outcome would be more than astonishing unless your emergency population or outpatient support are dramatically different than in high-income countries.

Revised: Thank you for your valuable comments.

We changed the sentence in conclusion:

Line 40. Conclusions: In one middle-income country, infectious diseases account for 14.5% of elderly ED patients. Almost two-thirds of patients presenting to ED with infection are admitted to hospital. One-third of elderly ED patients with infection died within 1 year. Age ≥ 85 years, Charlson Co-morbidity Index score ≥ 5, lactate ≥ 4 mmol/l, qSOFA score ≥ 2, and platelet count <100,000 cells/mm3 predicted 1-year mortality rate.
2. When using a p-value of \( \leq 0.01 \), male gender would not make the cut. Since you use this threshold for all the other predictors and the low end of the range of the O.R. would be one, would it be preferable to not list it as a predictor identified by your study?

Revised: Thank you for your valuable comments. We re-analysed for the model as per your recommendations. We found that male gender was not a significant predictor. We revised the results in the abstract, results and conclusion.

Line 35: Our multivariate analysis showed that age 85 years and older [odds ratio (OR)=1.89; 95% confidence interval (CI): 1.36-2.63], Charlson Co-morbidity Index score \( \geq 5 \) (OR=3.51; 95%CI 2.14-5.77), lactate \( \geq 4 \text{ mmol/l} \) (OR= 2.66;95%CI 1.32-5.38), quick Sequential Organ Failure Assessment (qSOFA) score \( \geq 2 \) (OR= 5.46; 95%CI 2.94-10.12), and platelet count <100,000 cells/mm3 (OR= 3.19; 95%CI 1.15-8.83) were associated with 1-year mortality.

Line 40: Conclusions: In one middle-income country, infectious diseases account for 14.5 % in elderly ED patients. Almost two-thirds of patients presenting with infection at the ED are admitted to hospital. One third of elderly ED patients with infection died within 1 year. Age \( \geq 85 \) years, Charlson Co-morbidity Index score \( \geq 5 \), lactate \( \geq 4 \text{ mmol/l} \), qSOFA score \( \geq 2 \), and platelet count <100,000 cells/mm3 predicted 1-year mortality rate.

Line 177. Our multivariate analysis showed that age 85 years and older [odds ratio (OR)=1.89; 95% confidence interval (CI): 1.36-2.63, p value <0.001], Charlson Co-morbidity Index score \( \geq 5 \) (OR=3.51; 95%CI 2.14-5.77, p value <0.001), lactate \( \geq 4 \text{ mmol/l} \) (OR= 2.66;95%CI 1.32-5.38, p value <0.001), quick Sequential Organ Failure Assessment (qSOFA) score \( \geq 2 \) (OR= 5.46; 95%CI 2.94-10.12, p value =0.025), and platelet count <100,000 cells/mm3 (OR= 3.19; 95%CI 1.15-8.83, p value <0.001) were associated with 1-year mortality (Table 4).

2.1 Serum lactate has been shown in many studies to be a predictor of mortality. Did analyze the predictive value with higher levels such as \( \geq 4 \). The same might apply to higher levels of serum creatinine. Did you consider assessing serum sodium levels or calculated osmolality which have been shown to be a predictor of mortality in ill medical patients?

Revised: Thank you for your valuable comments. We re-analysed for the model as per reviewer recommendations. We found that lactate \( \geq 4 \text{ mmol/l} \) was a significant variable that predicted 1-year mortality, on the other hand hyponatremia ( Na < 135 mmol/l) did not predict 1-year mortality rate. Even though we changed the cut point to Na < 130 mmol/l the result showed no difference (Table 4).
Reviewer 2.

Mette Søgaard (Reviewer 2): The authors have conducted a research study investigating the prevalence of infectious diseases and predictors of one-year mortality associated with infectious diseases among elderly patients presenting at a university hospital in Bangkok from January 1, 2016 through June 2016. The manuscript deals with an interesting topic, however as appears, I have a number of comments that needs to be addressed. Moreover, there are a number of linguistic errors and the language could be improved considerably. I therefore recommend having the manuscript revised by someone who is fluent in English.

Thank you for your valuable comments. We have Mr. Jason Cullen which is a native speaker editing our manuscript.

1. Abstract:

Conclusion - I suggested to also emphasize that almost two-thirds of patients presenting with infection at the ED are admitted to hospital.

Revised: Thank you for your valuable comments, we changed the sentences in conclusion:

Line 40 Conclusions: In one middle-income country, infectious diseases account for 14.5% in elderly ED patients. Almost two-thirds of patients presenting with infection at the ED are admitted to hospital. One third of elderly ED patients with infection died within 1 year. Age ≥ 85 years, Charlson Co-morbidity Index score ≥ 5, lactate ≥ 4 mmol/l, qSOFA score ≥ 2, and platelet count <100,000 cells/mm3 predicted 1-year mortality rate.

2. Background

Please define old and oldest-old.

Revised: We added the definition of the oldest-old populations in the background session.

Line 59: A study in the Netherlands found the oldest-old populations (age ≥ 85 years) who were independent in activities of daily living (ADL) became less able in ADLs with a diagnosis of infectious disease [9]

3. The Background section is quite long, and I suggest shortening this section to only 1 page by removing the detailed description of previous studies to the discussion

Revised: We have shortened the background by removing the detailed description of previous studies to the discussion.
IDs among elderly patients are different from younger patients because of the immune response that reduces complement activity, decreases Naïve T-cells, as well as anatomic and physiological changes with aging such as decreased acid-base in gastric secretions, decreased estrogen in menopause, increased risk of urinary tract infection, and polypharmacy. Multiple comorbidities increase older adults’ susceptibility to IDs [11-13].

4. Methods

4.1 I suggest providing all ICD-10 codes in a supplementary table in order to improve readability.

Revised: We have provided all ICD-10 codes in a supplementary Table 1

4.2 Do the authors have any information on the validity and completeness of the infectious disease coding in their database?

Revised: Line 102 Data were extracted from electronic medical records (EMR), which included ED diagnosis, laboratory information system, and ICD-10 codes. For in-hospital patients, we extracted diagnostic data from summaries of the notes of resident doctors who were in charge of each ward. Our hospital has a policy that attending physicians recheck diagnoses.

4.3.1 I think that it would improve readability and understanding if the authors moved the paragraph "Definitions" up before the description of "Data collection process".

Revised: We moved the paragraph "Definitions" up before the description of "Data collection process".

Line 89

Definitions

Polypharmacy was defined as the number of patients’ medications ≥ 5.

Sepsis fast track at this hospital was defined as patients who had at least 2 from 3 points of Systemic Inflammatory Response Syndrome (SIRS) criteria at triage; nurses then activated fast track by notifying EPs. SIRS at triage was defined as 1. body temperature < 36 °C or > 38 °C; 2. heart rate > 90 beats/min; and 3. respiratory rate (RR) > 20/min.

Quick Sequential Organ Failure Assessment (qSOFA) was defined as 1. systolic blood pressure (SBP) ≤ 100 mmHg; 2. respiratory rate ≥ 22/min; and 3. glasgow coma scale (GCS) <15.
Data collection process

The data collection was done by a third-year emergency resident, medical students in their sixth year, and a registered nurse who had three years’ practicing experience in ED. Data were extracted from electronic medical records (EMR), which included ED diagnosis, laboratory information system, and ICD-10 codes. For in-hospital patients, we extracted diagnostic data from summaries of the notes of resident doctors who were in charge of each ward. Our hospital has a policy that attending physicians recheck diagnoses.

4.3.2 Regarding definitions and baseline characteristics: How long of a lookback period did you use for diagnoses and medication, e.g. for assessment of the Charlson Comorbidity Index score?

Revised: We looked back at all records in medical records for diagnoses, and assessment of the Charlson Comorbidity Index score up to 1 year, except for current medications for which we looked back to up to 6 months.

4.3.3 Regarding data collection, it is somewhere unclear whether the data were extracted from the hospital's electronic system (ICD-10 codes) or from the medical record or laboratory information system?

Revised: Data were extracted from electronic medical records (EMR), which included ED diagnosis, laboratory information system, and ICD-10 codes. For in-hospital patients, we extracted diagnostic data from summaries of the notes of resident doctors who were in charge of each ward. Our hospital has a policy that attending physicians recheck diagnoses.

5. Results

5.1 The numbers in Figure 1 do not add up: 3467 patients - 271 non-urgent patients = 3196 patients and not 3217 patients? Please revise this.

Revised Figure 1

5.2 Table 1. Please clarify what 30 Baht healthcare scheme is? Moreover, please also define all abbreviations used in the table.

Revised: We clarify 30 Baht healthcare scheme as shown in the footnote of the table. We define all abbreviations in the Table 1.

5.3 Table 2. Could the patients have more than one type of infection, e.g. pneumonia AND sepsis? Regarding "Hospital admission diagnosis" was this defined as the primary diagnosis?
Revised: We used the data that doctor defined as principal diagnosis in medical records. Regarding "Hospital admission diagnosis" the infection was defined as the primary diagnosis.

5.4 Discussion

The authors conclude that infectious diseases account for 14.4% of ED contacts among elderly patients in their setting. I wonder how robust this estimate is and whether one could expect some form of seasonal variation in the prevalence of infectious diseases?

While the authors discuss study limitations, the paper could benefit from a more thorough discussion of the clinical implications of the study findings.

Revised: Line 235

Lactate concentration ≥ 4 mmol/l was associated with increased 1-year mortality rate, which was comparable to a study by Audren et al, which found lactate concentrations > 4 mmol/L had a specificity of 96% in predicting mortality in hospitalized non-hypotensive patients.29 Other studies found higher serum lactate levels were associated with higher mortality rate.30-32 Clinically, hyperlactatemia (≥ 4 mmol/l ) can be considered a warning signal for organ dysfunction and a guide for medical intervention among elderly patients.

Although our hospital has a sepsis fast track, following the sepsis-3 recommendations, still one-fifth of older adults died within 1 year. Sepsis guidelines for elderly ED patients that focus on and oldest-old population with Charlson co-morbidity index > 5, lactate concentration ≥ 4 mmol/l and qSOFA ≥ 2 points may be beneficial.