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DECAF score as a mortality predictor for acute exacerbation of chronic obstructive pulmonary disease: a systematic review and meta-analysis

Short title: DECAF score for patients with AECOPD

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Abstract

Objectives: This study was conducted to explore the prognostic effect of DECAF score (The Dyspnea, Eosinopenia, Consolidation, Acidemia, and Atrial Fibrillation) and optimal DECAF cutoff value for patients with acute exacerbation of chronic obstructive pulmonary disease (AECOPD), and aimed to provide an early warning score with promising feasibility and prognostic value for AECOPD patients.

Design: Systematic review and meta-analysis.

Participants: Adult patients diagnosed with AECOPD (over 18 years of age).

Primary and secondary outcome measures: Electronic databases and reference lists of the related reports were searched for studies published up to September 2019. Studies were identified that reported the prognostic value of DECAF scores in AECOPD patients. Seventeen studies involving 8329 participants were included in the study.

Results: Seventeen studies involving 8329 participants were included in the study. Quantitative analysis demonstrated that elevated DECAF scores were associated with high mortality risk (WMD = 1.87; 95% CI: 1.19 – 2.56). In the accuracy analysis, DECAF scores showed good prognostic accuracy for both in-hospital and 30-day mortality [AUC: 0.83 (0.79 – 0.86) and 0.79 (0.76 – 0.83), respectively]. The optimal cutoff value for DECAF scores was 3 and the optimal prognostic accuracy was detected with satisfactory sensitivity and specificity. When the prognostic value was compared to that of other scoring systems, DECAF scores showed better prognostic accuracy and stable clinical values than the modified DECAF, CAPS, BAP-65, CURB-65 or APACHE II scores.

Conclusion: The DECAF score is an effective and feasible predictor for short-term mortality. As a specific and easily scored predictor for AECOPD patients, DECAF scores are superior to other early warning scores. An optimal cutoff value of 3 was associated with satisfactory prognostic accuracy, sensitivity, and specificity.

Keywords: Dyspnoea, Eosinopenia, Consolidation, Acidaemia, and atrial Fibrillation (DECAF) score; early warning score; acute exacerbation of chronic obstructive pulmonary disease (AECOPD); meta-analysis; systematic review.

Strengths and limitations of this study

- This study not only evaluated the effectiveness of DECAF score, but also tested the optimal cut-off value of DECAF score in prognosis short-term mortality for AECOPD patients.
- In order to further evaluate the effectiveness of DECAF, this study compared the prognostic effects of DECAF scores with other early warning scores such as APACHE II, BAP-65 and CURB-65.
- This study assessed DECAF scores by quantitative analysis and accuracy analysis.
- The data and analyses were difficult to obtain due to a lack of original studies reporting the value of DECAF scores for predicting long-term mortality and other adverse outcomes in AECOPD patients.
- Although we analyzed the source of heterogeneity through subgroup analysis, heterogeneity in the results should still be considered carefully.

Introduction

Acute exacerbation of chronic obstructive pulmonary disease (AECOPD) is characterized by the deterioration of respiratory symptoms beyond normal daily variations [1]. AECOPD accounts for one in eight hospital admissions [2] and is associated with worsening lung function, health-related quality of life, and mortality risk. The in-hospital mortality of AECOPD patients ranges from 4.4% to 25%. The survivors have a readmission rate of 25% to 55% and 25% to 50% of these patients have a high risk of death within one year [2, 3].

Early warning scores can provide a strong indicator for identifying high-risk populations and assist in clinical management, including Hospital-at-Home or early supported discharge for low-risk groups, and early escalation or appropriate palliation for high-risk groups [4, 5]. The Dyspnea, Eosinopenia, Consolidation, Acidemia, and Atrial Fibrillation (DECAF) score is targeted at predicting the in-hospital mortality of patients with AECOPD [6], which can be easily applied at the bedside using indices routinely available at admission. The score includes five predictors, the strongest of which is stable state dyspnea, measured by the extended Medical Research Council Dyspnea score (eMRCD; Table 1) [7]. However, the prognostic effectiveness and optimal cutoff value of DECAF scores remain unclear.

This systematic review and meta-analysis evaluated the association between DECAF scores and the prognosis of patients with AECOPD, assessed the specific predictive value of DECAF scores, and explored the optimal cutoff value in clinical practice. To further assess the clinical value of DECAF scores, we compared the test to other commonly used predictors of mortality in patients with AECOPD, including the modified DECAF (the Dyspnoea, Eosinopenia, Consolidation, Acidemia, and Frequency of admission in AECOPD in the last year) [8], CAPS (COPD and Asthma Physiology Score)[9], BAP-65 (BUN, Altered mental status, Pulse and age > 65) [10], CURB-65 (Confusion, Urea, Respiratory Rate, Blood pressure, and age > 65) [11], and APACHE II

(Acute Physiology and Chronic Health Evaluation scoring system Ⅱ) scoring systems[12]. This study aimed to provide an effective and feasible prognostic tool for clinical management and improve the clinical course and outcome of AECOPD patients.

Materials and Methods

All methods of this systematic review and meta-analysis analysis followed the PRISMA guidelines [13, 14].

Data Sources and Searches

The review authors searched for medical literature before September 2019. The research was conducted in electronic databases including the Cochrane Library, PubMed, the Excerpt Medica Database (Embase), the Web of Science (WOS), and the reference lists from review articles, irrespective of publication dates, status or language. The search was conducted with the following keywords: *DECAF Score or Dyspnea, Eosinopenia, Consolidation, Acidemia and Atrial Fibrillation Score and AECOPD or Acute Exacerbations of Chronic Obstructive Pulmonary Disease.* Search strategies used in the Cochrane Library, PubMed, Embase, and WOS can be found in the Supplement.

This meta-analysis included studies that met the following criteria:

1. Adult patients diagnosed with AECOPD (over 18 years of age)
2. The studies included the results of DECAF score prognoses in patients with AECOPD. Study information could be extracted into a 2 × 2 contingency table. AECOPD was diagnosed based on the latest reference standard in the original study, such as the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guideline, which was defined as an acute event characterized by worsening of the patient's respiratory symptoms beyond normal day-to-day variations, leading to medication changes.

3. No publication date, status or language restrictions were applied. Clinical original articles were included, whereas secondary studies, conference abstracts, editorials, and animal experiments were excluded.

Study Selection

Two review authors (Q Huang and H Xiong) independently assessed the studies to be included based on the titles, abstracts, and keywords. If a study was found to be relevant to our topic, at least two reviewers further evaluated the full text to determine whether it met the inclusion criteria. In the case of inconsistencies between the reviewers, a third reviewer (J Liu) was consulted. The authors consulted the original authors to further ensure the eligibility of a study, when additional information on the details of the results and methods or allocation concealment was needed. A study diagram was prepared to illustrate the entire literature research process and the selection of the studies (Fig. 1).

Data Extraction and Quality Assessment

The data were independently extracted by two review authors (T Shuai and C Zhang) and the resulting differences were resolved by a third reviewer (C He). The extracted data included the lead author; publication year; the country of origin; the participant characteristics (age, sex, and mortality rate); the optimal cutoff threshold; values for sensitivity, specificity, true-positive, true-negative, false-positive, false-negative; and the area (AUC) under the receiver operating characteristic (ROC) curve. If data were missing, a letter was written to the authors to request the data. If there was no response to the letter after four weeks, an e-mail was sent. If there was no response to the e-mail, estimates were made based on available data and used.

Two review authors (J Liu and J Lu) independently applied the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [15] to evaluate each involved study. The quality and bias of the included studies were assessed using the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) [16] by two independent authors (J Liu and J Lu). In the case of any

inconsistencies, an agreement was reached through discussion between all of the authors. Quality was assessed from two perspectives that included bias risk and applicability concerns. Summary figures show an assessment of the risk of bias (Figs. S1 and S2).

Data Synthesis and Analysis

This study used StataSE15.0 (StataCorp; College Station, TX, USA) to analyze the extracted data. Continuous variables are expressed as weighted mean differences (WMD) with a 95% confidence interval (95% CI). The pooled effect size was calculated by the fixed effect model. When significant heterogeneity ($P < 0.05$, $I^2 \geq 50\%$) was observed, a randomized effect model was applied.

Spearman's correlation coefficient was used to evaluate the threshold of the DECAF score prognostic accuracy. The pooled sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NLR), and diagnostic odds ratio (DOR) were calculated. The accuracy of the diagnostic and prognostic effects was assessed by constructing a summary receiver operating characteristic (SROC) curve. The AUC reflects the accuracy of diagnostic experiments, where 0.5 – 0.7 indicates low accuracy, 0.7 – 0.9 indicates moderate accuracy, and > 0.9 indicates high accuracy.

Heterogeneity was assessed by the Q test (significant heterogeneity was indicated by $P < 0.05$) and the I^2 test (significant heterogeneity was indicated by $I^2 > 50\%$). If substantive heterogeneity ($I^2 > 50\%$) existed, subgroup analysis was performed to analyze the sources of the heterogeneity. Based on the results, forest plots were produced to demonstrate the cumulative effect of the DECAF scores. Deek's funnel plot was used to assess publication bias. The α value was set to 0.05.

Patient and public involvement

This study is a meta-analysis using data from previously published studies, hence patients and the general public were not involved in this study.

Results

Study Selection

A flow chart of the study selection process (Fig. 1) was prepared according to the PRISMA guidelines. After reviewing the title and abstract, 35 articles were screened for full-text review. Among them, 18 articles failed to meet the inclusion criteria. Seventeen studies involving a total of 8329 participants met all of the criteria [6, 8, 17-31]. Among them, Echevarria et al. [17, 19] and Shi et al. [18, 20] each produced two articles from two different studies.

Study Characteristics

As for the AECOPD definition, all studies were defined by the GOLD criteria, which is defined as an acute event characterized by worsening of the patient's respiratory symptoms beyond normal day-to-day variations and leading to medication changes [32]. All identified studies reported the results of DECAF scores for AECOPD prognosis. Among these studies, 15 studies reported the prognostic values of DECAF scores for in-hospital mortality [6, 8, 17, 19, 20, 22-31] and five studies reported 30-day mortality [18, 19, 21, 22, 24]. The optimal cutoff threshold for each study was retrospectively determined based on the ROC curve. For in-hospital mortality, the results of five studies were based on a cutoff value of 4 [8, 19, 26, 28, 30], four studies were based on a cutoff value of 3 [6, 23, 27, 31], three studies were based on a cut-off value of 2 [21, 24, 29], and the other three studies did not report an optimal cutoff threshold [17, 22, 25]. Five studies reported the prognostic value of CURB-65 scores [19, 21, 22, 24, 26], eight reported BAP-65 scores [19, 21, 22, 24-28], five reported APACHE Ⅱ scores [6, 18-20, 31], four reported CAPS scores [6, 19, 20, 31], and three reported the prognostic value of modified DECAF scores [8, 20, 28] for AECOPD patients. A summary of the characteristics of the included studies is shown in Table 2.

Methodological Quality

The methodological quality of the observational studies was rated as high and eight studies fulfilled all of the QUADAS-2 items [6, 19, 23, 24, 27-29, 31]. All of the included studies

met the low-risk criteria of the reference standard items. The overall bias risk was relatively low. However, the included studies yielded different baseline characteristics in the included population, which influenced the patient selection, flow, and timing (Figs. S1 and S2).

The Quantitative Analysis of DECAF scores in AECOPD

Three studies referred to DECAF scores between the survivor group and the non-survivor group. The randomized effect model showed a significant increase in DECAF scores in the non-survivor group compared to the survivor group (WMD = 1.87; 95% CI: 1.19 – 2.56; $P < 0.001$) (Table 3). The results indicate that the elevated DECAF scores were associated with high mortality risk.

As shown in Table 2, four other scoring systems have been proven to indicate poor outcomes of AECOPD. Compared to the survivor group, the results showed that CURB-65 scores, BAP-65 scores, modified DECAF scores, and APACHE Ⅱ scores were increased in the non-survivor group (WMD = 0.69, 95% CI: -0.08 – 1.45, $P = 0.078$; WMD = 0.75, 95% CI: -0.07 – 1.56, $P = 0.071$; WMD = 1.74, 95% CI: 1.36 – 2.13, $P = 0.001$; WMD = 5.24, 95% CI: 4.00 – 6.47, $P < 0.001$, respectively). The results showed that increases in DECAF scores, modified DECAF scores, and APACHE Ⅱ scores were associated with a high risk of mortality in AECOPD, suggesting that DECAF scores have the potential to be a prognostic indicator for patients with AECOPD.

Prognostic Value of DECAF Scores for AECOPD

Seventeen studies reported the prognostic value of DECAF scores. The pooled sensitivity of DECAF scores for predicting mortality was 0.76 [95% CI, 0.70 – 0.81; $I^2 = 45.24\%$, $Q = 29.22$ ($P = 0.02$)] with a specificity of 0.76 [95% CI, 0.68 – 0.83; $I^2 = 96.99\%$, $Q = 531.44$ ($P < 0.001$); Fig. 2]. The PLR and NLR were 3.2 (95% CI, 2.4 – 4.1) and 0.32 (95% CI, 0.27 – 0.37), respectively, and the DOR was 10 (95% CI, 8 – 13). The AUC was 0.82 (95% CI, 0.78 – 0.85; Fig. 3), indicating that the DECAF scores were moderately accurate in predicting mortality in AECOPD patients. Additionally, there was

no significant difference in threshold effect (Spearman's correlation coefficient = 0.467; $P = 0.059$).

Subgroup Analysis

In predicting in-hospital mortality, the pooled sensitivity of the DECAF scores was 0.77 (95% CI, 0.70 – 0.82; $I^2 = 47.24\%$, $P = 0.02$), the specificity was 0.76 (95% CI, 0.67 – 0.84; $I^2 = 96.5\%$, $P < 0.001$], and the AUC was 0.83 (95% CI, 0.79 –0.86). For 30-day mortality, the pooled sensitivity of the DECAF scores was 0.71 (95% CI, 0.53 – 0.84; $I^2 = 84.95\%$, $P < 0.001$), the specificity was 0.75 (95% CI, 0.58 – 0.86; $I^2 = 98.37\%$, $P < 0.001$), and the AUC was 0.79 (95% CI, 0.76 – 0.83).

The subgroup analyses were based on different cutoff values. For a cutoff value of 4, the pooled sensitivity of the DECAF scores was 0.75 (95% CI, 0.69 – 0.81; $I^2 = 0.00\%$, $P = 0.61$), the specificity was 0.80 (95% CI, 0.68 – 0.89; $I^2 = 95.84\%$, $P < 0.001$], and the AUC was 0.76 (95% CI, 0.72 – 0.80). For a cut-off value of 3, the pooled sensitivity was 0.77 (95% CI, 0.70 – 0.82; $I^2 = 0.00\%$, $P = 0.52$), the specificity was 0.76 (95% CI, 0.67 – 0.84; $I^2 = 29.09\%$, $P = 0.24$], and the AUC was 0.83 (95% CI, 0.79 – 0.86). For a cutoff value of 2, the pooled sensitivity was 0.84 (95% CI, 0.68 – 0.93; $I^2 = 0.00\%$, $P = 0.52$), the specificity was 0.53 (95% CI, 0.50 – 0.56; $I^2 = 0.00\%$, $P = 0.61$], and the AUC was 0.77 (95% CI, 0.73 – 0.80).

Other Early Warning Scores for Patients with AECOPD

In predicting the in-hospital mortality of patients with AECOPD, the pooled results showed that the sensitivity, specificity, and AUC of the CURB-65 scores were 0.46, 0.92, and 0.73, respectively. The sensitivity, specificity, and AUC of the BAP-65 scores were 0.70, 0.50, and 0.64, respectively. The sensitivity, specificity, and AUC of the APACHE Ⅱ scores were 0.70, 0.65, and 0.72, respectively. The sensitivity, specificity, and AUC of CAPS scores were 0.77, 0.62, and 0.75, respectively, and the sensitivity, specificity, and AUC of the m-DECAF scores were 0.84, 0.62, and 0.84, respectively.

Discussion

In stable COPD, prognostic indicators have been thoroughly investigated and tools to predict mortality risk, such as the BODE Score [32], have been well established. However, prognostic studies in patients with exacerbation requiring hospitalization are limited and the predictors of mortality between stable disease periods and AECOPD periods seem to have little in common [33]. In addition, the risk of mortality in AECOPD patients is much higher than in patients with stable COPD. Thus, there is an urgent need for effective reliable clinical tools that can be used to inform clinicians and patients of the risk of death during exacerbation.

The current study conducted a systematic review and meta-analysis to characterize and evaluate DECAF scores predicting mortality in patients with AECOPD. Six potential scoring systems were evaluated by comparing survivor and non-survivor scores and prognostic accuracy. Quantitative analysis demonstrated that elevated DECAF scores were significantly associated with high mortality risk. Among other potential scoring systems, only the modified DECAF and APACHE Ⅱ showed similar effects in predicting mortality for AECOPD patients. In the accuracy analysis, DECAF scores showed a better prognostic accuracy for both in-hospital and 30-day mortality. For the optimal cutoff DECAF values, the results showed that as the cutoff value increased, the sensitivity decreased and the specificity escalated. When the cutoff value was 3, the optimal prognostic accuracy was detected with satisfactory sensitivity and specificity. When the prognostic value was compared with other scoring systems, DECAF scores showed better prognostic accuracy and stable clinical value in predicting the in-hospital mortality and 30-day mortality of patients with AECOPD.

The DECAF scores increased significantly in the non-survivor group. This suggests that elevated DECAF scores have the potential to identify a high-risk population of AECOPD patients. The modified DECAF and APACHE Ⅱ scores had a similar relationship, which indicates that scoring systems have potential to aid clinical decisions

in risk stratification. However, the CURB-65 and BAP-65 scores did not show statistical differences between the survivor and non-survivor groups. Although studies have shown that CURB-65 and BAP-65 can be effective tools for predicting mortality [34], based on the results of this current study, we speculate that the potential prognostic value of CURB-65 and BAP-65 is relatively low.

The DECAF score is an effective predictor of mortality and can be easily scored at the bedside using indices routinely available at admission [6]. In clinical practice, an AUC above 0.8 is considered to be a very reliable test [35]. The results showed that the AUC of the DECAF scores was 0.83 for predicting in-hospital mortality and 0.79 for short-term mortality (30-day). This indicates that the DECAF test can be utilized as a promising prognosis tool with satisfactory sensitivity and specificity for AECOPD patients.

Mortality rates vary between clinical settings and cohorts. In this study, the mortality rate of patients in the included studies ranged from 2.38% to 33.93%. This largely reflects differences in baseline characteristics, especially in the proportion of patients admitted from institutional care and with coexisting pneumonia [11, 19]. In addition, this also partly leads to choosing different optimal cutoff values. To illustrate the relationship between the cutoff values for predicting mortality, subgroup analyses were performed. For cutoff values from 2 to 4, the sensitivity decreased from 0.84 to 0.75 and the specificity increased from 0.53 to 0.80. With an increase in the cutoff value, specificity increased significantly. Under the premise of ensuring sensitivity, improving specificity can effectively reduce the number of false positives and improve the clinical application value of an early warning score. When the cutoff value was 3, the optimal prognostic accuracy (AUC = 0.83) was detected with satisfactory sensitivity and specificity.

The CURB-65 and BAP-65 tests can also be easily scored on admission [36]. However, according to the results of this study, the CURB-65 and BAP-65 scores had low prognostic value for predicting in-hospital and 30-day mortality, which were consistent

with the lack of statistical difference in CURB-65 and BAP-65 scores between survivors and non-survivors.

APACHE II uses point scores based on the initial values of 12 routine physiological measurements, age, and previous health status to provide a general measure of disease severity [37]. APACHE II is not a specific predictor for AECOPD but is still commonly used in clinical practice to predict mortality in AECOPD patients [38]. Based on our results, APACHE II scores showed no superiority to DECAF scores in prognostic accuracy, sensitivity or specificity. In addition, it contains cumbersome test items, thus increasing the workload of clinicians in clinical practice. For AECOPD patients, the APACHE II test may not be the preferred early warning scoring system.

As for the modified DECAF, Zidan et al. [8] attempted to replace the atrial fibrillation item in the DECAF test with admission frequency for AECOPD during the last year and named the revision the modified DECAF. They concluded that the modified DECAF test was more sensitive and specific in predicting in-hospital mortality during acute exacerbation of COPD than the DECAF test. However, there was no significant difference between the two scores [8], which was consistent with the results of this current study. In addition, only 3 studies reported the predictive value of modified DECAF test for in-hospital mortality in AECOPD patients, and no study reported the effectiveness of the test in terms of 30-day mortality. Therefore, more evidence is needed to evaluate the prognostic value of modified DECAF scores and further compare the clinical value between DECAF scores and modified DECAF scores.

Examination of early warning scores can contribute to clinical management, early risk-stratification, and the prevention of poor outcomes, as well as monitoring during treatment [39]. Clinicians are constantly seeking predictors of mortality for patients with AECOPD. As a promising predictor, DECAF scores can be used in a variety of hospital settings to accurately stratify mortality risk. As a specific and easily scored predictor for AECOPD patients, DECAF is superior to other early warning scores in predicting short-

term mortality. Although we detected an optimal cutoff value of 3 for DECAF score prognostic accuracy, further studies are still needed for validation.

Compared to the meta-analyses of interventions, including randomized controlled trials, those including diagnostic studies have more publication bias [40]. Publication bias exists in studies that report prognostic value. Excluding studies that do not have sufficient data can lead to publication and reporting bias. Therefore, the prognostic value of DECAF may be overestimated. As for the significant degree of heterogeneity, we conducted a subgroup analysis to explore the source of the heterogeneity. The subgroup analysis revealed that the heterogeneity was mainly derived from the choice of cutoff value. When the cut-off value was 2, 3 or 4, the heterogeneity of sensitivity decreased to 0. However, the heterogeneity of specificity was still substantive when the cutoff value was 4. This largely reflect differences in the baseline characteristics of the involved population.

This meta-analysis had some limitations. First, the data and analyses were difficult to obtain due to a lack of original studies reporting the value of DECAF scores for predicting long-term mortality and other adverse outcomes in AECOPD patients. Further studies are needed for validation. Second, it was difficult to obtain raw data for each of the included studies, which limited us to determining the optimal DECAF cutoff point for predicting AECOPD. Finally, although we analyzed the source of heterogeneity through subgroup analysis, heterogeneity in the results should still be considered carefully.

Conclusion

In conclusion, the results of this systematic review and meta-analysis indicated that the DECAF score was an effective and feasible predictor of short-term mortality in patients with AECOPD. As a specific and easily scored predictor for AECOPD patients, DECAF scores are superior to other early warning scores. The optimal cutoff value was 3, with satisfactory prognostic accuracy, sensitivity, and specificity. Further clinical practice experience is needed for validation.

List of abbreviations

AECOPD: acute exacerbation of chronic obstructive pulmonary disease; DECAF: Dyspnoea, Eosinopenia, Consolidation, Acidaemia, and atrial Fibrillation score; the modified DECAF: the Dyspnoea, Eosinopenia, Consolidation, Acidaemia and Frequency of admission in AECOPD in the last year; CAPS: COPD and Asthma Physiology Score; BAP-65: BUN, Altered mental status, Pulse and Age > 65; CURB-65: Confusion, Urea, Respiratory Rate, Blood pressure, Age > 65; APACHE II: acute physiology and chronic health evaluation scoring system Ⅱ scores; QUADAS-2: the Quality Assessment of Diagnostic Accuracy Studies-2; WOS: web of science; WMD: weighted mean difference; AUC: the area under the receiver operating characteristic curve; PRISMA: the preferred reporting items for systematic reviews and meta-analyses; PLR: positive likelihood ratio; NLR: negative likelihood ratio; DOR: diagnostic odds ratio; SROC: summary receiver operating characteristic; CIs: confidence intervals;

Additional Information

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Competing interests

The authors each individually and collectively declare there are no competing interests.

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Availability of data and materials

All data generated or analyzed during this study are included in this published article and its supplementary information files.

References

1. Rodriguez-Roisin R. Toward a consensus definition for COPD exacerbations. Chest. 2000;117(5 Suppl 2):398s-401s.

2. Johannesdottir SA, Christiansen CF, Johansen MB, et al. Hospitalization with acute exacerbation of chronic obstructive pulmonary disease and associated health resource utilization: a population-based Danish cohort study. Journal of medical economics 2013;16:897-906.

3. de Miguel-Diez J, Jimenez-Garcia R, Hernandez-Barrera V, et al. Trends in hospital admissions for acute exacerbation of COPD in Spain from 2006 to 2010. Respiratory medicine 2013;107:717-23.

4. Wildman MJ, Sanderson C, Groves J, et al. Predicting mortality for patients with exacerbations of COPD and Asthma in the COPD and Asthma Outcome Study (CAOS). QJM : monthly journal of the Association of Physicians 2009;102:389-99.

5. Doll H, Miravitlles M. Health-related QOL in acute exacerbations of chronic bronchitis and chronic obstructive pulmonary disease: a review of the literature. PharmacoEconomics 2005;23:345-63.

6. Steer J, Gibson J, Bourke SC. The DECAF Score: predicting hospital mortality in exacerbations of chronic obstructive pulmonary disease. Thorax 2012;67:970-6.

7. Steer J, Norman EM, Afolabi OA, et al. Dyspnoea severity and pneumonia as predictors of in-hospital mortality and early readmission in acute exacerbations of COPD. Thorax 2012;67:117-21.

8. Zidan MH, Rabie AK, Megahed MM, et al. The usefulness of the DECAF score in predicting hospital mortality in Acute exacerbations of chronic obstructive pulmonary disease. Egyptian Journal of Chest Diseases and Tuberculosis 2015;64:75-80.

9. Wildman MJ, Harrison DA, Welch CA, et al. A new measure of acute physiological derangement for patients with exacerbations of obstructive airways disease: the COPD and Asthma Physiology Score. Respiratory medicine 2007;101:1994-2002.

10. Shorr AF, Sun X, Johannes RS, et al. Validation of a novel risk score for severity of illness in acute exacerbations of COPD. Chest 2011;140:1177-83.

11. Lim WS, van der Eerden MM, Laing R, et al. Defining community acquired pneumonia severity on presentation to hospital: an international derivation and validation study. Thorax 2003;58:377-82.

12. Jacobs S, Chang RW, Lee B. One year's experience with the APACHE II severity of disease classification system in a general intensive care unit. Anaesthesia 1987;42:738-44.

13. Wang X, Chen Y, Yao L, et al. Reporting of declarations and conflicts of interest in WHO guidelines can be further improved. Journal of clinical epidemiology 2018;98:1-8.

14. Ge L, Tian JH, Li YN, et al. Association between prospective registration and overall reporting and methodological quality of systematic reviews: a meta-epidemiological study. Journal of clinical epidemiology 2018;93:45-55.

15. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. Journal of clinical epidemiology 2009;62:e1-34.

16. Whiting PF, Rutjes AW, Westwood ME, et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. Annals of internal medicine 2011;155:529-36.

17. Echevarria C, Steer J, Bourke SC. Comparison of early warning scores in patients with COPD exacerbation: DECAF and NEWS score. Thorax 2019;74:941-6.

18. Shi QF, Sheng Y, Zhu N, et al. The v-DECAF score can predict 90-day all-cause mortality in patients with COPD exacerbation requiring invasive mechanical ventilation. The clinical respiratory journal 2019.

19. Echevarria C, Steer J, Heslop-Marshall K, et al. Validation of the DECAF score to predict hospital mortality in acute exacerbations of COPD. Thorax 2016;71:133-40.

20. Sweeney D, Pham J, Reekie C, et al. ACUTE EXACERBATIONS OF COPD: 'DECAF' VALIDATION AND QUALITY-CARE ASSESSMENT. Respirology 2019;24:133.

21. Bastidas AR, Hincapie Diaz G, Mantilla Cardozo B, et al. Validity CURB 65, BAP 65, DECAF for predicting outcomes in exacerbation of COPD. American Journal of Respiratory and Critical Care Medicine 2018;197.

22. Shafuddin E, Chang CL, Hancox RJ. Comparing severity scores in exacerbations of chronic obstructive pulmonary disease. The clinical respiratory journal 2018;12:2668-75.

23. Bisquera RR, Cruz BOD. Prognostic utility of the DECAF score to predict in-hospital mortality among patients with acute exacerbation of chronic obstructive pulmonary disease admitted at Chinese general hospital. Respirology 2018;23:128-9.

24. Mantilla BM, Ramírez CA, Valbuena S, et al. Saturación de oxígeno/fracción inspirada de oxígeno como predictor de mortalidad en pacientes con exacerbación de EPOC atendidos en el Hospital Militar Central. Acta Medica Colombiana 2017;42:215-23.

25. Sangwan V, Chaudhry D, Malik R. Dyspnea, Eosinopenia, Consolidation, Acidemia and Atrial Fibrillation Score and BAP-65 Score, Tools for Prediction of Mortality in

Acute Exacerbations of Chronic Obstructive Pulmonary Disease: A Comparative Pilot Study. Indian journal of critical care medicine : peer-reviewed, official publication of Indian Society of Critical Care Medicine 2017;21:671-7.

26. Soe AK, Avdeev SN, Nuralieva GS, et al. Predictors of poor outcomes in acute exacerbations of chronic obstructive pulmonary disease. Pul'monologiya 2018;28:446-52.

27. Parras AMV, Bautista CL, Chica GP, et al. Evaluation of DECAF, CURB-65 and BAP-65 scales as predictor of mortality risk in acute exacerbation of COPD in a retrospective cohort. European Respiratory Journal 2017;50.

28. Yousif M, El Wahsh RA. Predicting in-hospital mortality in acute exacerbation of COPD: Is there a golden score? Egyptian Journal of Chest Diseases and Tuberculosis 2016;65:579-84.

29. Collier L, David T, Craig C, et al. PRACTICAL USE OF THE DECAF SCORE: CAN WE IMPROVE OUTCOMES IN ACUTE EXACERBATION OF COPD ADMISSIONS? Thorax 2015;70:A98-A.

30. Rabbani B, Brammer P. CAN THE DECAF SCORE BE USED TO GUIDE PROGNOSIS AFTER AN ACUTE ADMISSION FOR COPD EXACERBATION? Thorax 2014;69:A139-A40.

31. Nafae R, Embarak S, Gad DM. Value of the DECAF score in predicting hospital mortality in patients with acute exacerbation of chronic obstructive pulmonary disease admitted to Zagazig University Hospitals, Egypt. Egyptian Journal of Chest Diseases and Tuberculosis 2015;64:35-40.

32. Celli BR, Cote CG, Marin JM, et al. The body-mass index, airflow obstruction, dyspnea, and exercise capacity index in chronic obstructive pulmonary disease. The New England journal of medicine 2004;350:1005-12.

33. Steer J, Gibson GJ, Bourke SC. Predicting outcomes following hospitalization for acute exacerbations of COPD. QJM : monthly journal of the Association of Physicians 2010;103:817-29.

34. Shorr AF, Sun X, Johannes RS, et al. Predicting the need for mechanical ventilation in acute exacerbations of chronic obstructive pulmonary disease: comparing the CURB-65 and BAP-65 scores. Journal of critical care 2012;27:564-70.

35. Memon MA, Faryal S, Brohi N, et al. Role of the DECAF Score in Predicting In-hospital Mortality in Acute Exacerbation of Chronic Obstructive Pulmonary Disease. Cureus 2019;11:e4826.

36. Patil SP, Krishnan JA, Lechtzin N, et al. In-hospital mortality following acute exacerbations of chronic obstructive pulmonary disease. Archives of internal medicine 2003;163:1180-6.

37. Mach K. [Staphylococcus epidermidis infection. Results of three groups evaluated according to APACHE II--severity of disease classification system--with reference to risk, mortality and prognosis]. Wiener klinische Wochenschrift 1992;104:540-2.

38. Akhter S, Warraich UA, Ghazal S, et al. Assessment and comparison of APACHE II (Acute Physiology and Chronic Health Evaluation), SOFA (Sequential Organ Failure Assessment) score and CURB 65 (Confusion; Urea; Respiratory Rate; Blood Pressure), for prediction of inpatient mortality in Acute Exacerbation of Chronic Obstructive Pulmonary Disease. JPMA The Journal of the Pakistan Medical Association 2019;69:211-5.

39. Costello RW, Cushen B. A risk stratification tool for exacerbations of COPD: time to switch to DECAF. Thorax 2016;71:489-90.

40. Irwig L, Macaskill P, Glasziou P, et al. Meta-analytic methods for diagnostic test accuracy. Journal of clinical epidemiology 1995;48:119-30.

Authors' contributions

The authors Jian Liu, Qiangru Huang, Chengying He, Meng Zhang, Chuchu Zhang, Huaiyu Xiong and Tiankui Shuai participated in the design of the project, conducted the literature review, and participated in the analysis. The authors Qiangru Huang, Yalei

Wang wrote this paper. The authors Lei Zhu and Jiaju Lu were responsible for the statistical analysis and participated in data interpretation. The author Jian Liu was the principal investigator for the project. All authors approved the final version of the article.

Table 1. DECAF score

Variables	Score
Dyspnea	1
eMRCD 5a (too breathless to leave the house unassisted but independent in washing and/or dressing)	2
eMRCD 5b (too breathless to leave the house unassisted and requires help with washing and dressing)	1
Eosinopenia (eosinophils <0.05×109/L)	1
Consolidation	1
Moderate or severe acidemia (pH <7.3)	1
Atrial fibrillation (including history of paroxysmal atrial fibrillation)	1
Maximum DECAF score	6

DECAF: dyspnea, eosinopenia, consolidation, acidemia, and atrial fibrillation; eMRCD, extended Medical Research Council dyspnea score

Table 2. Characteristics of included studies

Author/Year	Study Inception (Year)	Country	Study design	Sample size	Male	Age (years)	Mortality (%)	Measured time	Cut-off value	Early warning scores
Echevarria 2019	NA	UK	PC	2645	1217	73.10	8.62	in-hospital	NA	DECAF
Shi 2019	2016.1-2017.12	China	PC	112	73	77.57	33.93	30d	3	DECAF
Bastidas 2018	NA	Colombia	PC	462	229	79.00	2.38	30d	2	DECAF, BAP-65 and CURB-65
Shafuddin 2018	2006.7-2007.7 2012.8-2013.7	New Zealand	PC	423	190	71.00	4.49 7.33	in-hospital 30d	NA	DECAF, CURB-65, CRB-65, and BAP-65
Bisquera 2018	NA	Philippines	PC	77	68	72.50	6.49	in-hospital	3	DECAF
Mantilla 2017	2014.2-2017.1	Colombia	PC	462	233	79.00	2.60 5.84	in-hospital 30d	2	DECAF, BAP-65 and CURB-65
Sangwan 2017	NA	India	PC	50	43	61.20	18.00	in-hospital	NA	DECAF and BAP-65
Xu 2017	2014.1-2016.1	China	RC	302	150	75.50	7.95	28d	4	DECAF, BAP-65 and CURB-65
Parras 2017	NA	Spain	RC	164	153	76.14	20.12	in-hospital	3	DECAF

Shi 2016	2014.1-2016.6	China	RC	186	108	66.20	15.59	in-hospital	3	DECAF, m-DECAF, CAPS and APACHE Ⅱ
Yousif 2016	2014.1-2015.9	Egypt	PC	264	176	63.61	7.58	in-hospital	4	DECAF, m-DECAF and BAP-65
Echevarria 2016	2012.1-2014.5	UK	PC	1725	788	73.10	7.65 28.35	in-hospital 30d	4	DECAF, CAPS, APACHE Ⅱ, CURB-65 and BAP-65
Zidan 2015	NA	Egypt	PC	100	58	46.46	11.00	in-hospital	4	DECAF and m-DECAF
Collier 2015	2014.12-2015.3	UK	PC	78	47	72.70	15.38	in-hospital	2	DECAF
Rabbani 2014	2012.12-2013.1	UK	RC	159	92	72.14	9.43	30d	4	DECAF
Nafae 2014	2010.10-2013.4	Egypt	PC	200	102	68.50	12.50	in-hospital	3	DECAF, CAPS and APACHE Ⅱ
Steer 2012	2008.12-2010.6	UK	PC	920	424	73.10	10.43	in-hospital	3	DECAF, CAPS and APACHE Ⅱ

Abbreviations: PC, prospective cohort; RC, retrospective cohort; NA, not available.

Table 3. The Quantitative Analysis of scores in AECOPD mortality

Variables	Studies, No.	Patients, No.	WMD	95%CI	P value
DECAF	3	600	1.87	1.19-2.56	<0.001
CURB-65	2	414	0.69	-1.53	0.078
BAP-65	2	414	0.75	-1.63	0.071
Modified DECAF	2	298	1.74	1.36-2.13	0.001
APACHE II	2	298	5.24	4.00-6.47	<0.001

Abbreviations: WMD, weighted mean difference; 95% CI, 95% confidence interval

Table 4. Subgroup analysis of the prognostic value of DECAF based on different variables.

Variables	Studies, No. (Patients, No.)	Sensitivity (95%CI)	Specificity (95%CI)	PLR (95%CI)	NLR (95%CI)	DOR (95%CI)	AUC (95%CI)
Overall	17(8329)	0.76(0.70-0.81)	0.76(0.68-0.83)	3.20(2.40-4.10)	0.32(0.27-0.37)	10(8-13)	0.82(0.78-0.85)
in-hospital	15(7655)	0.77(0.70-0.82)	0.76(0.67-0.84)	3.20(2.40-4.40)	0.31(0.25-0.37)	11(8-15)	0.83(0.79-0.86)
30d	5(3084)	0.71(0.53-0.84)	0.75(0.58-0.86)	2.80(2.00-4.10)	0.39(0.27-0.56)	7(6-9)	0.79(0.76-0.83)
cut-off= 4	5(2550)	0.75(0.69-0.81)	0.80(0.68-0.89)	3.80(2.20-6.60)	0.31(0.23-0.41)	12(6-26)	0.76(0.72-0.80)
cut-off= 3	4(1361)	0.77(0.70-0.82)	0.76(0.67-0.84)	3.20(2.40-4.40)	0.31(0.25-0.37)	11(8-15)	0.83(0.79-0.86)
cut-off= 2	3(1002)	0.84(0.68-0.93)	0.53(0.50-0.56)	1.80(1.50-2.10)	0.31(0.15-0.64)	6(2-14)	0.77(0.73-0.80)

Abbreviations: CI, confidence interval; PLR, positive likelihood ratio; NLR, negative likelihood ratio; DOR, diagnostic odds ratio; AUC, area under the receiver operating characteristic curve.

Table 5. The prognostic value of early warning scores for predicting in-hospital mortality in patients with AECOPD.

Variables	Studies, No. (Patients, No.)	Sensitivity (95%CI)	Specificity (95%CI)	PLR (95%CI)	NLR (95%CI)	DOR (95%CI)	AUC (95%CI)
DECAF	15(7655)	0.77(0.70-0.82)	0.76(0.67-0.84)	3.20(2.40-4.40)	0.31(0.25-0.37)	11(8-15)	0.83(0.79-0.86)
CURB-65	4(2912)	0.46(0.21-0.72)	0.92(0.63-0.99)	6.00(1.70-21.60)	0.59(0.40-0.86)	10(4-28)	0.73(0.69-0.77)
BAP-65	6(3226)	0.70(0.46-0.87)	0.50(0.31-0.70)	1.40(0.90-2.20)	0.59(0.29-1.20)	2(1-7)	0.64(0.59-0.68)
APACHE II	4(3031)	0.70(0.63-0.76)	0.65(0.58-0.72)	2.00(1.60-2.50)	0.46(0.37-0.57)	4(3-7)	0.72(0.68-0.76)
CAPS	4(3031)	0.77(0.60-0.88)	0.62(0.46-0.76)	2.00(1.50-2.70)	0.37(0.24-0.58)	5(3-9)	0.75(0.71-0.79)
Modified DECAF	3(666)	0.84(0.71-0.91)	0.62(0.46-0.75)	2.20(1.40-3.40)	0.27(0.13-0.55)	8(3-25)	0.84(0.81-0.87)

Abbreviations: CI, confidence interval; PLR, positive likelihood ratio; NLR, negative likelihood ratio; DOR, diagnostic odds ratio; AUC, area under the receiver operating characteristic curve.

Table 6. The prognostic value of early warning scores for predicting 30-day mortality in patients with AECOPD.

Variables	Studies, No. (Patients, No.)	Sensitivity (95%CI)	Specificity (95%CI)	PLR (95%CI)	NLR (95%CI)	DOR (95%CI)	AUC (95%CI)
DECAF	5(3084)	0.71(0.53-0.84)	0.75(0.58-0.86)	2.80(2.00-4.10)	0.39(0.27-0.56)	7(6-9)	0.79(0.76-0.83)
CURB-65	4(3072)	0.52(0.48-0.56)	0.85(0.56-0.96)	3.50(1.00-12.50)	0.56(0.45-0.71)	6(1-28)	0.53(0.49-0.57)
BAP-65	5(3236)	0.61(0.34-0.82)	0.57(0.23-0.85)	1.40(0.80-2.40)	0.70(0.46-1.06)	2(1-5)	0.62(0.57-0.66)
APACHE Ⅱ	2(1837)	0.68(0.52-0.80)	0.73(0.66-0.79)	2.50(1.60-3.90)	0.44(0.26-0.74)	6(2-15)	0.77(0.73-0.80)

Abbreviations: CI, confidence interval; PLR, positive likelihood ratio; NLR, negative likelihood ratio; DOR, diagnostic odds ratio; AUC, area under the receiver operating characteristic curve.

Figure Legends

Figure 1 : PRISMA (preferred reporting items for systematic reviews and meta-analyses) flow diagram and exclusion criteria

Figure 2: Forest plot of sensitivity and specificity of DECAF for the prediction of mortality in AECOPD.

Figure 3: Summary receiver operating characteristics curve for evaluating prognostic value of mortality of DECAF in AECOPD.

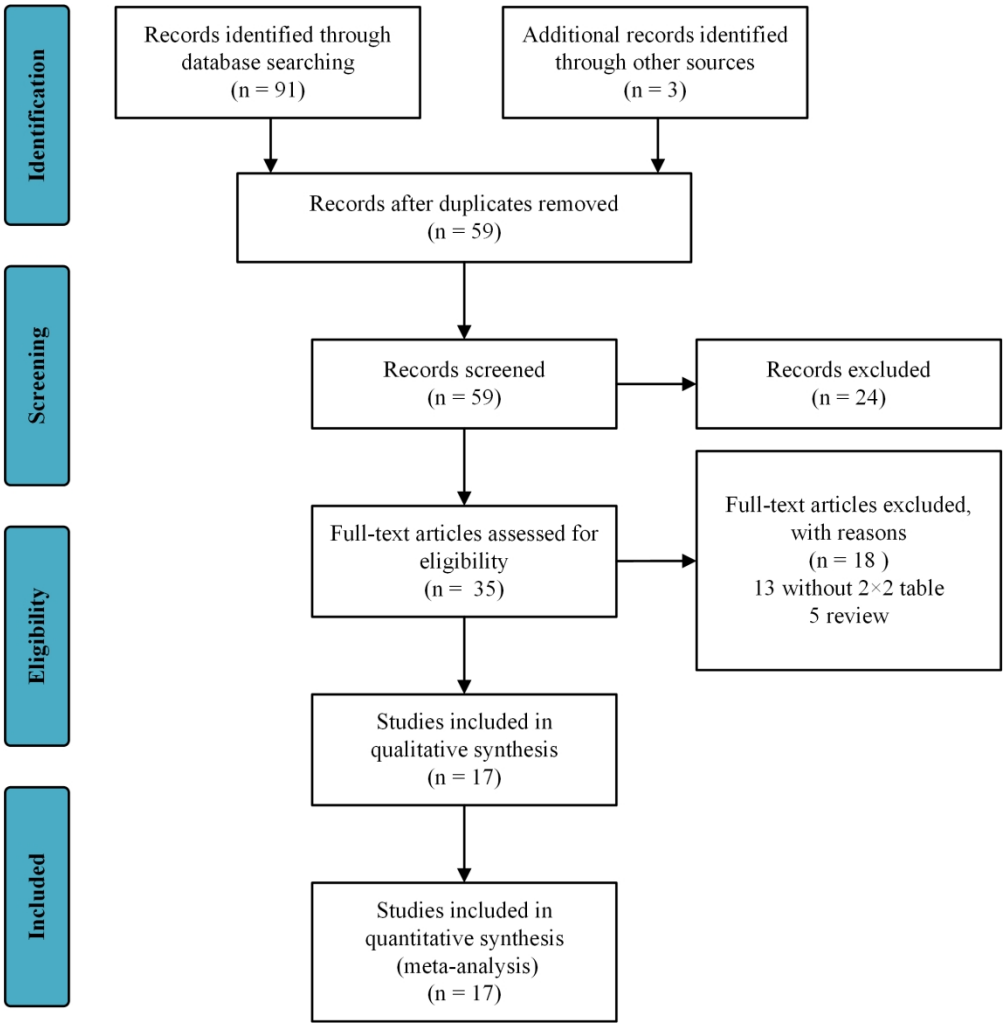

Figure 1 : PRISMA (preferred reporting items for systematic reviews and meta-analyses) flow diagram and exclusion criteria

183x186mm (300 x 300 DPI)

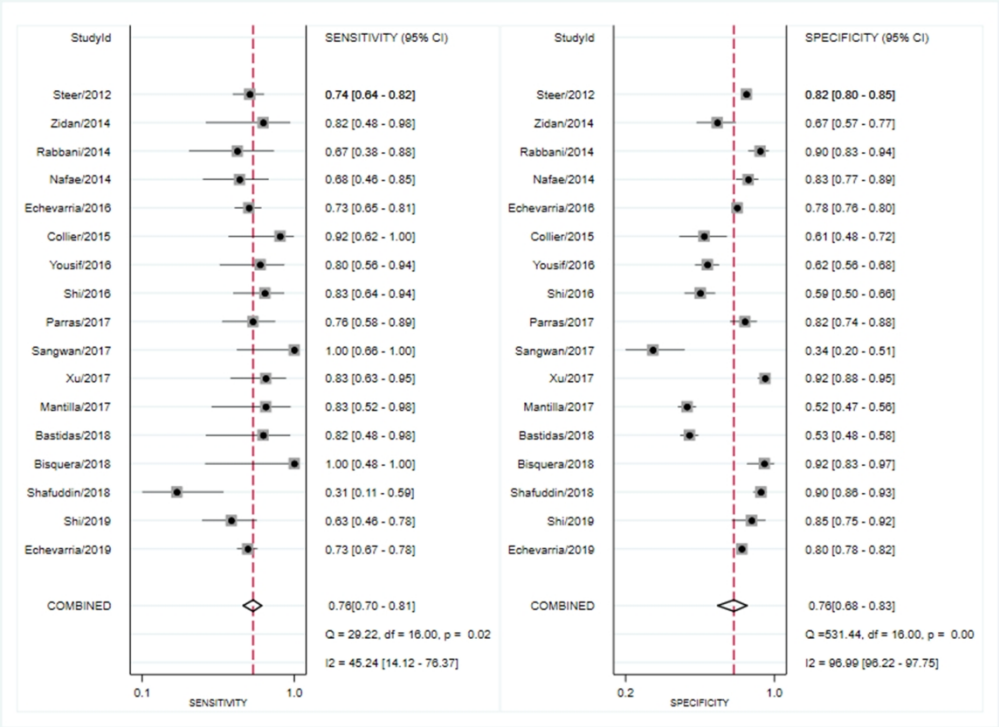

Figure 2: Forest plot of sensitivity and specificity of DECAF for the prediction of mortality in AECOPD.

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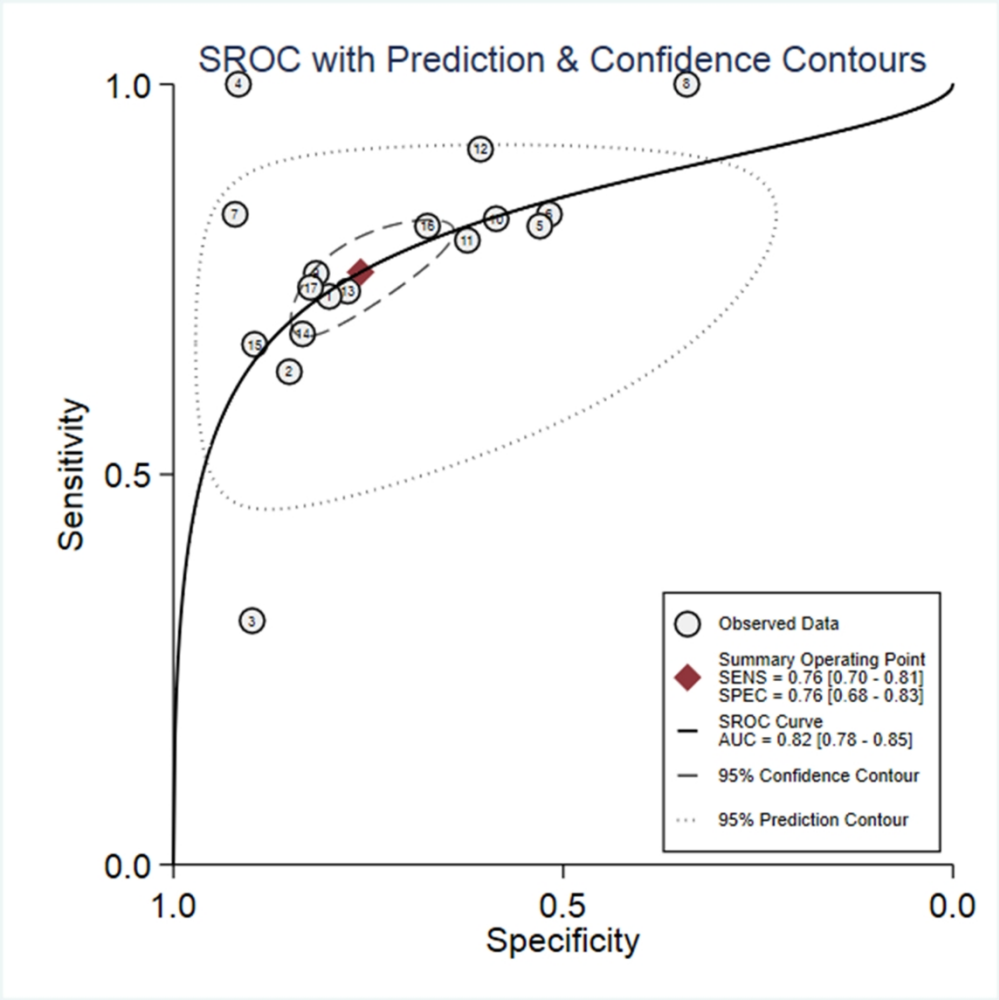

Figure 3: Summary receiver operating characteristics curve for evaluating prognostic value of mortality of DECAF in AECOPD.

215x215mm (300 x 300 DPI)

Supplementary

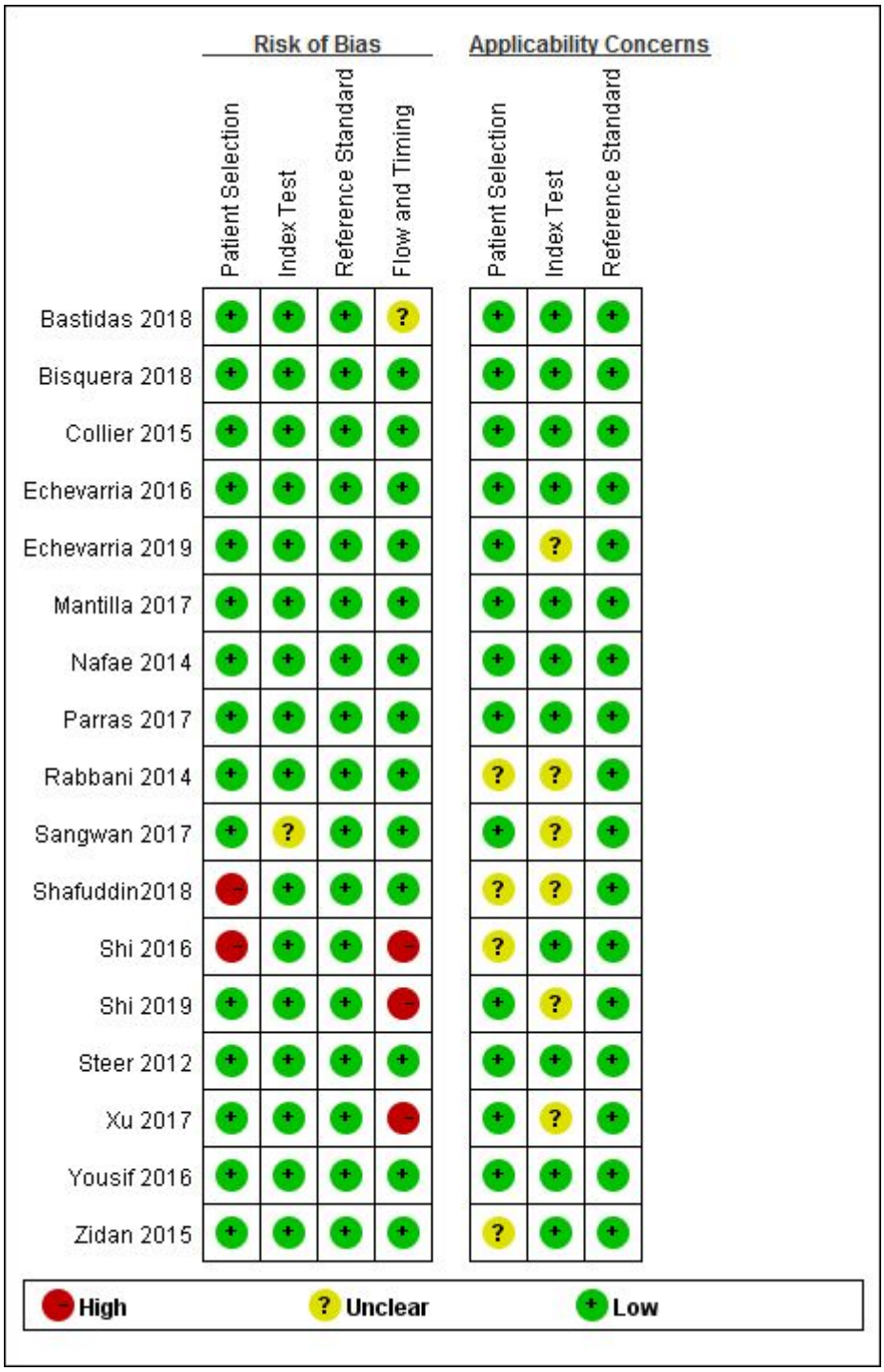

Figure S1: The quality evaluation and risk of bias in included studies.

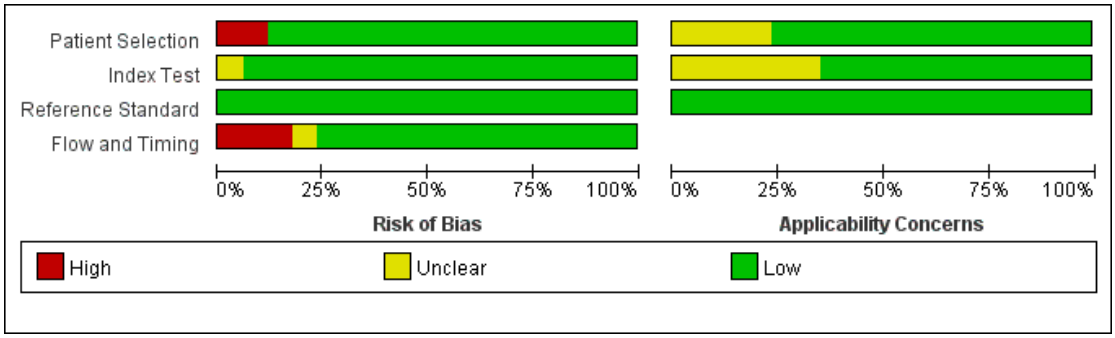

Figure S2: Methodological quality graph in included studies.

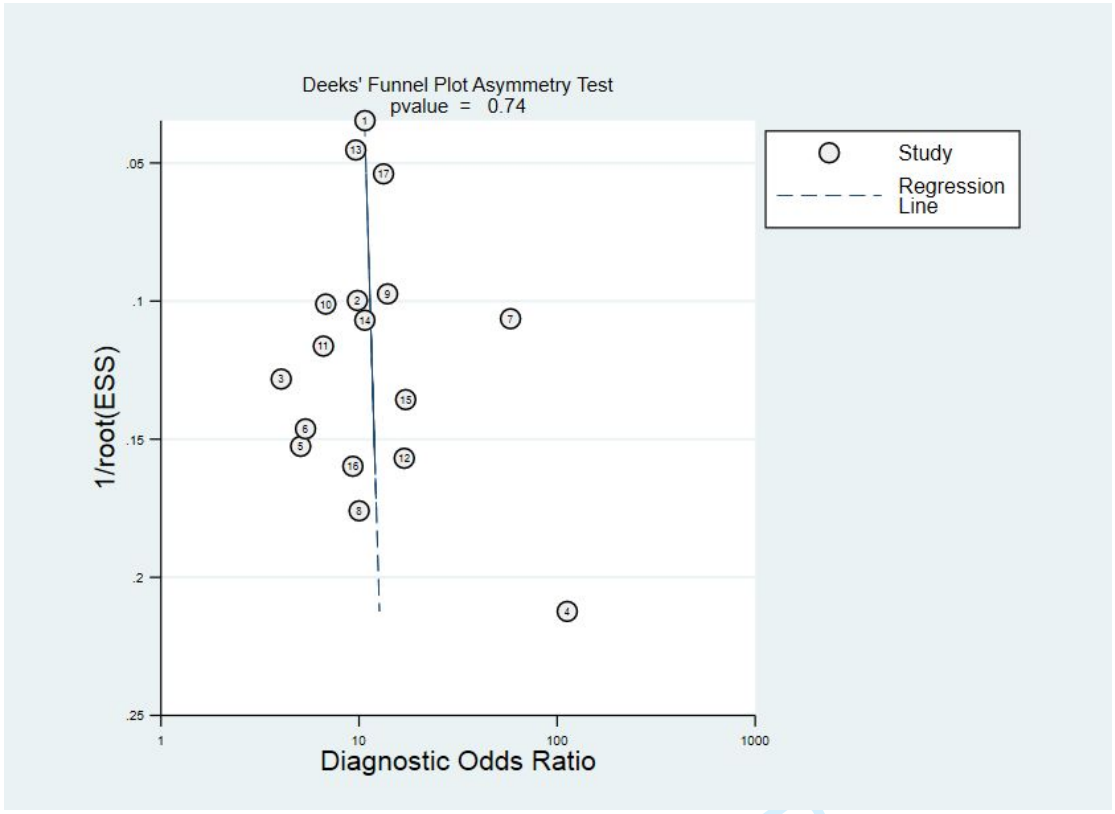

Figure S3: Deek's funnel plot asymmetry test for publication bias of studies evaluating the value of DECAF for the prognosis of AECOPD

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Search Strategies

1. Pubmed

Search ((("Pulmonary Disease, Chronic Obstructive"[Mesh]) OR ((((((((((((COPD[Title/Abstract]) OR Chronic Obstructive Pulmonary Disease[Title/Abstract]) OR Chronic Airflow Obstructions[Title/Abstract]) OR Chronic Airflow Obstruction[Title/Abstract]) OR COAD[Title/Abstract]) OR Chronic Obstructive Airway Disease[Title/Abstract]) OR Airflow Obstruction, Chronic[Title/Abstract]) OR Airflow Obstructions, Chronic[Title/Abstract]) OR

Chronic Obstructive Lung Disease[Title/Abstract]) OR Chronic Obstructive Lung Disease[Title/Abstract]) OR airways obstruction[Title/Abstract]) OR obstructive lung disease[Title/Abstract]) OR emphysema[Title/Abstract]) OR bronchitis[Title/Abstract]))) AND ((DECAF score[Title/Abstract]) OR DECAF[Title/Abstract])

2. The Cochrane Library

#1 MeSH descriptor: [undefined] explode all trees
#2 (Chronic Obstructive Lung Disease):ti,ab,kw
#3 (Chronic Obstructive Pulmonary Disease):ti,ab,kw
#4 (COPD):ti,ab,kw
#5 (COAD):ti,ab,kw
#6 (Chronic Obstructive Airway Disease):ti,ab,kw
#7 (Airflow Obstruction, Chronic):ti,ab,kw
#8 (Chronic Airflow Obstruction):ti,ab,kw
#9 (Airflow Obstructions, Chronic):ti,ab,kw
#10 (Chronic Airflow Obstructions):ti,ab,kw
#11 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10
#12 MeSH descriptor: [Lung Diseases, Obstructive] explode all trees
#13 (Pulmonary Disease, Obstructive):ti,ab,kw
#14 (Obstructive Pulmonary Diseases):ti,ab,kw
#15 (Obstructive Lung Diseases):ti,ab,kw
#16 (Obstructive Lung Disease):ti,ab,kw
#17 (Lung Disease, Obstructive):ti,ab,kw
#18 (Pulmonary Diseases, Obstructive):ti,ab,kw
#19 (Obstructive Pulmonary Disease):ti,ab,kw
#20 #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19
#21 MeSH descriptor: [Pulmonary Emphysema] explode all trees
#22 (Emphysema, Centrilobular):ti,ab,kw
#23 (Centrilobular Emphysema):ti,ab,kw
#24 (Emphysemas, Pulmonary):ti,ab,kw
#25 (Emphysema, Pulmonary):ti,ab,kw
#26 (Pulmonary Emphysemas):ti,ab,kw
#27 (Emphysema, Panlobular):ti,ab,kw
#28 (Panlobular Emphysema):ti,ab,kw
#29 (Focal Emphysema):ti,ab,kw
#30 (Emphysema, Focal):ti,ab,kw
#31 #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30
#32 MeSH descriptor: [Bronchitis, Chronic] explode all trees
#33 (Chronic Bronchitis):ti,ab,kw
#34 #32 or #33
#35 #11 or #20 or #31 or #34
#36 MeSH descriptor: [Pulmonary Disease, Chronic Obstructive] explode all trees
#37 #35 or #36

#38 (DECAF):ti,ab,kw
#39 (DECAF score):ti,ab,kw
#40 #38 or #39
#41 #37 and #40

3. Web of Science (WOS)

1 TOPIC: (Pulmonary Disease, Chronic Obstructive) OR TOPIC: (COPD) OR TOPIC: (Chronic Obstructive Pulmonary Disease) OR TOPIC: (COAD) OR TOPIC: (Chronic Obstructive Airway Disease) OR TOPIC: (Chronic Obstructive Lung Disease) OR TOPIC: (Airflow Obstruction, Chronic) OR TOPIC: (Airflow Obstructions, Chronic) OR TOPIC: (Chronic Airflow Obstructions) OR TOPIC: (Chronic Airflow Obstruction) OR TOPIC: (Lung Diseases, Obstructive) OR TOPIC: (Lung Disease, Obstructive) OR TOPIC: (Obstructive Lung Disease) OR TOPIC: (Obstructive Lung Diseases) OR TOPIC: (Obstructive Pulmonary Diseases) OR TOPIC: (Obstructive Pulmonary Disease) OR TOPIC: (Pulmonary Disease, Obstructive) OR TOPIC: (Pulmonary Diseases, Obstructive) OR TOPIC: (Bronchitis, Chronic) OR TOPIC: (Chronic Bronchitis) OR TOPIC: (Pulmonary Emphysema) OR TOPIC: (Emphysema)
2 TOPIC: (DECAF) OR TOPIC: (DECAF score) OR TOPIC: (decaf score)
3 #2 AND #1

4. Embase

#5 #3 AND #4
#4 decaf:ab,ti OR 'decaf score':ab,ti
#3 #1 OR #2
#2 'chronic airflow obstruction':ab,ti OR 'chronic airway obstruction':ab,ti OR 'chronic obstructive bronchitis':ab,ti OR 'chronic obstructive bronchopulmonary disease':ab,ti OR 'chronic obstructive lung disorder':ab,ti OR 'chronic obstructive pulmonary disease':ab,ti OR 'chronic obstructive pulmonary disorder':ab,ti OR 'chronic obstructive respiratory disease':ab,ti OR copd:ab,ti OR 'lung chronic obstructive disease':ab,ti OR 'lung disease, chronic obstructive':ab,ti OR 'lung diseases, obstructive':ab,ti OR 'obstructive lung disease':ab,ti OR 'obstructive lung disease, chronic':ab,ti OR 'obstructive pulmonary disease':ab,ti OR 'obstructive respiratory disease':ab,ti OR 'obstructive respiratory tract disease':ab,ti OR 'pulmonary disease, chronic obstructive':ab,ti OR 'pulmonary disorder, chronic obstructive':ab,ti
#1 'chronic obstructive lung disease'/exp

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	page1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	page2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	page3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	page 3
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	page 4
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	page 4
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	page 4
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	page 4
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	page 4
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	page 4-5
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	page 5
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	page 5
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	page 5
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	page 5

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	page 5
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	page 5
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	page 5 and Fig. 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	page5, 7, 8
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	page6
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Page9-11
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Page9-11
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Page6 and Fig.S1
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	Page 10-11
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	Page12
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	Page13
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	Page14
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	Page14

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DECAF score as a mortality predictor for acute exacerbation of chronic obstructive pulmonary disease: a systematic review and meta-analysis

Short title: DECAF score for patients with AECOPD

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Abstract

Objectives: This study was conducted to assess the association between DECAF scores (The Dyspnea, Eosinopenia, Consolidation, Acidemia, and Atrial Fibrillation) and the prognosis of patients with acute exacerbation of chronic obstructive pulmonary disease (AECOPD), and to evaluate the specific predictive and prognostic value of DECAF scores, and to explore the effectiveness of different cut-off values in risk stratification of AECOPD patients.

Design: Systematic review and meta-analysis.

Participants: Adult patients diagnosed with AECOPD (over 18 years of age).

Primary and secondary outcome measures: Electronic databases, including the Cochrane Library, PubMed, the EMBASE, and the WOS, and the reference lists in related articles were searched for studies published up to September 2019. The identified studies reported the prognostic value of DECAF scores in AECOPD patients.

Results: Seventeen studies involving 8329 participants were included in the study. Quantitative analysis demonstrated that elevated DECAF scores were associated with high mortality risk (WMD = 1.87; 95% CI: 1.19 – 2.56). In the accuracy analysis, DECAF scores showed good prognostic accuracy for both in-hospital and 30-day mortality [AUC: 0.83 (0.79 – 0.86) and 0.79 (0.76 – 0.83), respectively]. When the prognostic value was compared to that of other scoring systems, DECAF scores showed better prognostic accuracy and stable clinical values than the modified DECAF, CAPS, BAP-65, CURB-65 or APACHE II scores.

Conclusion: The DECAF score is an effective and feasible predictor for short-term mortality. As a specific and easily scored predictor for AECOPD patients, DECAF score is superior to other prognostic scores. The DECAF score can correctly identify most AECOPD patients as low risk, and with the increase of cut-off value, the risk stratification of DECAF score in high-risk population increases significantly.

Keywords: Dyspnoea, Eosinopenia, Consolidation, Acidaemia, and atrial Fibrillation (DECAF) score; early warning score; acute exacerbation of chronic obstructive pulmonary disease (AECOPD); meta-analysis; systematic review.

Strengths and limitations of this study

- This study not only evaluated the effectiveness of DECAF score on prognosis short-term mortality of AECOPD patients, but also explored the effectiveness of different cut-off values in risk stratification of AECOPD patients.
- In order to further evaluate the effectiveness of DECAF score, this study compared the prognostic effects of DECAF scores with other prognostic scores, such as APACHE II, BAP-65, and CURB-65.
- This study assessed DECAF scores by quantitative analysis and accuracy analysis.
- The data and analyses were difficult to obtain due to a lack of original studies reporting the value of DECAF scores for predicting long-term mortality and other adverse outcomes in AECOPD patients.
- Although we analyzed the source of heterogeneity through subgroup analysis, heterogeneity in the results should still be considered carefully.

Introduction

Acute exacerbation of chronic obstructive pulmonary disease (AECOPD) is characterized by the deterioration of respiratory symptoms beyond normal daily variations[1]. AECOPD accounts for one in eight hospital admissions[2] and is associated with worsening lung function, health-related quality of life, and mortality risk. The in-hospital mortality of AECOPD patients ranges from 4.4% to 25%. The survivors have a readmission rate of 25% to 55% and 25% to 50% of these patients have a high risk of death within one year[2, 3].

Prognostic score can provide a strong indicator for risk stratification and assist clinical management, including Hospital-at-Home or early supported discharge for low-risk groups, and early escalation or appropriate palliation for high-risk groups[4, 5]. The Dyspnea, Eosinopenia, Consolidation, Acidemia, and Atrial Fibrillation (DECAF) score is designed to predict in-hospital mortality of AECOPD patients[6], and can be easily applied at the bedside using indices routinely available at admission. The score includes five predictors, the strongest of which is stable state dyspnea, measured by the extended Medical Research Council Dyspnea score (eMRCD; Table 1)[7]. The DECAF score showed promising performance in derivative studies, and was superior to other prognostic tools for AECOPD patients[6]. The UK National COPD audit recommends that DECAF scores be recorded for AECOPD patients. However, it is also pointed out that the application of DECAF score still needs evidence and validation[8]. In addition, the prognosis value of DECAF score is still unclear and needs to be verified, which is essential to prove the generalization of prognosis scores.

This systematic review and meta-analysis evaluated the association between DECAF scores and the prognosis of AECOPD patients, assessed the specific predictive and prognostic value of DECAF scores, and explored the effectiveness of different cut-off values in risk stratification of AECOPD patients. To further assess the clinical value of DECAF scores, we compared the test to other commonly used prognostic scores,,

including the modified DECAF (the Dyspnoea, Eosinopenia, Consolidation, Acidemia, and Frequency of admission in AECOPD in the last year)[9], CAPS (COPD and Asthma Physiology Score)[10], BAP-65 (BUN, Altered mental status, Pulse and age > 65)[11], CURB-65 (Confusion, Urea, Respiratory Rate, Blood pressure, and age > 65)[12], and APACHE II (Acute Physiology and Chronic Health Evaluation scoring system Ⅱ) scoring systems[13]. Although these scores are not designed or proposed for AECOPD, they are still commonly used in clinical practice for the prediction and prognostic evaluation of AECOPD patients. This study aimed to evaluate and validate the effectiveness of the DECAF score and improve the clinical course and outcome of AECOPD patients.

Materials and Methods

All methods of this systematic review and meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines[14, 15].

Data Sources and Searches

The review authors searched for medical literature before September 2019. The research was conducted in electronic databases including the Cochrane Library, PubMed, the Excerpt Medica Database (Embase), the Web of Science (WOS), and the reference lists from review articles, irrespective of publication dates, status or language. The search was conducted with the following keywords: *DECAF Score or Dyspnea, Eosinopenia, Consolidation, Acidemia and Atrial Fibrillation Score and AECOPD or Acute Exacerbations of Chronic Obstructive Pulmonary Disease.* Search strategies used in the Cochrane Library, PubMed, Embase, and WOS can be found in the Supplement (Supplementary File: Search strategies).

This meta-analysis included studies that met the following criteria:

1. Adult patients diagnosed with AECOPD (over 18 years of age)
2. The studies included the results of DECAF score prognoses in patients with AECOPD. Study information could be extracted into a 2 × 2 contingency table.

AECOPD was diagnosed based on the latest reference standard in the original study, such as the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guideline, which was defined as an acute event characterized by worsening of the patient's respiratory symptoms beyond normal day-to-day variations, leading to medication changes.

3. No publication date, status or language restrictions were applied. Clinical original articles were included, whereas secondary studies, conference abstracts, editorials, and animal experiments were excluded.

Study Selection

Two review authors (Q Huang and H Xiong) independently assessed the studies to be included based on the titles, abstracts, and keywords. If a study was found to be relevant to our topic, at least two reviewers further evaluated the full text to determine whether it met the inclusion criteria. In the case of inconsistencies between the reviewers, a third reviewer (J Liu) was consulted. The authors consulted the original authors to further ensure the eligibility of a study, when additional information on the details of the results and methods or allocation concealment was needed. A study diagram was prepared to illustrate the entire literature research process and the selection of the studies (Fig. 1).

Data Extraction and Quality Assessment

The data were independently extracted by two review authors (T Shuai and C Zhang) and the resulting differences were resolved by a third reviewer (C He). The extracted data included the lead author; publication year; the country of origin; the participant characteristics (age, sex, and mortality rate); the statements for collection of DECAF; the optimal cut-off threshold in original study; values for sensitivity, specificity, true-positive, true-negative, false-positive, false-negative; and the area (AUC) under the receiver operating characteristic (ROC) curve. If data were missing, a letter was written to the authors to request the data. If there was no response to the letter after four weeks, an e-

mail was sent. If there was no response to the e-mail, estimates were made based on available data and used.

Two review authors (J Liu and J Lu) independently applied the guidelines of the PRISMA statement[16] to evaluate each involved study. The Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) was conducted by two independent authors (J Liu and J Lu) to assess the quality and risk of bias for diagnostic or prognostic studies[17]. In case of any inconsistency, all authors reach an agreement through discussion. The quality and risk of bias were assessed from two perspectives, including bias risk and applicability concerns, and evaluated from four aspects, including patient selection, index test, reference standard, and flow and timing.

Data Synthesis and Analysis

This study used Stata SE 15.0 (Stata Corp; College Station, TX, USA) to analyze the extracted data. Continuous variables are expressed as weighted mean differences (WMD) with a 95% confidence interval (95% CI).

The mixed bivariate random-effects regression model was used to analyze and pool the diagnostic accuracy measurements across studies[18]. To derive summary estimates, we plotted estimates of the observed sensitivities and specificities for each test in forest plots and hierarchical summary receiver operating characteristic (HSROC) curves derived from individual study results[19, 20]. These results were plotted using HSROC curves with 95% confidence and prediction regions. Additionally, pooled sensitivity (SEN), specificity (SPE), diagnostic odds ratio (DOR), positive likelihood ratio (PLR), and negative likelihood ratio (NLR) were calculated[21]. The AUC was also calculated to show the prognostic performance of DECAF. In clinical practice, tests with AUC above 0.8 are considered to be very reliable[22].

The heterogeneity of eligible studies was assessed by the Cochrane Q test (significant heterogeneity was indicated by $P < 0.05$) and the I^2 test (significant heterogeneity was indicated by $I^2 > 50\%$)[23]. If substantive heterogeneity ($I^2 > 50\%$)

existed, subgroup analysis and sensitivity analysis were performed to analyze the sources of the heterogeneity. The α value was set to 0.05.

To assess the heterogeneity from the threshold effect, the Spearman correlation coefficient between the logit of sensitivity and the logit of (1−specificity) was computed to assess the threshold effect on the prognostic accuracy of DECAF score. If the Spearman correlation coefficient was greater than or equal to 0.6 ($p<0.05$), there was a threshold effect[24]. The Deek's funnel plot asymmetry test was used to assess for publication bias, when the included studies were greater than 10 studies [25].

Patient and public involvement

Patients and the public were not involved in the development of the research question, the outcome measures, the design or conduct of this systematic review. Patients and the public were not asked to advise on interpretation of results or to contribute to the writing or editing of this document.

Results

Study Selection

A flow chart of the study selection process (Fig. 1) was prepared according to the PRISMA guidelines. After reviewing the title and abstract, 35 articles were screened for full-text review. Among them, 18 articles failed to meet the inclusion criteria. Seventeen studies involving a total of 8329 participants met all of the criteria [6, 9, 26-40]. Among them, Echevarria et al.[26, 28] and Shi et al.[27, 29] each produced two articles from two different studies.

Study Characteristics

As for the AECOPD definition, all studies were defined by the GOLD criteria, which is defined as an acute event characterized by worsening of the patient's respiratory symptoms beyond normal day-to-day variations and leading to medication changes[41]. All identified studies reported the results of DECAF scores for AECOPD prognosis. Among

these studies, 15 studies reported the prognostic values of DECAF scores for in-hospital mortality[6, 9, 26, 28, 29, 31-40] and five studies reported 30-day mortality[27, 28, 30, 31, 33]. The cutoff threshold for each study was retrospectively determined based on the ROC curve. For in-hospital mortality, the results of five studies were based on a cutoff value of 4[9, 28, 35, 37, 39], four studies were based on a cutoff value of 3[6, 32, 36, 40], three studies were based on a cut-off value of 2[30, 33, 38], and the other three studies did not report a cut-off threshold[17, 22, 25]. With regard to the collection of DECAF score, eight studies collected the score on admission[9, 27, 30, 32-34, 38, 40], one reported that the collection was pre-specified in the original study protocol[26], one was collected within 24 hours after admission [35], one recorded DECAF score as part of routine practice[28], and the other six reported that the DECAF score was compiled based on admission data[6, 29, 31, 36, 37, 39]. As for other prognostic scores, five studies reported the prognostic value of CURB-65 scores[28, 30, 31, 33, 35], eight reported BAP-65 scores[28, 30, 31, 33-37], five reported APACHE Ⅱ scores[6, 27-29, 40], four reported CAPS scores[6, 28, 29, 40], and three reported the prognostic value of modified DECAF scores[9, 29, 37] for AECOPD patients. A summary of the characteristics of the included studies is shown in Table 2.

Methodological Quality and Risk of Bias

Only one study was a case-control design without blinding statements, which could not prevent the occurrence of observer bias, thus the risk of bias was related high [35]. All studies included patients diagnosed with AECOPD, and eight studies reported consecutive enrollment[6, 9, 26-28, 30, 34, 40]. Most of studies included did not pre-specify the cut-off value for risk stratification. Since the main outcome is the mortality of AECOPD patients, for which the reference standard is survival or non-survival, all included studies met the low-risk criteria of the reference standard items. However, the included studies yielded different baseline characteristics in the included population, which affected patient selection, flow, and timing. The quality and bias of each included studies was

shown in Table 3, and the summary figures of risk of bias were shown in Figs. S1 and S2.

The Quantitative Analysis of DECAF scores in AECOPD

Three studies referred to DECAF scores between the survivor group and the non-survivor group. The randomized effect model showed a significant increase in DECAF scores in the non-survivor group compared to the survivor group (WMD = 1.87; 95% CI: 1.19 – 2.56; $P < 0.001$) (Table 4). The results indicate that the elevated DECAF scores were associated with high mortality risk.

As shown in Table 4, four other scoring systems have been proven to indicate poor outcomes of AECOPD. Compared to the survivor group, the results showed that CURB-65 scores, BAP-65 scores, modified DECAF scores, and APACHE Ⅱ scores were increased in the non-survivor group (WMD = 0.69, 95% CI: -0.08 – 1.45, $P = 0.078$; WMD = 0.75, 95% CI: -0.07 – 1.56, $P = 0.071$; WMD = 1.74, 95% CI: 1.36 – 2.13, $P = 0.001$; WMD = 5.24, 95% CI: 4.00 – 6.47, $P < 0.001$, respectively). The results showed that increases in DECAF scores, modified DECAF scores, and APACHE Ⅱ scores were associated with a high risk of mortality in AECOPD, suggesting that DECAF scores have the potential to be a prognostic indicator for patients with AECOPD.

Prognostic Value of DECAF Scores for AECOPD

Seventeen studies reported the prognostic value of DECAF scores. The pooled sensitivity of DECAF scores for predicting mortality was 0.76 [95% CI, 0.70 – 0.81; $I^2 = 45.24\%$, $Q = 29.22$ ($P = 0.02$)] with a specificity of 0.76 [95% CI, 0.68 – 0.83; $I^2 = 96.99\%$, $Q = 531.44$ ($P < 0.001$); Fig. 2]. The PLR and NLR were 3.2 (95% CI, 2.4 – 4.1) and 0.32 (95% CI, 0.27 – 0.37), respectively, and the DOR was 10 (95% CI, 8 – 13). The AUC of the HSROC was 0.82 (95% CI, 0.78 – 0.85; Fig. 3), indicating that the DECAF score had a reliable accuracy in predicting mortality for AECOPD patients. Additionally, there was no significant difference in threshold effect (Spearman's correlation coefficient = 0.467;

$P = 0.059$). No publication bias was found in Deek's funnel plot asymmetry test ($P = 0.74$; Fig. S3).

Subgroup Analysis

In predicting in-hospital mortality, the pooled sensitivity of the DECAF scores was 0.77 (95% CI, 0.70 – 0.82; $I^2 = 47.24\%$, $P = 0.02$), the specificity was 0.76 (95% CI, 0.67 – 0.84; $I^2 = 96.5\%$, $P < 0.001$], and the AUC of the HSROC was 0.83 (95% CI, 0.79 – 0.86). For 30-day mortality, the pooled sensitivity of the DECAF scores was 0.71 (95% CI, 0.53 – 0.84; $I^2 = 84.95\%$, $P < 0.001$), the specificity was 0.75 (95% CI, 0.58 – 0.86; $I^2 = 98.37\%$, $P < 0.001$), and the AUC of the HSROC was 0.79 (95% CI, 0.76 – 0.83) (Table 5).

The subgroup analyses were based on different cut-off values (Table 5). For a cut-off value of 4, five studies included 2,550 participants reported the prognostic value of DECAF. The pooled sensitivity of the DECAF scores was 0.75 (95% CI, 0.69 – 0.81; $I^2 = 0.00\%$, $P = 0.61$), the specificity was 0.80 (95% CI, 0.68 – 0.89; $I^2 = 95.84\%$, $P < 0.001$], and the AUC of the HSROC was 0.76 (95% CI, 0.72 – 0.80), the PLR was 3.80 (95% CI, 2.20 – 6.60), and the NLR was 0.31 (95% CI, 0.23 – 0.41). Four studies included 1,361 participants reported the results of a cut-off value was 3. The pooled sensitivity was 0.77 (95% CI, 0.70 – 0.82; $I^2 = 0.00\%$, $P = 0.52$), the specificity was 0.76 (95% CI, 0.67 – 0.84; $I^2 = 29.09\%$, $P = 0.24$], the AUC of the HSROC was 0.83 (95% CI, 0.79 – 0.86), the PLR was 3.20 (95% CI, 2.40 – 4.40), and the NLR was 0.31 (95% CI, 0.25 – 0.37). For a cut-off value of 2, three studies included 1,002 participants reported the results. The pooled sensitivity was 0.84 (95% CI, 0.68 – 0.93; $I^2 = 0.00\%$, $P = 0.52$), the specificity was 0.53 (95% CI, 0.50 – 0.56; $I^2 = 0.00\%$, $P = 0.61$], the AUC of the HSROC was 0.77 (95% CI, 0.73 – 0.80), the PLR was 1.80 (95% CI, 1.50 – 2.10), and the NLR was 0.31 (95% CI, 0.15 – 0.64). The results of PLR and NLR at different cut-off values suggest that DECAF score can correctly identify most of AECOPD patients as low risk, and with

the increase of cut-off value, the risk stratification of DECAF score for high-risk population increased significantly.

Other Prognostic Scores for Patients with AECOPD

In predicting the in-hospital mortality of patients with AECOPD, the pooled results showed that the sensitivity, specificity, and AUC of the CURB-65 scores were 0.46, 0.92, and 0.73, respectively. The sensitivity, specificity, and AUC of the BAP-65 scores were 0.70, 0.50, and 0.64, respectively. The sensitivity, specificity, and AUC of the APACHE Ⅱ scores were 0.70, 0.65, and 0.72, respectively. The sensitivity, specificity, and AUC of CAPS scores were 0.77, 0.62, and 0.75, respectively, and the sensitivity, specificity, and AUC of the m-DECAF scores were 0.84, 0.62, and 0.84, respectively (Table 6).

When predicting the 30-day mortality in COPD patients, the pooled results showed that the sensitivity, specificity, and AUC of the CURB-65 scores were 0.52, 0.85, and 0.53, respectively. The sensitivity, specificity, and AUC of the BAP-65 scores were 0.61, 0.57, and 0.62, respectively. The sensitivity, specificity, and AUC of the APACHE Ⅱ scores were 0.68, 0.73, and 0.77, respectively (Table 7).

Discussion

In stable COPD, prognostic indicators have been thoroughly investigated and tools to predict mortality risk, such as the BODE Score[41], have been well established. However, prognostic studies in patients with exacerbation requiring hospitalization are limited and the predictors of mortality between stable disease periods and AECOPD periods seem to have little in common[42]. In addition, the risk of mortality in AECOPD patients is much higher than in patients with stable COPD. Thus, there is an urgent need for effective reliable clinical tools that can be used to inform clinicians and patients of the risk of death during exacerbation.

The current study conducted a systematic review and meta-analysis to characterize and evaluate DECAF scores predicting mortality in patients with AECOPD. Six potential scoring systems were evaluated by comparing survivor and non-survivor scores and

prognostic accuracy. Quantitative analysis demonstrated that elevated DECAF scores were significantly associated with high mortality risk. In other potential scoring systems, compared with the survivor group, the results showed that only the modified DECAF and APACHE Ⅱ scores increased in the non-survivor group. In the accuracy analysis, DECAF scores showed a reliable prognostic accuracy for both in-hospital and 30-day mortality. When the prognostic value was compared with other prognostic scores, DECAF scores showed better prognostic accuracy and stable clinical value in predicting the in-hospital mortality and 30-day mortality of patients with AECOPD. The results showed that for the different cut-off values of DECAF score, as the cut-off value increased, the sensitivity decreased and the specificity escalated. The results of PLR and NLR at different cut-off values suggest that DECAF score can correctly identify most AECOPD patients as low risk, and with the increase of cut-off value, the risk stratification of DECAF score for high-risk population increased significantly.

The DECAF scores increased significantly in the non-survivor group. This suggests that elevated DECAF scores have the potential to stratify a high-risk population from low-risk patients. The modified DECAF and APACHE Ⅱ scores had a similar relationship, which indicates that scoring systems have potential to aid clinical decisions in risk stratification. However, the CURB-65 and BAP-65 scores did not show statistical differences between the survivor and non-survivor groups. Although studies have shown that CURB-65 and BAP-65 can be effective tools for predicting mortality[43], based on the results of this current study, we speculate that the potential prognostic value of CURB-65 and BAP-65 is relatively low.

The DECAF score is an effective predictor of mortality and can be easily scored at the bedside using indices routinely available at admission[6]. In clinical practice, test with AUC greater than 0.8 is considered to be very reliable[22]. The results showed that the AUC of the DECAF scores was 0.83 for predicting in-hospital mortality and 0.79 for short-

term mortality (30-day). This indicates that the DECAF test can be utilized as a promising prognosis tool with satisfactory sensitivity and specificity for AECOPD patients.

Mortality rates vary between clinical settings and cohorts. In this study, the mortality rate of patients in the included studies ranged from 2.38% to 33.93%. This largely reflects differences in baseline characteristics, especially in the proportion of patients admitted from institutional care and with coexisting pneumonia[12, 28]. In addition, this also partly leads to choosing different cut-off values. To illustrate the relationship between the cut-off values for risk stratification, subgroup analyses were performed. For cut-off values from 2 to 4, the sensitivity decreased from 0.84 to 0.75 and the specificity increased from 0.53 to 0.80. With an increase in the cut-off value, specificity increased significantly. Under the premise of ensuring sensitivity, improving specificity can effectively reduce the number of false positives and improve the clinical application value of a prognostic score.

In clinical practice, the greater the PLR value, the greater the likelihood of true positive when the test result is positive; the smaller the NLR value, the greater the likelihood of true negative when the test result is negative. PLR is more important in stratification of high-risk groups, while NLR is more important in low-risk groups. From the results, the NLR was very small, 0.31, which indicated that the DECAF score could correctly identify most AECOPD patients as a low-risk group. For the cut-off value from 2 to 4, the PLR value increased from 1.80 to 3.80, indicating that with the increase of the cut-off value, the risk stratification of the DECAF score in high-risk groups increased significantly.

The CURB-65 and BAP-65 tests can also be easily scored on admission[44]. However, according to the results of this study, the CURB-65 and BAP-65 scores had low prognostic value for predicting in-hospital and 30-day mortality, which were consistent with the lack of statistical difference in CURB-65 and BAP-65 scores between survivors and non-survivors.

APACHE II uses point scores based on the initial values of 12 routine physiological measurements, age, and previous health status to provide a general measure of disease severity[45]. APACHE II is not a specific predictor for AECOPD but is still commonly used in clinical practice to predict mortality in AECOPD patients[46]. Based on our results, APACHE II scores showed no superiority to DECAF scores in prognostic accuracy, sensitivity or specificity. In addition, it contains cumbersome test items, thus increasing the workload of clinicians in clinical practice. For AECOPD patients, the APACHE II test may not be the preferred early warning scoring system.

As for the modified DECAF, Zidan et al.[9] attempted to replace the atrial fibrillation item in the DECAF test with admission frequency for AECOPD during the last year and named the revision the modified DECAF. They concluded that the modified DECAF test was more sensitive and specific in predicting in-hospital mortality during acute exacerbation of COPD than the DECAF test. However, there was no significant difference between the two scores[9], which was consistent with the results of this current study. In addition, only three studies reported the predictive value of modified DECAF test for in-hospital mortality in AECOPD patients, and no study reported the effectiveness of the test in terms of 30-day mortality. Therefore, more evidence is needed to evaluate the prognostic value of modified DECAF scores and further compare the clinical value between DECAF scores and modified DECAF scores.

Examination of prognostic scores can contribute to clinical management, early risk-stratification, and the prevention of poor outcomes, as well as monitoring during treatment[47]. Clinicians are constantly seeking predictors of mortality for patients with AECOPD. As a promising predictor, DECAF scores can be used in a variety of hospital settings to accurately stratify mortality risk. As a specific and easily scored predictor for AECOPD patients, DECAF is superior to other prognostic scores in predicting short-term mortality. From the results of different cut-off values, the DECAF score showed a promising potential. It can correctly identify most AECOPD patients as low-risk group,

which is related to the reduction of in-hospital stay. Compared to the meta-analyses of interventions, including randomized controlled trials, those including diagnostic studies have more publication bias[48]. Excluding studies that do not have sufficient data may lead to publication and reporting bias. Therefore, the prognostic value of DECAF may be overestimated. As for the significant degree of heterogeneity, we conducted a subgroup analysis to explore the source of the heterogeneity. The subgroup analysis revealed that the heterogeneity was mainly derived from the choice of cut-off value. When the cut-off value was 2, 3 or 4, the heterogeneity of sensitivity decreased to 0. However, the heterogeneity of specificity was still substantive when the cut-off value was 4. This largely reflect differences in the baseline characteristics of the patient selection. The biases between included studies can also lead to heterogeneity. The DECAF score needs to be collected at admission or pre-specified in the original study protocol. However, the collection of DECAF score varied between the included studies, which may result in variable performance of DECAF. In addition, different included studies yielded different baseline characteristics in the included population, which affected patient selection and also led to the different selection of cut-off value between studies.

This meta-analysis had some limitations. Firstly, the data and analyses were difficult to obtain due to a lack of original studies reporting the value of DECAF scores for predicting long-term mortality and other adverse outcomes in AECOPD patients. Further studies are needed for validation. Secondly, it was difficult to obtain raw data for each of the included studies, which limited us to determining the optimal DECAF cut-off point for predicting AECOPD. Thirdly, because of the lack of original research comparing DECAF with other predictive scores, we can only compare the predictive value of DECAF and other predictive scores to AECOPD patients in general. With the increase of related original research, it is possible to further explore the effectiveness of different prognostic scores in risk stratification of AECOPD patients. In addition,

although the source of heterogeneity was analyzed by subgroup analysis, heterogeneity in the results should still be considered carefully.

Conclusion

In conclusion, the results of this systematic review and meta-analysis indicated that the DECAF score was an effective and feasible predictor of short-term mortality in patients with AECOPD. As a specific and easily scored predictor for AECOPD patients, DECAF scores are superior to other prognostic scores. The DECAF score can correctly identify most AECOPD patients as low risk, and with the increase of cut-off value, the risk stratification of DECAF score for high-risk population increased significantly.

List of abbreviations

AECOPD: acute exacerbation of chronic obstructive pulmonary disease; DECAF: Dyspnoea, Eosinopenia, Consolidation, Acidaemia, and atrial Fibrillation score; the modified DECAF: the Dyspnoea, Eosinopenia, Consolidation, Acidaemia and Frequency of admission in AECOPD in the last year; CAPS: COPD and Asthma Physiology Score; BAP-65: BUN, Altered mental status, Pulse and Age > 65; CURB-65: Confusion, Urea, Respiratory Rate, Blood pressure, Age > 65; APACHE II: acute physiology and chronic health evaluation scoring system Ⅱ scores; QUADAS-2: the Quality Assessment of Diagnostic Accuracy Studies-2; WOS: web of science; WMD: weighted mean difference; AUC: the area under the receiver operating characteristic curve; PRISMA: the preferred reporting items for systematic reviews and meta-analyses; PLR: positive likelihood ratio; NLR: negative likelihood ratio; DOR: diagnostic odds ratio; HSROC: hierarchical summary receiver operating characteristic; CIs: confidence intervals;

Additional Information

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The authors each individually and collectively declare there are no competing interests.

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All data generated or analyzed during this study are included in this published article and its supplementary information files, and no unpublished data are available.

References

1. Rodriguez-Roisin R. Toward a consensus definition for COPD exacerbations. Chest. 2000;117(5 Suppl 2):398s-401s.

2. Johannesdottir SA, Christiansen CF, Johansen MB, et al. Hospitalization with acute exacerbation of chronic obstructive pulmonary disease and associated health resource utilization: a population-based Danish cohort study. Journal of medical economics 2013;16:897-906.

3. de Miguel-Diez J, Jimenez-Garcia R, Hernandez-Barrera V, et al. Trends in hospital admissions for acute exacerbation of COPD in Spain from 2006 to 2010. Respiratory medicine 2013;107:717-23.

4. Wildman MJ, Sanderson C, Groves J, et al. Predicting mortality for patients with exacerbations of COPD and Asthma in the COPD and Asthma Outcome Study (CAOS). QJM : monthly journal of the Association of Physicians 2009;102:389-99.

5. Doll H, Miravitlles M. Health-related QOL in acute exacerbations of chronic bronchitis and chronic obstructive pulmonary disease: a review of the literature. PharmacoEconomics 2005;23:345-63.

6. Steer J, Gibson J, Bourke SC. The DECAF Score: predicting hospital mortality in exacerbations of chronic obstructive pulmonary disease. Thorax 2012;67:970-6.

7. Steer J, Norman EM, Afolabi OA, et al. Dyspnoea severity and pneumonia as predictors of in-hospital mortality and early readmission in acute exacerbations of COPD. Thorax 2012;67:117-21.

8. Stone RA, Holzhauer-Barrie J, Lowe D, et al. COPD: Who cares matters. National Chronic Obstructive Pulmonary Disease (COPD) Audit Programme: Clinical audit of COPD exacerbations admitted to acute units in England and Wales 2014, 2015.

9. Zidan MH, Rabie AK, Megahed MM, et al. The usefulness of the DECAF score in predicting hospital mortality in Acute exacerbations of chronic obstructive pulmonary disease. Egyptian Journal of Chest Diseases and Tuberculosis 2015;64:75-80.

10. Wildman MJ, Harrison DA, Welch CA, et al. A new measure of acute physiological derangement for patients with exacerbations of obstructive airways disease: the COPD and Asthma Physiology Score. Respiratory medicine 2007;101:1994-2002.

11. Shorr AF, Sun X, Johannes RS, et al. Validation of a novel risk score for severity of illness in acute exacerbations of COPD. Chest 2011;140:1177-83.

12. Lim WS, van der Eerden MM, Laing R, et al. Defining community acquired pneumonia severity on presentation to hospital: an international derivation and validation study. Thorax 2003;58:377-82.

13. Jacobs S, Chang RW, Lee B. One year's experience with the APACHE II severity of disease classification system in a general intensive care unit. Anaesthesia 1987;42:738-44.

14. Wang X, Chen Y, Yao L, et al. Reporting of declarations and conflicts of interest in WHO guidelines can be further improved. Journal of clinical epidemiology 2018;98:1-8.

15. Ge L, Tian JH, Li YN, et al. Association between prospective registration and overall reporting and methodological quality of systematic reviews: a meta-epidemiological study. Journal of clinical epidemiology 2018;93:45-55.

16. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. Journal of clinical epidemiology 2009;62:e1-34.

17. Whiting PF, Rutjes AW, Westwood ME, et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. Annals of internal medicine 2011;155:529-36.

18. Kim KW, Lee J, Choi SH, et al. Systematic Review and Meta-Analysis of Studies Evaluating Diagnostic Test Accuracy: A Practical Review for Clinical Researchers-Part I. General Guidance and Tips. Korean J Radiol 2015;16:1175-87.

19. Lee J, Kim KW, Choi SH, et al. Systematic Review and Meta-Analysis of Studies Evaluating Diagnostic Test Accuracy: A Practical Review for Clinical Researchers-Part II. Statistical Methods of Meta-Analysis. Korean J Radiol 2015;16:1188-96.

20. Rutter C M., Gatsonis C A. A hierarchical regression approach to meta-analysis of diagnostic test accuracy evaluations. Stat Med 2001, 20:2865-84.

21. Chu H, Cole SR. Bivariate meta-analysis of sensitivity and specificity with sparse data: a generalized linear mixed model approach. J Clin Epidemiol 2006;59:1331–1332.

22. Memon MA, Faryal S, Brohi N, et al. Role of the DECAF Score in Predicting In-hospital Mortality in Acute Exacerbation of Chronic Obstructive Pulmonary Disease. Cureus 2019;11:e4826.

23. Higgins J, Green S. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0. Cochrane Collaboration; 2008.

24. Deville WL, Buntinx F, Bouter LM, et al. Conducting systematic reviews of diagnostic studies: didactic guidelines. BMC Med Res Methodol 2002;2:9.

25. Deeks JJ, Macaskill P, Irwig L. The performance of tests of publication bias and other sample size effects in systematic reviews of diagnostic test accuracy was assessed. J Clin Ep- idemiol 2005;58:882–893.

26. Echevarria C, Steer J, Bourke SC. Comparison of early warning scores in patients with COPD exacerbation: DECAF and NEWS score. Thorax 2019;74:941-6.

27. Shi QF, Sheng Y, Zhu N, et al. The v-DECAF score can predict 90-day all-cause mortality in patients with COPD exacerbation requiring invasive mechanical ventilation. The clinical respiratory journal 2019.

28. Echevarria C, Steer J, Heslop-Marshall K, et al. Validation of the DECAF score to predict hospital mortality in acute exacerbations of COPD. Thorax 2016;71:133-40.

29. Shi QF, Sheng Y, Wang SY. Comparison of four score modes in prognosis assessment of AECOPD patients with respiratory failure. Journal of Practical Medicine 2017; 33: 242-5

30. Bastidas AR, Hincapie Diaz G, Mantilla Cardozo B, et al. Validity CURB 65, BAP 65, DECAF for predicting outcomes in exacerbation of COPD. American Journal of Respiratory and Critical Care Medicine 2018;197.

31. Shafuddin E, Chang CL, Hancox RJ. Comparing severity scores in exacerbations of chronic obstructive pulmonary disease. The clinical respiratory journal 2018;12:2668-75.

32. Bisquera RR, Cruz BOD. Prognostic utility of the DECAF score to predict in-hospital mortality among patients with acute exacerbation of chronic obstructive pulmonary disease admitted at Chinese general hospital. Respirology 2018;23:128-9.

33. Mantilla BM, Ramírez CA, Valbuena S, et al. Saturación de oxígeno/fracción inspirada de oxígeno como predictor de mortalidad en pacientes con exacerbación de EPOC atendidos en el Hospital Militar Central. Acta Medica Colombiana 2017;42:215-23.

34. Sangwan V, Chaudhry D, Malik R. Dyspnea, Eosinopenia, Consolidation, Acidemia and Atrial Fibrillation Score and BAP-65 Score, Tools for Prediction of Mortality in Acute Exacerbations of Chronic Obstructive Pulmonary Disease: A Comparative Pilot Study. Indian journal of critical care medicine : peer-reviewed, official publication of Indian Society of Critical Care Medicine 2017;21:671-7.

35. Xu MM, Yu SY, Zhang TT. Evaluation of the three scores to assess the severity of chronic obstructive pulmonary disease exacerbation. Journal of Tianjin Medical University 2017; 23:530-3.

36. Parras AMV, Bautista CL, Chica GP, et al. Evaluation of DECAF, CURB-65 and BAP-65 scales as predictor of mortality risk in acute exacerbation of COPD in a retrospective cohort. European Respiratory Journal 2017;50.

37. Yousif M, El Wahsh RA. Predicting in-hospital mortality in acute exacerbation of COPD: Is there a golden score? Egyptian Journal of Chest Diseases and Tuberculosis 2016;65:579-84.

38. Collier L, David T, Craig C, et al. PRACTICAL USE OF THE DECAF SCORE: CAN WE IMPROVE OUTCOMES IN ACUTE EXACERBATION OF COPD ADMISSIONS? Thorax 2015;70:A98-A.

39. Rabbani B, Brammer P. CAN THE DECAF SCORE BE USED TO GUIDE PROGNOSIS AFTER AN ACUTE ADMISSION FOR COPD EXACERBATION? Thorax 2014;69:A139-A40.

40. Nafae R, Embarak S, Gad DM. Value of the DECAF score in predicting hospital mortality in patients with acute exacerbation of chronic obstructive pulmonary disease admitted to Zagazig University Hospitals, Egypt. Egyptian Journal of Chest Diseases and Tuberculosis 2015;64:35-40.

41. Celli BR, Cote CG, Marin JM, et al. The body-mass index, airflow obstruction, dyspnea, and exercise capacity index in chronic obstructive pulmonary disease. The New England journal of medicine 2004;350:1005-12.

42. Steer J, Gibson GJ, Bourke SC. Predicting outcomes following hospitalization for acute exacerbations of COPD. QJM : monthly journal of the Association of Physicians 2010;103:817-29.

43. Shorr AF, Sun X, Johannes RS, et al. Predicting the need for mechanical ventilation in acute exacerbations of chronic obstructive pulmonary disease: comparing the CURB-65 and BAP-65 scores. Journal of critical care 2012;27:564-70.

44. Patil SP, Krishnan JA, Lechtzin N, et al. In-hospital mortality following acute exacerbations of chronic obstructive pulmonary disease. Archives of internal medicine 2003;163:1180-6.

45. Mach K. [Staphylococcus epidermidis infection. Results of three groups evaluated according to APACHE II--severity of disease classification system--with reference to risk, mortality and prognosis]. Wiener klinische Wochenschrift 1992;104:540-2.

46. Akhter S, Warraich UA, Ghazal S, et al. Assessment and comparison of APACHE II (Acute Physiology and Chronic Health Evaluation), SOFA (Sequential Organ Failure Assessment) score and CURB 65 (Confusion; Urea; Respiratory Rate; Blood Pressure), for prediction of inpatient mortality in Acute Exacerbation of Chronic Obstructive Pulmonary Disease. JPMA The Journal of the Pakistan Medical Association 2019;69:211-5.

47. Costello RW, Cushen B. A risk stratification tool for exacerbations of COPD: time to switch to DECAF. Thorax 2016;71:489-90.

48. Irwig L, Macaskill P, Glasziou P, et al. Meta-analytic methods for diagnostic test accuracy. Journal of clinical epidemiology 1995;48:119-30.

Authors' contributions

The authors Jian Liu, Qiangru Huang, Chengying He, Meng Zhang, Chuchu Zhang, Huaiyu Xiong and Tiankui Shuai participated in the design of the project, conducted the literature review, and participated in the analysis. The authors Qiangru Huang, Yalei Wang wrote this paper. The authors Lei Zhu and Jiaju Lu were responsible for the statistical analysis and participated in data interpretation. The author Jian Liu was the principal investigator for the project. All authors approved the final version of the article.

Table 1. DECAF score

Variables	Score
Dyspnea	1
eMRCD 5a (too breathless to leave the house unassisted but independent in washing and/or dressing)	1
eMRCD 5b (too breathless to leave the house unassisted and requires help with washing and dressing)	2
Eosinopenia (eosinophils <0.05×109/L)	1
Consolidation	1
Moderate or severe acidemia (pH <7.3)	1
Atrial fibrillation (including history of paroxysmal atrial fibrillation)	1
Maximum DECAF score	6

DECAF: dyspnea, eosinopenia, consolidation, acidemia, and atrial fibrillation; eMRCD, extended Medical Research Council dyspnea score

Table 2. Characteristics of included studies

Author/Year	Study Inception (Year)	Country	Study design	Sample size	Male	Age (years)	Mortality (%)	Measured time	Collection of DECAF	DECAF Cut-off value	Early warning scores
Echevarria 2019	NA	UK	PC	2645	1217	73.10	8.62	in-hospital	Pre-specified in the original study protocol	NA	DECAF
Shi 2019	2016.1-2017.12	China	PC	112	73	77.57	33.93	28d	At admission	3	DECAF
Bastidas 2018	NA	Colombia	PC	462	229	79.00	2.38	30d	At admission	2	DECAF, BAP-65 and CURB-65
Shafuddin 2018	2006.7-2007.7 2012.8-2013.7	New Zealand	RC	423	190	71.00	4.49 7.33	in-hospital 30d	Compiled by admission data	NA	DECAF, CURB-65, CRB-65, and BAP-65
Bisquera 2018	NA	Philippines	PC	77	68	72.50	6.49	in-hospital	At admission	3	DECAF
Mantilla 2017	2014.2-2017.1	Colombia	PC	462	233	79.00	2.60 5.84	in-hospital 30d	At admission	2	DECAF, BAP-65 and CURB-65
Sangwan 2017	NA	India	PC	50	43	61.20	18.00	in-hospital	At admission	NA	DECAF and BAP-65
Xu 2017	2014.1-2016.1	China	CC	302	150	75.50	7.95	28d	Within 24h after admission	4	DECAF, BAP-65 and CURB-65
Parras 2017	NA	Spain	RC	164	153	76.14	20.12	in-hospital	Compiled by admission data	3	DECAF
Shi 2016	2014.1-2016.6	China	RC	186	108	66.20	15.59	in-hospital	Compiled by admission data	3	DECAF, m-DECAF, CAPS and APACHE Ⅱ

Yousif 2016	2014.1-2015.9	Egypt	R&PC	264	176	63.61	7.58	in-hospital	Compiled by admission data	4	DECAF, m-DECAF and BAP-65
Echevarria 2016	2012.1-2014.5	UK	R&PC	1725	788	73.10	7.65 28.35	in-hospital 30d	Recorded as routine practice	3	DECAF, CAPS, APACHE Ⅱ, CURB-65 and BAP-65
Zidan 2015	NA	Egypt	PC	100	58	46.46	11.00	in-hospital	At admission	4	DECAF and m-DECAF
Collier 2015	2014.12-2015.3	UK	PC	78	47	72.70	15.38	in-hospital	At admission	2	DECAF
Rabbani 2014	2012.12-2013.1	UK	RC	159	92	72.14	9.43	30d	Compiled by admission data	4	DECAF
Nafae 2014	2010.10-2013.4	Egypt	PC	200	102	68.50	12.50	in-hospital	At admission	3	DECAF, CAPS and APACHE Ⅱ
Steer 2012	2008.12-2010.6	UK	PC	920	424	73.10	10.43	in-hospital	Compiled by admission data	3	DECAF, CAPS and APACHE Ⅱ

Abbreviations: PC, prospective cohort; RC, retrospective cohort; R&PC, retrospective and prospective cohort; CC, case-control; NA, not available.

Table 3 The Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) for included studies

Studies	Patient Selection				Index Test			Reference Standard			Flow and Timing				Scores
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
Echevarria 2019	Y	Y	U	Low	Y	Y	Low	Y	U	Low	Y	Y	Y	Low	12
Shi 2019	Y	Y	Y	Low	U	U	Unclear	Y	U	Low	U	Y	Y	Low	9
Bastidas 2018	Y	Y	U	Low	Y	U	Unclear	Y	U	Low	Y	Y	Y	Low	10
Shafuddin 2018	U	Y	Y	Unclear	Y	U	Unclear	Y	U	Low	Y	Y	N	High	7
Bisquera 2018	U	Y	U	Unclear	Y	U	Low	Y	U	Low	Y	Y	U	Unclear	7
Mantilla 2017	U	Y	U	Unclear	Y	U	Low	Y	U	Low	Y	Y	Y	Low	9
Sangwan 2017	Y	Y	Y	Low	Y	U	Low	Y	U	Low	Y	Y	U	Unclear	10
Xu 2017	U	N	Y	High	N	U	High	Y	N	High	U	Y	Y	Unclear	4
Parras 2017	U	Y	Y	Unclear	Y	U	Low	Y	U	Low	U	Y	Y	Low	9
Shi 2016	U	Y	Y	Unclear	Y	U	Low	Y	Y	Low	U	Y	Y	Low	10
Yousif 2016	U	Y	Y	Unclear	Y	U	Unclear	Y	U	Low	U	Y	Y	Low	8
Echevarria 2016	Y	Y	Y	Low	Y	U	Unclear	Y	U	Low	Y	Y	Y	Low	11

Zidan 2015	Y	Y	Y	Low	Y	U	Low	Y	U	Low	Y	Y	Y	Low	12
Collier 2015	U	Y	U	Unclear	Y	U	Low	Y	U	Low	U	Y	U	Unclear	6
Rabbani 2014	U	Y	U	Unclear	U	U	Unclear	Y	U	Low	U	Y	Y	Low	6
Nafae 2014	Y	Y	Y	Low	Y	U	Low	Y	U	Low	Y	Y	Y	Low	12
Steer 2012	Y	Y	Y	Low	U	U	Unclear	Y	U	Low	Y	Y	Y	Low	10

Y = Yes, represents certain answer for the corresponding question; N = no, represents negative answer for the corresponding question; U = unclear, i.e. the information provided in the individual studies was insufficient to answer the corresponding question. QUADAS-2 criteria: 1. Was a consecutive or random sample of patients enrolled? 2. Was a case-control design avoided? 3. Did the study avoid inappropriate exclusions? 4. Could the selection of patients have introduced bias? 5. Were the index test results interpreted without knowledge of the results of the reference standard? 6. If a threshold was used, was it pre-specified? 7. Could the conduct or interpretation of the index test have introduced bias? 8. Is the reference standards likely to correctly classify the target condition? 9. Were the reference standard results interpreted without knowledge of the results of the index tests? 10. Could the reference standard, its conduct, or its interpretation have introduced bias? 11. Was there an appropriate interval between index test and reference standard? 12. Did all patients receive the same reference standard? 13. Were all patients included in the analysis? 14. Could the patient flow have introduced bias?

Table 4. The Quantitative Analysis of scores in AECOPD mortality

Variables	Studies, No.	Patients, No.	WMD	95%CI	P value
DECAF	3	600	1.87	1.19-2.56	<0.001
CURB-65	2	414	0.69	-0.08-1.45	0.078
BAP-65	2	414	0.75	-0.07-1.56	0.071
Modified DECAF	2	298	1.74	1.36-2.13	0.001
APACHE II	2	298	5.24	4.00-6.47	<0.001

Abbreviations: WMD, weighted mean difference; 95% CI, 95% confidence interval

Table 5. Subgroup analysis of the prognostic value of DECAF based on different variables.

Variables	Studies, No. (Patients, No.)	Sensitivity (95%CI)	Specificity (95%CI)	PLR (95%CI)	NLR (95%CI)	DOR (95%CI)	AUC (95%CI)
Overall	17(8329)	0.76(0.70-0.81)	0.76(0.68-0.83)	3.20(2.40-4.10)	0.32(0.27-0.37)	10(8-13)	0.82(0.78-0.85)
in-hospital	15(7655)	0.77(0.70-0.82)	0.76(0.67-0.84)	3.20(2.40-4.40)	0.31(0.25-0.37)	11(8-15)	0.83(0.79-0.86)
30d	5(3084)	0.71(0.53-0.84)	0.75(0.58-0.86)	2.80(2.00-4.10)	0.39(0.27-0.56)	7(6-9)	0.79(0.76-0.83)
cut-off= 4	5(2550)	0.75(0.69-0.81)	0.80(0.68-0.89)	3.80(2.20-6.60)	0.31(0.23-0.41)	12(6-26)	0.76(0.72-0.80)
cut-off= 3	4(1361)	0.77(0.70-0.82)	0.76(0.67-0.84)	3.20(2.40-4.40)	0.31(0.25-0.37)	11(8-15)	0.83(0.79-0.86)
cut-off= 2	3(1002)	0.84(0.68-0.93)	0.53(0.50-0.56)	1.80(1.50-2.10)	0.31(0.15-0.64)	6(2-14)	0.77(0.73-0.80)

Abbreviations: CI, confidence interval; PLR, positive likelihood ratio; NLR, negative likelihood ratio; DOR, diagnostic odds ratio; AUC, area under the receiver operating characteristic curve.

Table 6. The prognostic value of prognostic scores for predicting in-hospital mortality in patients with AECOPD.

Variables	Studies, No. (Patients, No.)	Sensitivity (95%CI)	Specificity (95%CI)	PLR (95%CI)	NLR (95%CI)	DOR (95%CI)	AUC (95%CI)
DECAF	15(7655)	0.77(0.70-0.82)	0.76(0.67-0.84)	3.20(2.40-4.40)	0.31(0.25-0.37)	11(8-15)	0.83(0.79-0.86)
CURB-65	4(2912)	0.46(0.21-0.72)	0.92(0.63-0.99)	6.00(1.70-21.60)	0.59(0.40-0.86)	10(4-28)	0.73(0.69-0.77)
BAP-65	6(3226)	0.70(0.46-0.87)	0.50(0.31-0.70)	1.40(0.90-2.20)	0.59(0.29-1.20)	2(1-7)	0.64(0.59-0.68)
APACHE II	4(3031)	0.70(0.63-0.76)	0.65(0.58-0.72)	2.00(1.60-2.50)	0.46(0.37-0.57)	4(3-7)	0.72(0.68-0.76)
CAPS	4(3031)	0.77(0.60-0.88)	0.62(0.46-0.76)	2.00(1.50-2.70)	0.37(0.24-0.58)	5(3-9)	0.75(0.71-0.79)
Modified DECAF	3(666)	0.84(0.71-0.91)	0.62(0.46-0.75)	2.20(1.40-3.40)	0.27(0.13-0.55)	8(3-25)	0.84(0.81-0.87)

Abbreviations: CI, confidence interval; PLR, positive likelihood ratio; NLR, negative likelihood ratio; DOR, diagnostic odds ratio; AUC, area under the receiver operating characteristic curve.

Table 7. The prognostic value of prognostic scores for predicting 30-day mortality in patients with AECOPD.

Variables	Studies, No. (Patients, No.)	Sensitivity (95%CI)	Specificity (95%CI)	PLR (95%CI)	NLR (95%CI)	DOR (95%CI)	AUC (95%CI)
DECAF	5(3084)	0.71(0.53-0.84)	0.75(0.58-0.86)	2.80(2.00-4.10)	0.39(0.27-0.56)	7(6-9)	0.79(0.76-0.83)
CURB-65	4(3072)	0.52(0.48-0.56)	0.85(0.56-0.96)	3.50(1.00-12.50)	0.56(0.45-0.71)	6(1-28)	0.53(0.49-0.57)
BAP-65	5(3236)	0.61(0.34-0.82)	0.57(0.23-0.85)	1.40(0.80-2.40)	0.70(0.46-1.06)	2(1-5)	0.62(0.57-0.66)
APACHE Ⅱ	2(1837)	0.68(0.52-0.80)	0.73(0.66-0.79)	2.50(1.60-3.90)	0.44(0.26-0.74)	6(2-15)	0.77(0.73-0.80)

Abbreviations: CI, confidence interval; PLR, positive likelihood ratio; NLR, negative likelihood ratio; DOR, diagnostic odds ratio; AUC, area under the receiver operating characteristic curve.

Figure Legends

Figure 1： PRISMA (preferred reporting items for systematic reviews and meta-analyses) flow diagram and exclusion criteria

Figure 2: Forest plot of sensitivity and specificity of DECAF for the prediction of mortality in AECOPD.

Figure 3: Hierarchical summary receiver operating characteristic curve for evaluating prognostic value of mortality of DECAF in AECOPD.

The HSROC curves was conducted which plots sensitivity versus specificity. All studies were presented as a circle and plotted with the HSROC curve. The summary point (red box) indicates that the summary sensitivity was 0.76 and the summary specificity was 0.76. The summary results are displayed as the 95% confidence region and 95% prediction region in the HSROC curve plot. The size of the marker is scaled according to the total number of patients in each study.

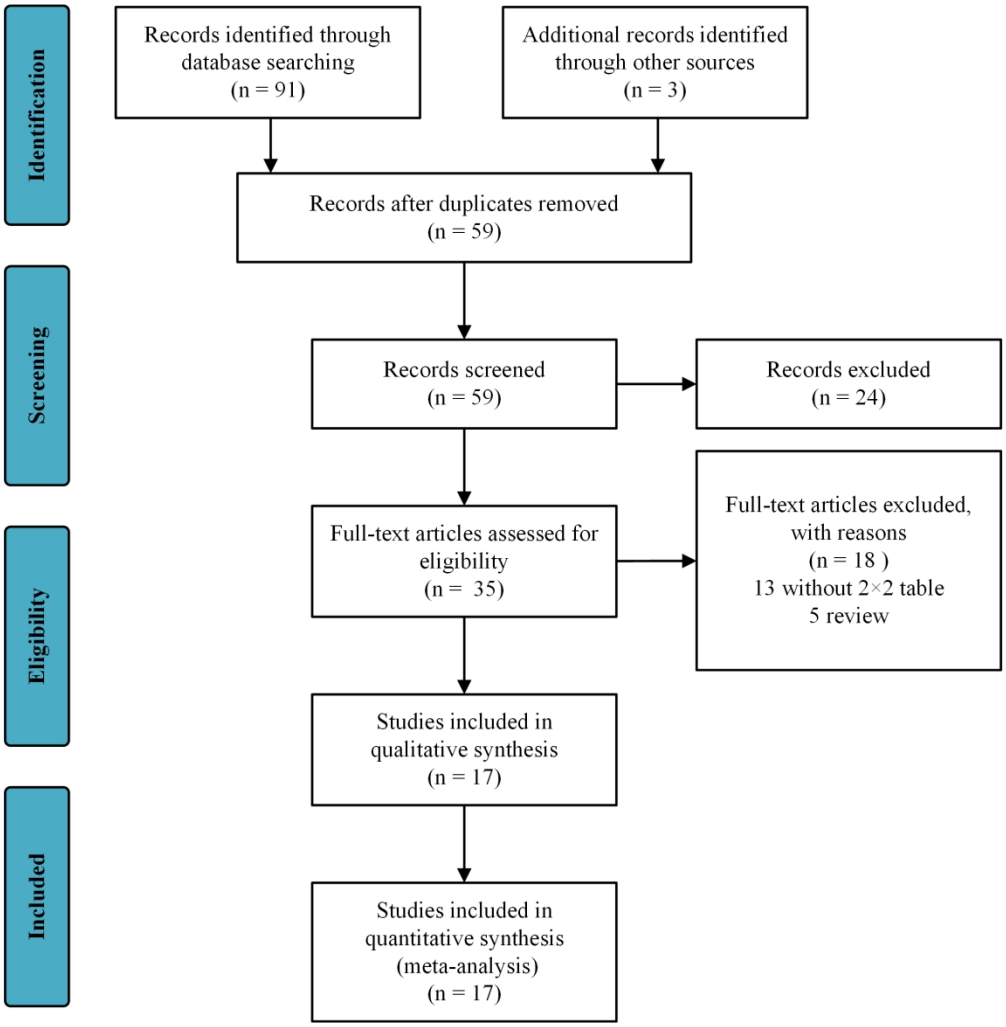

Figure 1 : PRISMA (preferred reporting items for systematic reviews and meta-analyses) flow diagram and exclusion criteria

183x186mm (300 x 300 DPI)

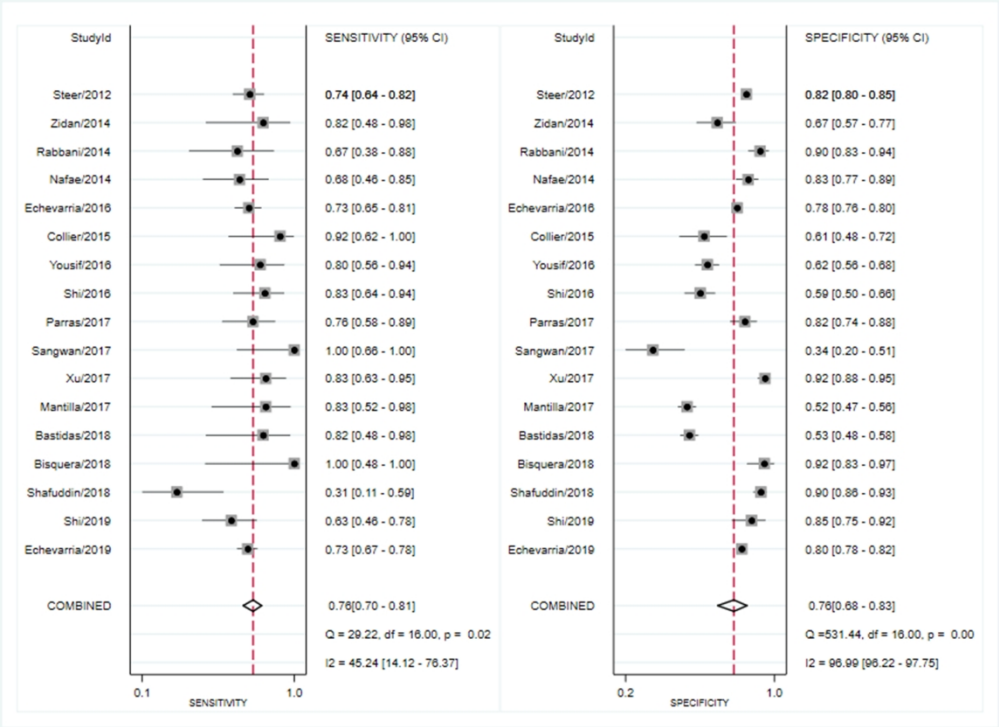

Figure 2: Forest plot of sensitivity and specificity of DECAF for the prediction of mortality in AECOPD.

296x215mm (300 x 300 DPI)

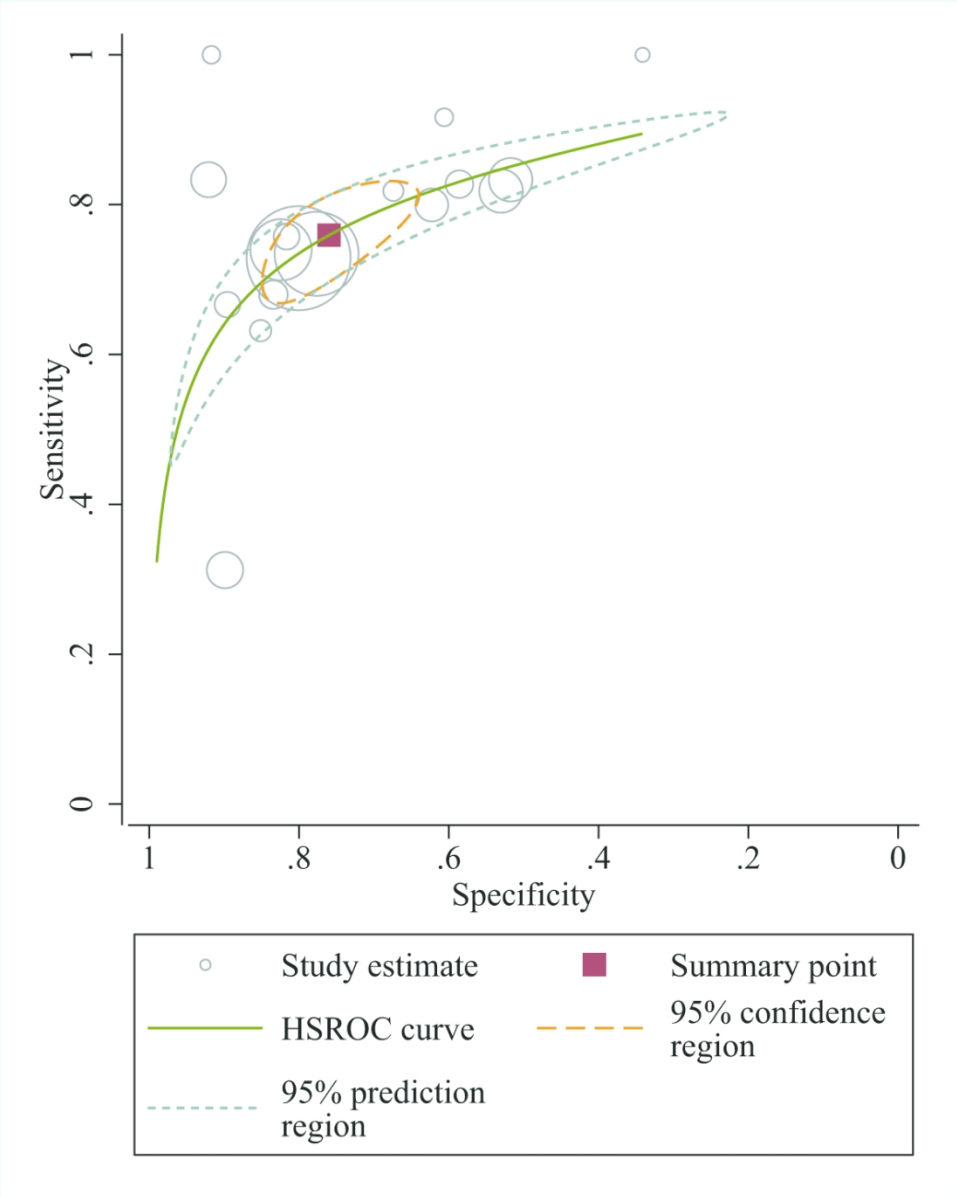

Figure 3: Hierarchical summary receiver operating characteristic curve for evaluating prognostic value of mortality of DECAF in AECOPD.
The HSROC curves was conducted which plots sensitivity versus specificity. All studies were presented as a circle and plotted with the HSROC curve. The summary point (red box) indicates that the summary sensitivity was 0.76 and the summary specificity was 0.76. The summary results are displayed as the 95% confidence region and 95% prediction region in the HSROC curve plot. The size of the marker is scaled according to the total number of patients in each study.

99x124mm (300 x 300 DPI)

Supplementary

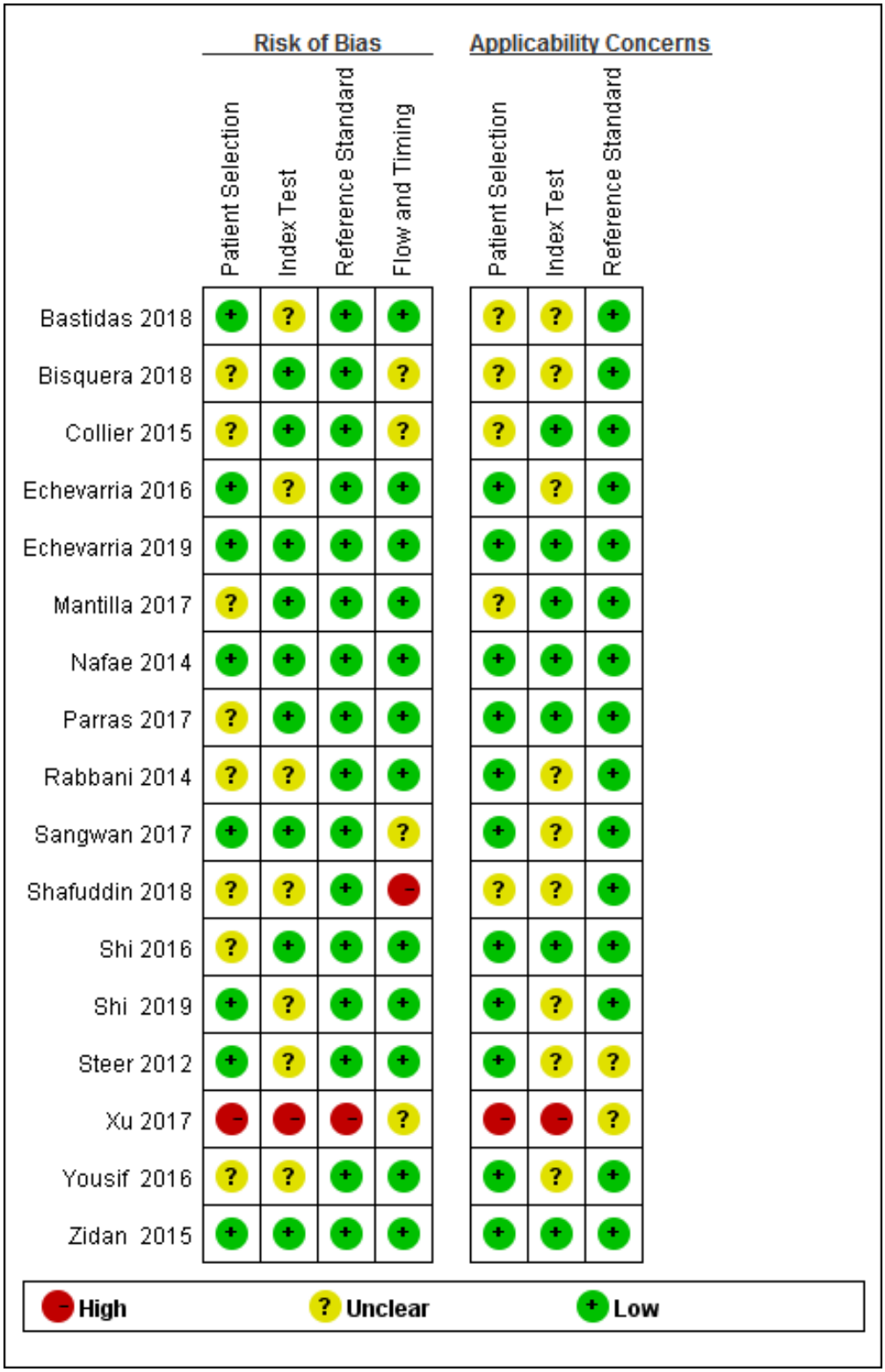

Figure S1: The quality evaluation and risk of bias in included studies.

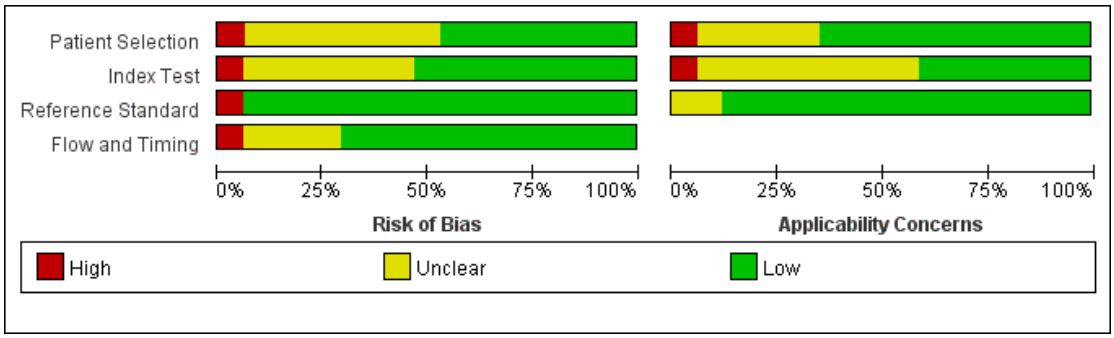

Figure S2: Methodological quality graph in included studies.

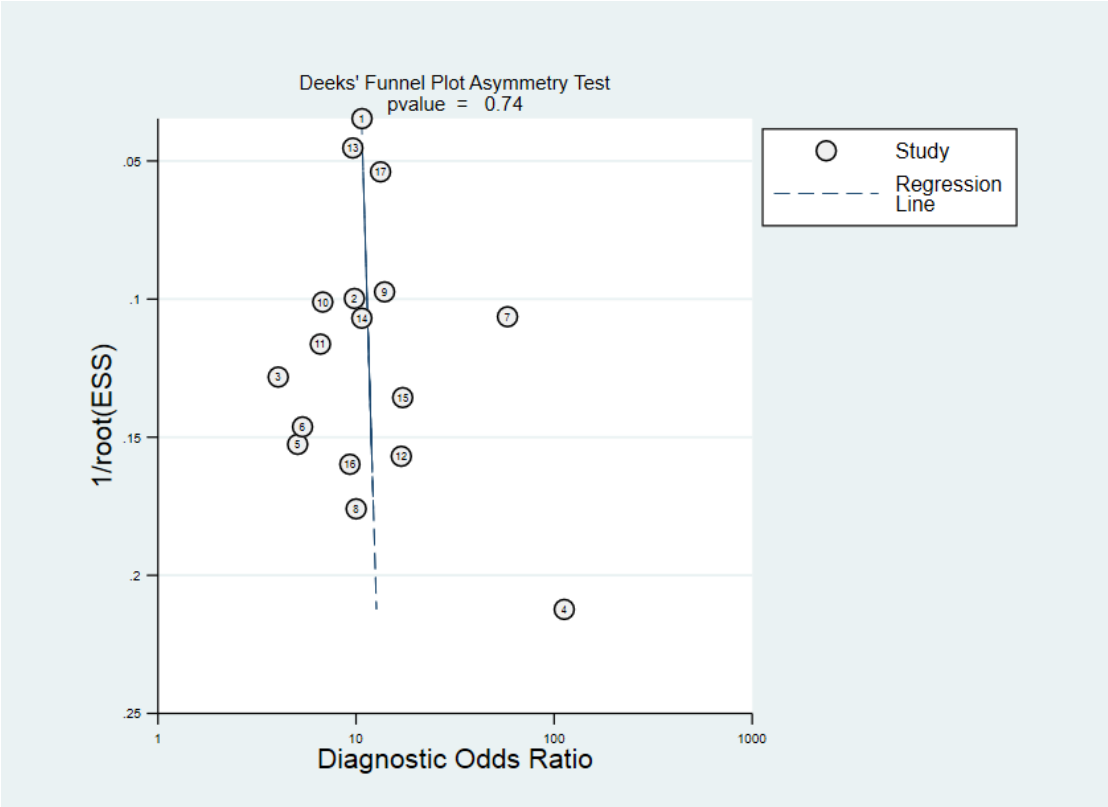

Figure S3: Deek's funnel plot asymmetry test for publication bias of studies evaluating the value of DECAF for the prognosis of AECOPD

.

Search Strategies

1. Pubmed

Search ((("Pulmonary Disease, Chronic Obstructive"[Mesh]) OR ((((((((((((COPD[Title/Abstract]) OR Chronic Obstructive Pulmonary Disease[Title/Abstract]) OR Chronic Airflow Obstructions[Title/Abstract]) OR Chronic Airflow Obstruction[Title/Abstract]) OR COAD[Title/Abstract]) OR Chronic Obstructive Airway Disease[Title/Abstract]) OR Airflow Obstruction, Chronic[Title/Abstract]) OR Airflow Obstructions, Chronic[Title/Abstract]) OR

Chronic Obstructive Lung Disease[Title/Abstract]) OR Chronic Obstructive Lung Disease[Title/Abstract]) OR airways obstruction[Title/Abstract]) OR obstructive lung disease[Title/Abstract]) OR emphysema[Title/Abstract]) OR bronchitis[Title/Abstract]))) AND ((DECAF score[Title/Abstract]) OR DECAF[Title/Abstract])

2. The Cochrane Library

#1 MeSH descriptor: [undefined] explode all trees
#2 (Chronic Obstructive Lung Disease):ti,ab,kw
#3 (Chronic Obstructive Pulmonary Disease):ti,ab,kw
#4 (COPD):ti,ab,kw
#5 (COAD):ti,ab,kw
#6 (Chronic Obstructive Airway Disease):ti,ab,kw
#7 (Airflow Obstruction, Chronic):ti,ab,kw
#8 (Chronic Airflow Obstruction):ti,ab,kw
#9 (Airflow Obstructions, Chronic):ti,ab,kw
#10 (Chronic Airflow Obstructions):ti,ab,kw
#11 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10
#12 MeSH descriptor: [Lung Diseases, Obstructive] explode all trees
#13 (Pulmonary Disease, Obstructive):ti,ab,kw
#14 (Obstructive Pulmonary Diseases):ti,ab,kw
#15 (Obstructive Lung Diseases):ti,ab,kw
#16 (Obstructive Lung Disease):ti,ab,kw
#17 (Lung Disease, Obstructive):ti,ab,kw
#18 (Pulmonary Diseases, Obstructive):ti,ab,kw
#19 (Obstructive Pulmonary Disease):ti,ab,kw
#20 #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19
#21 MeSH descriptor: [Pulmonary Emphysema] explode all trees
#22 (Emphysema, Centrilobular):ti,ab,kw
#23 (Centrilobular Emphysema):ti,ab,kw
#24 (Emphysemas, Pulmonary):ti,ab,kw
#25 (Emphysema, Pulmonary):ti,ab,kw
#26 (Pulmonary Emphysemas):ti,ab,kw
#27 (Emphysema, Panlobular):ti,ab,kw
#28 (Panlobular Emphysema):ti,ab,kw
#29 (Focal Emphysema):ti,ab,kw
#30 (Emphysema, Focal):ti,ab,kw
#31 #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30
#32 MeSH descriptor: [Bronchitis, Chronic] explode all trees
#33 (Chronic Bronchitis):ti,ab,kw
#34 #32 or #33
#35 #11 or #20 or #31 or #34
#36 MeSH descriptor: [Pulmonary Disease, Chronic Obstructive] explode all trees
#37 #35 or #36

#38 (DECAF):ti,ab,kw
#39 (DECAF score):ti,ab,kw
#40 #38 or #39
#41 #37 and #40

3. Web of Science (WOS)

1 TOPIC: (Pulmonary Disease, Chronic Obstructive) OR TOPIC: (COPD) OR TOPIC: (Chronic Obstructive Pulmonary Disease) OR TOPIC: (COAD) OR TOPIC: (Chronic Obstructive Airway Disease) OR TOPIC: (Chronic Obstructive Lung Disease) OR TOPIC: (Airflow Obstruction, Chronic) OR TOPIC: (Airflow Obstructions, Chronic) OR TOPIC: (Chronic Airflow Obstructions) OR TOPIC: (Chronic Airflow Obstruction) OR TOPIC: (Lung Diseases, Obstructive) OR TOPIC: (Lung Disease, Obstructive) OR TOPIC: (Obstructive Lung Disease) OR TOPIC: (Obstructive Lung Diseases) OR TOPIC: (Obstructive Pulmonary Diseases) OR TOPIC: (Obstructive Pulmonary Disease) OR TOPIC: (Pulmonary Disease, Obstructive) OR TOPIC: (Pulmonary Diseases, Obstructive) OR TOPIC: (Bronchitis, Chronic) OR TOPIC: (Chronic Bronchitis) OR TOPIC: (Pulmonary Emphysema) OR TOPIC: (Emphysema)
2 TOPIC: (DECAF) OR TOPIC: (DECAF score) OR TOPIC: (decaf score)
3 #2 AND #1

4. Embase

#5 #3 AND #4
#4 decaf:ab,ti OR 'decaf score':ab,ti
#3 #1 OR #2
#2 'chronic airflow obstruction':ab,ti OR 'chronic airway obstruction':ab,ti OR 'chronic obstructive bronchitis':ab,ti OR 'chronic obstructive bronchopulmonary disease':ab,ti OR 'chronic obstructive lung disorder':ab,ti OR 'chronic obstructive pulmonary disease':ab,ti OR 'chronic obstructive pulmonary disorder':ab,ti OR 'chronic obstructive respiratory disease':ab,ti OR copd:ab,ti OR 'lung chronic obstructive disease':ab,ti OR 'lung disease, chronic obstructive':ab,ti OR 'lung diseases, obstructive':ab,ti OR 'obstructive lung disease':ab,ti OR 'obstructive lung disease, chronic':ab,ti OR 'obstructive pulmonary disease':ab,ti OR 'obstructive respiratory disease':ab,ti OR 'obstructive respiratory tract disease':ab,ti OR 'pulmonary disease, chronic obstructive':ab,ti OR 'pulmonary disorder, chronic obstructive':ab,ti
#1 'chronic obstructive lung disease'/exp

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	page1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	page2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	page3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	page 3
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	page 4
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	page 4
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	page 4
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	page 4
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	page 4
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	page 4-5
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	page 5
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	page 5
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	page 5
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	page 5

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	page 5
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	page 5
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	page 5 and Fig. 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	page5, 7, 8
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	page6
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Page9-11
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Page9-11
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Page6 and Fig.S1
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	Page 10-11
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	Page12
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	Page13
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	Page14
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	Page14

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

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DECAF score as a mortality predictor for acute exacerbation of chronic obstructive pulmonary disease: a systematic review and meta-analysis

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Primary Subject Heading:	Respiratory medicine
Secondary Subject Heading:	Intensive care, Respiratory medicine
Keywords:	Adult intensive & critical care < INTENSIVE & CRITICAL CARE, RESPIRATORY MEDICINE (see Thoracic Medicine), Chronic airways disease < THORACIC MEDICINE

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DECAF score as a mortality predictor for acute exacerbation of chronic obstructive pulmonary disease: a systematic review and meta-analysis

Short title: DECAF score for patients with AECOPD

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Abstract

Objectives: This study was conducted to assess the association between DECAF scores (The Dyspnea, Eosinopenia, Consolidation, Acidemia, and Atrial Fibrillation) and the prognosis of patients with acute exacerbation of chronic obstructive pulmonary disease (AECOPD), and to evaluate the specific predictive and prognostic value of DECAF scores, and to explore the effectiveness of different cutoff values in risk stratification of AECOPD patients.

Design: Systematic review and meta-analysis.

Participants: Adult patients diagnosed with AECOPD (over 18 years of age).

Primary and secondary outcome measures: Electronic databases, including the Cochrane Library, PubMed, the EMBASE, and the WOS, and the reference lists in related articles were searched for studies published up to September 2019. The identified studies reported the prognostic value of DECAF scores in AECOPD patients.

Results: Seventeen studies involving 8329 participants were included in the study. Quantitative analysis demonstrated that elevated DECAF scores were associated with high mortality risk (WMD = 1.87; 95% CI: 1.19 – 2.56). In the accuracy analysis, DECAF scores showed good prognostic accuracy for both in-hospital and 30-day mortality [AUC: 0.83 (0.79 – 0.86) and 0.79 (0.76 – 0.83), respectively]. When the prognostic value was compared to that of other scoring systems, DECAF scores showed better prognostic accuracy and stable clinical values than the modified DECAF, CAPS, BAP-65, CURB-65 or APACHE II scores.

Conclusion: The DECAF score is an effective and feasible predictor for short-term mortality. As a specific and easily scored predictor for AECOPD patients, DECAF score is superior to other prognostic scores. The DECAF score can correctly identify most AECOPD patients as low risk, and with the increase of cutoff value, the risk stratification of DECAF score in high-risk population increases significantly.

Keywords: Dyspnoea, Eosinopenia, Consolidation, Acidaemia, and atrial Fibrillation (DECAF) score; early warning score; acute exacerbation of chronic obstructive pulmonary disease (AECOPD); meta-analysis; systematic review.

Strengths and limitations of this study

- This study not only evaluated the effectiveness of DECAF score on prognosis short-term mortality of AECOPD patients, but also explored the effectiveness of different cutoff values in risk stratification of AECOPD patients.
- In order to further evaluate the effectiveness of DECAF score, this study compared the prognostic effects of DECAF scores with other prognostic scores, such as APACHE II, BAP-65, and CURB-65.
- This study assessed DECAF scores by quantitative analysis and accuracy analysis.
- The data and analyses were difficult to obtain due to a lack of original studies reporting the value of DECAF scores for predicting long-term mortality and other adverse outcomes in AECOPD patients.
- Although we analyzed the source of heterogeneity through subgroup analysis, heterogeneity in the results should still be considered carefully.

Introduction

Acute exacerbation of chronic obstructive pulmonary disease (AECOPD) is characterized by the deterioration of respiratory symptoms beyond normal daily variations[1]. AECOPD accounts for one in eight hospital admissions[2] and is associated with worsening lung function, health-related quality of life, and mortality risk. The in-hospital mortality of AECOPD patients ranges from 4.4% to 25%. The survivors have a readmission rate of 25% to 55% and 25% to 50% of these patients have a high risk of death within one year[2, 3].

Prognostic score can provide a strong indicator for risk stratification and assist clinical management, including Hospital-at-Home or early supported discharge for low-risk groups, and early escalation or appropriate palliation for high-risk groups[4, 5]. The Dyspnea, Eosinopenia, Consolidation, Acidemia, and Atrial Fibrillation (DECAF) score is a risk stratification tool designed to predict risk of death in AECOPD patients[6], and can be easily applied at the bedside to guide treatment, such as hospital at home for low-risk patients[7]. The DECAF score using indices routinely available at admission. The score includes five predictors, the strongest of which is stable state dyspnea, measured by the extended Medical Research Council Dyspnea score (eMRCD; Table 1)[8]. The DECAF score showed promising performance in derivative studies, and was superior to other prognostic tools for AECOPD patients[6]. In 2014, the UK National COPD audit recommends that DECAF scores be recorded for AECOPD patients[9]. Subsequently, an increasing number of original studies conducted derivation, internal and external validation, and implementation of the DECAF score. The prognostic value of DECAF score still needs to be further verified by the methods of systematic review and meta-analysis, which is essential to prove the generalization of prognosis scores.

This systematic review and meta-analysis evaluated the association between DECAF scores and the prognosis of AECOPD patients, assessed the specific predictive and prognostic value of DECAF scores, and explored the effectiveness of different cutoff

values in risk stratification of AECOPD patients. To further assess the clinical value of DECAF scores, we compared the test to other commonly used prognostic scores,, including the modified DECAF (the Dyspnoea, Eosinopenia, Consolidation, Acidemia, and Frequency of admission in AECOPD in the last year)[10], CAPS (COPD and Asthma Physiology Score)[11], BAP-65 (BUN, Altered mental status, Pulse and age > 65)[12], CURB-65 (Confusion, Urea, Respiratory Rate, Blood pressure, and age > 65)[13], and APACHE II (Acute Physiology and Chronic Health Evaluation scoring system Ⅱ) scoring systems[14]. Although these scores are not designed or proposed for AECOPD, they are still commonly used in clinical practice for the prediction and prognostic evaluation of AECOPD patients. This study aimed to evaluate and validate the effectiveness of the DECAF score and improve the clinical course and outcome of AECOPD patients.

Materials and Methods

All methods of this systematic review and meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines[15].

Data Sources and Searches

The review authors searched for medical literature before September 2019. The research was conducted in electronic databases including the Cochrane Library, PubMed, the Excerpt Medica Database (Embase), the Web of Science (WOS), and the reference lists from review articles, irrespective of publication dates, status or language. The search was conducted with the following keywords: *DECAF Score or Dyspnea, Eosinopenia, Consolidation, Acidemia and Atrial Fibrillation Score and AECOPD or Acute Exacerbations of Chronic Obstructive Pulmonary Disease.* Search strategies used in the Cochrane Library, PubMed, Embase, and WOS can be found in the Supplement (Supplementary File: Search strategies).

This meta-analysis included studies that met the following criteria:

1. Adult patients diagnosed with AECOPD (over 18 years of age)

2. The studies included the results of DECAF score prognoses in patients with AECOPD. Study information could be extracted into a 2 × 2 contingency table. AECOPD was diagnosed based on the latest reference standard in the original study, such as the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guideline, which was defined as an acute event characterized by worsening of the patient's respiratory symptoms beyond normal day-to-day variations, leading to medication changes.

3. No publication date, status or language restrictions were applied. Clinical original articles were included, whereas secondary studies, conference abstracts, editorials, and animal experiments were excluded.

Study Selection

Two review authors (Q Huang and H Xiong) independently assessed the studies to be included based on the titles, abstracts, and keywords. If a study was found to be relevant to our topic, at least two reviewers further evaluated the full text to determine whether it met the inclusion criteria. In the case of inconsistencies between the reviewers, a third reviewer (J Liu) was consulted. The authors consulted the original authors to further ensure the eligibility of a study, when additional information on the details of the results and methods or allocation concealment was needed. A study diagram was prepared to illustrate the entire literature research process and the selection of the studies (Fig. 1).

Data Extraction and Quality Assessment

The data were independently extracted by two review authors (T Shuai and C Zhang) and the resulting differences were resolved by a third reviewer (C He). The extracted data included the lead author; publication year; the country of origin; the participant characteristics (age, sex, and mortality rate); the statements for collection of DECAF; the optimal cutoff threshold in original study; values for sensitivity, specificity, true-positive, true-negative, false-positive, false-negative; and the area (AUC) under the receiver operating characteristic (ROC) curve. If data were missing, a letter was written to the

authors to request the data. If there was no response to the letter after four weeks, an e-mail was sent. If there was no response to the e-mail, estimates were made based on available data and used.

Two review authors (J Liu and J Lu) independently applied the guidelines of the PRISMA statement[16] to evaluate each involved study. The Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) was conducted by two independent authors (J Liu and J Lu) to assess the quality and risk of bias for diagnostic or prognostic studies[17]. In case of any inconsistency, all authors reach an agreement through discussion. The quality and risk of bias were assessed from two perspectives, including bias risk and applicability concerns, and evaluated from four aspects, including patient selection, index test, reference standard, and flow and timing.

Data Synthesis and Analysis

This study used Stata SE 15.0 (Stata Corp; College Station, TX, USA) to analyze the extracted data. Continuous variables are expressed as weighted mean differences (WMD) with a 95% confidence interval (95% CI).

The mixed bivariate random-effects regression model was used to analyze and pool the diagnostic accuracy measurements across studies[18]. To derive summary estimates, we plotted estimates of the observed sensitivities and specificities for each test in forest plots and hierarchical summary receiver operating characteristic (HSROC) curves derived from individual study results[19, 20]. These results were plotted using HSROC curves with 95% confidence and prediction regions. Additionally, pooled sensitivity (SEN), specificity (SPE), diagnostic odds ratio (DOR), positive likelihood ratio (PLR), and negative likelihood ratio (NLR) were calculated[21]. The AUC was also calculated to show the prognostic performance of DECAF. In clinical practice, tests with AUC above 0.8 are considered to be very reliable[22].

The heterogeneity of eligible studies was assessed by the Cochrane Q test (significant heterogeneity was indicated by $P < 0.05$) and the I^2 test (significant

heterogeneity was indicated by I^2 > 50%)[23]. If substantive heterogeneity (I^2 > 50%) existed, subgroup analysis and sensitivity analysis were performed to analyze the sources of the heterogeneity. The α value was set to 0.05.

To assess the heterogeneity from the threshold effect, the Spearman correlation coefficient between the logit of sensitivity and the logit of (1−specificity) was computed to assess the threshold effect on the prognostic accuracy of DECAF score. If the Spearman correlation coefficient was greater than or equal to 0.6 ($p<0.05$), there was a threshold effect[24]. The Deek's funnel plot asymmetry test was used to assess for publication bias, when the included studies were greater than 10 studies [25].

Patient and public involvement

Patients and the public were not involved in the development of the research question, the outcome measures, the design or conduct of this systematic review. Patients and the public were not asked to advise on interpretation of results or to contribute to the writing or editing of this document.

Results

Study Selection

A flow chart of the study selection process (Fig. 1) was prepared according to the PRISMA guidelines. After reviewing the title and abstract, 35 articles were screened for full-text review. Among them, 18 articles failed to meet the inclusion criteria. Seventeen studies involving a total of 8329 participants met all of the criteria [6, 9, 26-40]. Among them, Echevarria et al.[26, 28] and Shi et al.[27, 29] each produced two articles from two different studies.

Study Characteristics

As for the AECOPD definition, all studies were defined by the GOLD criteria, which is defined as an acute event characterized by worsening of the patient's respiratory symptoms beyond normal day-to-day variations and leading to medication changes[41]. All

identified studies reported the results of DECAF scores for AECOPD prognosis. Among these studies, 15 studies reported the prognostic values of DECAF scores for in-hospital mortality[6, 9, 26, 28, 29, 31-40] and five studies reported 30-day mortality[27, 28, 30, 31, 33]. The cutoff threshold for each study was retrospectively determined based on the ROC curve. For in-hospital mortality, the results of five studies were based on a cutoff value of 4[9, 28, 35, 37, 39], four studies were based on a cutoff value of 3[6, 32, 36, 40], three studies were based on a cutoff value of 2[30, 33, 38], and the other three studies did not report a cutoff threshold[17, 22, 25]. With regard to the collection of DECAF score, eight studies collected the score on admission[9, 27, 30, 32-34, 38, 40], one reported that the collection was pre-specified in the original study protocol[26], one was collected within 24 hours after admission [35], one recorded DECAF score as part of routine practice[28], and the other six reported that the DECAF score was compiled based on admission data[6, 29, 31, 36, 37, 39]. As for other prognostic scores, five studies reported the prognostic value of CURB-65 scores[28, 30, 31, 33, 35], eight reported BAP-65 scores[28, 30, 31, 33-37], five reported APACHE Ⅱ scores[6, 27-29, 40], four reported CAPS scores[6, 28, 29, 40], and three reported the prognostic value of modified DECAF scores[9, 29, 37] for AECOPD patients. A summary of the characteristics of the included studies is shown in Table 2.

Methodological Quality and Risk of Bias

Only one study was a case-control design without blinding statements, which could not prevent the occurrence of observer bias, thus the risk of bias was related high [35]. All studies included patients diagnosed with AECOPD, and eight studies reported consecutive enrollment[6, 9, 26-28, 30, 34, 40]. Most of studies included did not pre-specify the cutoff value for risk stratification. Since the main outcome is the mortality of AECOPD patients, for which the reference standard is survival or non-survival, all included studies met the low-risk criteria of the reference standard items. However, the included studies yielded different baseline characteristics in the included population, which affected patient selection, flow, and timing. The quality and bias of each included studies was

shown in Table 3, and the summary figures of risk of bias were shown in Figs. S1 and S2.

The Quantitative Analysis of DECAF scores in AECOPD

Three studies referred to DECAF scores between the survivor group and the non-survivor group. The randomized effect model showed a significant increase in DECAF scores in the non-survivor group compared to the survivor group (WMD = 1.87; 95% CI: 1.19 – 2.56; $P < 0.001$) (Table 4). The results indicate that the elevated DECAF scores were associated with high mortality risk.

As shown in Table 4, four other scoring systems have been proven to indicate poor outcomes of AECOPD. Compared to the survivor group, the results showed that CURB-65 scores, BAP-65 scores, modified DECAF scores, and APACHE Ⅱ scores were increased in the non-survivor group (WMD = 0.69, 95% CI: -0.08 – 1.45, $P = 0.078$; WMD = 0.75, 95% CI: -0.07 – 1.56, $P = 0.071$; WMD = 1.74, 95% CI: 1.36 – 2.13, $P = 0.001$; WMD = 5.24, 95% CI: 4.00 – 6.47, $P < 0.001$, respectively). The results showed that increases in DECAF scores, modified DECAF scores, and APACHE Ⅱ scores were associated with a high risk of mortality in AECOPD, suggesting that DECAF scores have the potential to be a prognostic indicator for patients with AECOPD.

Prognostic Value of DECAF Scores for AECOPD

Seventeen studies reported the prognostic value of DECAF scores. The pooled sensitivity of DECAF scores for predicting mortality was 0.76 [95% CI, 0.70 – 0.81; $I^2 = 45.24\%$, $Q = 29.22$ ($P = 0.02$)] with a specificity of 0.76 [95% CI, 0.68 – 0.83; $I^2 = 96.99\%$, $Q = 531.44$ ($P < 0.001$); Fig. 2]. The PLR and NLR were 3.2 (95% CI, 2.4 – 4.1) and 0.32 (95% CI, 0.27 – 0.37), respectively, and the DOR was 10 (95% CI, 8 – 13). The AUC of the HSROC was 0.82 (95% CI, 0.78 – 0.85; Fig. 3), indicating that the DECAF score had a reliable accuracy in predicting mortality for AECOPD patients. Additionally, there was no significant difference in threshold effect (Spearman's correlation coefficient = 0.467;

$P = 0.059$). No publication bias was found in Deek's funnel plot asymmetry test ($P = 0.74$; Fig. S3).

Subgroup Analysis

In predicting in-hospital mortality, the pooled sensitivity of the DECAF scores was 0.77 (95% CI, 0.70 – 0.82; $I^2 = 47.24\%$, $P = 0.02$), the specificity was 0.76 (95% CI, 0.67 – 0.84; $I^2 = 96.5\%$, $P < 0.001$], and the AUC of the HSROC was 0.83 (95% CI, 0.79 – 0.86). For 30-day mortality, the pooled sensitivity of the DECAF scores was 0.71 (95% CI, 0.53 – 0.84; $I^2 = 84.95\%$, $P < 0.001$), the specificity was 0.75 (95% CI, 0.58 – 0.86; $I^2 = 98.37\%$, $P < 0.001$), and the AUC of the HSROC was 0.79 (95% CI, 0.76 – 0.83) (Table 5).

The subgroup analyses were based on different cutoff values (Table 5). For a cutoff value of 4, five studies included 2,550 participants reported the prognostic value of DECAF. The pooled sensitivity of the DECAF scores was 0.75 (95% CI, 0.69 – 0.81; $I^2 = 0.00\%$, $P = 0.61$), the specificity was 0.80 (95% CI, 0.68 – 0.89; $I^2 = 95.84\%$, $P < 0.001$], and the AUC of the HSROC was 0.76 (95% CI, 0.72 – 0.80), the PLR was 3.80 (95% CI, 2.20 – 6.60), and the NLR was 0.31 (95% CI, 0.23 – 0.41). Four studies included 1,361 participants reported the results of a cutoff value was 3. The pooled sensitivity was 0.77 (95% CI, 0.70 – 0.82; $I^2 = 0.00\%$, $P = 0.52$), the specificity was 0.76 (95% CI, 0.67 – 0.84; $I^2 = 29.09\%$, $P = 0.24$], the AUC of the HSROC was 0.83 (95% CI, 0.79 – 0.86), the PLR was 3.20 (95% CI, 2.40 – 4.40), and the NLR was 0.31 (95% CI, 0.25 – 0.37). For a cutoff value of 2, three studies included 1,002 participants reported the results. The pooled sensitivity was 0.84 (95% CI, 0.68 – 0.93; $I^2 = 0.00\%$, $P = 0.52$), the specificity was 0.53 (95% CI, 0.50 – 0.56; $I^2 = 0.00\%$, $P = 0.61$], the AUC of the HSROC was 0.77 (95% CI, 0.73 – 0.80), the PLR was 1.80 (95% CI, 1.50 – 2.10), and the NLR was 0.31 (95% CI, 0.15 – 0.64). The results of PLR and NLR at different cutoff values suggest that DECAF score can correctly identify most of AECOPD patients as low risk, and with the

increase of cutoff value, the risk stratification of DECAF score for high-risk population increased significantly.

Other Prognostic Scores for Patients with AECOPD

In predicting the in-hospital mortality of patients with AECOPD, the pooled results showed that the sensitivity, specificity, and AUC of the CURB-65 scores were 0.46, 0.92, and 0.73, respectively. The sensitivity, specificity, and AUC of the BAP-65 scores were 0.70, 0.50, and 0.64, respectively. The sensitivity, specificity, and AUC of the APACHE Ⅱ scores were 0.70, 0.65, and 0.72, respectively. The sensitivity, specificity, and AUC of CAPS scores were 0.77, 0.62, and 0.75, respectively, and the sensitivity, specificity, and AUC of the m-DECAF scores were 0.84, 0.62, and 0.84, respectively (Table 6).

When predicting the 30-day mortality in COPD patients, the pooled results showed that the sensitivity, specificity, and AUC of the CURB-65 scores were 0.52, 0.85, and 0.53, respectively. The sensitivity, specificity, and AUC of the BAP-65 scores were 0.61, 0.57, and 0.62, respectively. The sensitivity, specificity, and AUC of the APACHE Ⅱ scores were 0.68, 0.73, and 0.77, respectively (Table 7).

Discussion

In stable COPD, prognostic indicators have been thoroughly investigated and tools to predict mortality risk, such as the BODE Score[41], have been well established. However, prognostic studies in patients with exacerbation requiring hospitalization are limited and the predictors of mortality between stable disease periods and AECOPD periods seem to have little in common[42]. In addition, the risk of mortality in AECOPD patients is much higher than in patients with stable COPD. Thus, there is an urgent need for effective reliable clinical tools that can be used to inform clinicians and patients of the risk of death during exacerbation.

The current study conducted a systematic review and meta-analysis to characterize and evaluate DECAF scores predicting mortality in patients with AECOPD. Six potential scoring systems were evaluated by comparing survivor and non-survivor scores and

prognostic accuracy. Quantitative analysis demonstrated that elevated DECAF scores were significantly associated with high mortality risk. In other potential scoring systems, compared with the survivor group, the results showed that only the modified DECAF and APACHE Ⅱ scores increased in the non-survivor group. In the accuracy analysis, DECAF scores showed a reliable prognostic accuracy for both in-hospital and 30-day mortality. When the prognostic value was compared with other prognostic scores, DECAF scores showed better prognostic accuracy and stable clinical value in predicting the in-hospital mortality and 30-day mortality of patients with AECOPD. The results showed that for the different cutoff values of DECAF score, as the cutoff value increased, the sensitivity decreased and the specificity escalated. The results of PLR and NLR at different cutoff values suggest that DECAF score can correctly identify most AECOPD patients as low risk, and with the increase of cutoff value, the risk stratification of DECAF score for high-risk population increased significantly.

The DECAF scores increased significantly in the non-survivor group. This suggests that elevated DECAF scores have the potential to stratify a high-risk population from low-risk patients. The modified DECAF and APACHE Ⅱ scores had a similar relationship, which indicates that scoring systems have potential to aid clinical decisions in risk stratification. However, the CURB-65 and BAP-65 scores did not show statistical differences between the survivor and non-survivor groups. Although studies have shown that CURB-65 and BAP-65 can be effective tools for predicting mortality[43], based on the results of this current study, we speculate that the potential prognostic value of CURB-65 and BAP-65 is relatively low.

The DECAF score is an effective predictor of mortality and can be easily scored at the bedside using indices routinely available at admission[6]. In clinical practice, test with AUC greater than 0.8 is considered to be very reliable[22]. The results showed that the AUC of the DECAF scores was 0.83 for predicting in-hospital mortality and 0.79 for short-

term mortality (30-day). This indicates that the DECAF test can be utilized as a promising prognosis tool with satisfactory sensitivity and specificity for AECOPD patients.

In a randomized controlled trial and economic evaluation study of DECAF implementation, the low-risk patients (DECAF 0 or 1) selected by DECAF were more cost-effective than the usual care, mainly manifested in a 5-fold reduction in the median of 90 days of hospitalization[7]. The study showed that the DECAF score was easily applied at the bedside to guide treatment, and about twice as many patients were eligible compared with earlier models[7]. It was safe, clinically effective, cost-effective to use DECAF score at home in low-risk patients, and preferred by most patients[7].

Mortality rates vary between clinical settings and cohorts. In this study, the mortality rate of patients in the included studies ranged from 2.38% to 33.93%. This largely reflects differences in baseline characteristics, especially in the proportion of patients admitted from institutional care and with coexisting pneumonia[12, 28]. In addition, this also partly leads to choosing different cutoff values. To illustrate the relationship between the cutoff values for risk stratification, subgroup analyses were performed. For cutoff values from 2 to 4, the sensitivity decreased from 0.84 to 0.75 and the specificity increased from 0.53 to 0.80. With an increase in the cutoff value, specificity increased significantly. Under the premise of ensuring sensitivity, improving specificity can effectively reduce the number of false positives and improve the clinical application value of a prognostic score.

In clinical practice, the greater the PLR value, the greater the likelihood of true positive when the test result is positive; the smaller the NLR value, the greater the likelihood of true negative when the test result is negative. PLR is more important in stratification of high-risk groups, while NLR is more important in low-risk groups. From the results, the NLR was very small, 0.31, which indicated that the DECAF score could correctly identify most AECOPD patients as a low-risk group. For the cutoff value from 2 to 4, the PLR value increased from 1.80 to 3.80, indicating that with the increase of the

cutoff value, the risk stratification of the DECAF score in high-risk groups increased significantly.

The CURB-65 and BAP-65 tests can also be easily scored on admission[44]. However, according to the results of this study, the CURB-65 and BAP-65 scores had low prognostic value for predicting in-hospital and 30-day mortality, which were consistent with the lack of statistical difference in CURB-65 and BAP-65 scores between survivors and non-survivors.

APACHE II uses point scores based on the initial values of 12 routine physiological measurements, age, and previous health status to provide a general measure of disease severity[45]. APACHE II is not a specific predictor for AECOPD but is still commonly used in clinical practice to predict mortality in AECOPD patients[46]. Based on our results, APACHE II scores showed no superiority to DECAF scores in prognostic accuracy, sensitivity or specificity. In addition, it contains cumbersome test items, thus increasing the workload of clinicians in clinical practice. For AECOPD patients, the APACHE II test may not be the preferred early warning scoring system.

As for the modified DECAF, Zidan et al.[9] attempted to replace the atrial fibrillation item in the DECAF test with admission frequency for AECOPD during the last year and named the revision the modified DECAF. They concluded that the modified DECAF test was more sensitive and specific in predicting in-hospital mortality during acute exacerbation of COPD than the DECAF test. However, there was no significant difference between the two scores[9], which was consistent with the results of this current study. In addition, only three studies reported the predictive value of modified DECAF test for in-hospital mortality in AECOPD patients, and no study reported the effectiveness of the test in terms of 30-day mortality. Therefore, more evidence is needed to evaluate the prognostic value of modified DECAF scores and further compare the clinical value between DECAF scores and modified DECAF scores.

Examination of prognostic scores can contribute to clinical management, early risk-stratification, and the prevention of poor outcomes, as well as monitoring during treatment[47]. Clinicians are constantly seeking predictors of mortality for patients with AECOPD. As a promising predictor, DECAF scores can be used in a variety of hospital settings to accurately stratify mortality risk. As a specific and easily scored predictor for AECOPD patients, DECAF is superior to other prognostic scores in predicting short-term mortality. From the results of different cutoff values, the DECAF score showed a promising potential. It can correctly identify most AECOPD patients as low-risk group, which is related to the reduction of in-hospital stay. Compared to the meta-analyses of interventions, including randomized controlled trials, those including diagnostic studies have more publication bias[48]. Excluding studies that do not have sufficient data may lead to publication and reporting bias. Therefore, the prognostic value of DECAF may be overestimated. As for the significant degree of heterogeneity, we conducted a subgroup analysis to explore the source of the heterogeneity. The subgroup analysis revealed that the heterogeneity was mainly derived from the choice of cutoff value. When the cutoff value was 2, 3 or 4, the heterogeneity of sensitivity decreased to 0. However, the heterogeneity of specificity was still substantive when the cutoff value was 4. This largely reflect differences in the baseline characteristics of the patient selection. The biases between included studies can also lead to heterogeneity. The DECAF score needs to be collected at admission or pre-specified in the original study protocol. However, the collection of DECAF score varied between the included studies, which may result in variable performance of DECAF. In addition, different included studies yielded different baseline characteristics in the included population, which affected patient selection and also led to the different selection of cutoff value between studies.

This meta-analysis had some limitations. Firstly, the data and analyses were difficult to obtain due to a lack of original studies reporting the value of DECAF scores for predicting long-term mortality and other adverse outcomes in AECOPD patients.

Further studies are needed for validation. Secondly, it was difficult to obtain raw data for each of the included studies, which limited us to determining the optimal DECAF cutoff point for predicting AECOPD. Thirdly, because of the lack of original research comparing DECAF with other predictive scores, we can only compare the predictive value of DECAF and other predictive scores to AECOPD patients in general. With the increase of related original research, it is possible to further explore the effectiveness of different prognostic scores in risk stratification of AECOPD patients. In addition, although the source of heterogeneity was analyzed by subgroup analysis, heterogeneity in the results should still be considered carefully.

Conclusion

In conclusion, the results of this systematic review and meta-analysis indicated that the DECAF score was an effective and feasible predictor of short-term mortality in patients with AECOPD. As a specific and easily scored predictor for AECOPD patients, DECAF scores are superior to other prognostic scores. The DECAF score can correctly identify most AECOPD patients as low risk, and with the increase of cutoff value, the risk stratification of DECAF score for high-risk population increased significantly.

List of abbreviations

AECOPD: acute exacerbation of chronic obstructive pulmonary disease; DECAF: Dyspnoea, Eosinopenia, Consolidation, Acidaemia, and atrial Fibrillation score; the modified DECAF: the Dyspnoea, Eosinopenia, Consolidation, Acidaemia and Frequency of admission in AECOPD in the last year; CAPS: COPD and Asthma Physiology Score; BAP-65: BUN, Altered mental status, Pulse and Age > 65; CURB-65: Confusion, Urea, Respiratory Rate, Blood pressure, Age > 65; APACHE II: acute physiology and chronic health evaluation scoring system Ⅱ scores; QUADAS-2: the Quality Assessment of Diagnostic Accuracy Studies-2; WOS: web of science; WMD: weighted mean difference;

AUC: the area under the receiver operating characteristic curve; PRISMA: the preferred reporting items for systematic reviews and meta-analyses; PLR: positive likelihood ratio; NLR: negative likelihood ratio; DOR: diagnostic odds ratio; HSROC: hierarchical summary receiver operating characteristic; CIs: confidence intervals;

Additional Information

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Competing interests

The authors each individually and collectively declare there are no competing interests.

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Data sharing statement

All data generated or analyzed during this study are included in this published article and its supplementary information files, and no unpublished data are available.

References

1. Rodriguez-Roisin R. Toward a consensus definition for COPD exacerbations. Chest. 2000;117(5 Suppl 2):398s-401s.

2. Johannesdottir SA, Christiansen CF, Johansen MB, et al. Hospitalization with acute exacerbation of chronic obstructive pulmonary disease and associated health resource utilization: a population-based Danish cohort study. Journal of medical economics 2013;16:897-906.

3. de Miguel-Diez J, Jimenez-Garcia R, Hernandez-Barrera V, et al. Trends in hospital admissions for acute exacerbation of COPD in Spain from 2006 to 2010. Respiratory medicine 2013;107:717-23.

4. Wildman MJ, Sanderson C, Groves J, et al. Predicting mortality for patients with exacerbations of COPD and Asthma in the COPD and Asthma Outcome Study (CAOS). QJM : monthly journal of the Association of Physicians 2009;102:389-99.

5. Doll H, Miravitlles M. Health-related QOL in acute exacerbations of chronic bronchitis and chronic obstructive pulmonary disease: a review of the literature. PharmacoEconomics 2005;23:345-63.

6. Steer J, Gibson J, Bourke SC. The DECAF Score: predicting hospital mortality in exacerbations of chronic obstructive pulmonary disease. Thorax 2012;67:970-6.

7. Echevarria C, Gray J, Hartley T, et al. Home treatment of COPD exacerbation selected by DECAF score: a non-inferiority, randomised controlled trial and economic evaluation. Thorax 2018; 73:713-22.

8. Steer J, Norman EM, Afolabi OA, et al. Dyspnoea severity and pneumonia as predictors of in-hospital mortality and early readmission in acute exacerbations of COPD. Thorax 2012;67:117-21.

9. Stone RA, Holzhauer-Barrie J, Lowe D, et al. COPD: Who cares matters. National Chronic Obstructive Pulmonary Disease (COPD) Audit Programme: Clinical audit of COPD exacerbations admitted to acute units in England and Wales 2014, 2015.

10. Zidan MH, Rabie AK, Megahed MM, et al. The usefulness of the DECAF score in predicting hospital mortality in Acute exacerbations of chronic obstructive pulmonary disease. Egyptian Journal of Chest Diseases and Tuberculosis 2015;64:75-80.

11. Wildman MJ, Harrison DA, Welch CA, et al. A new measure of acute physiological derangement for patients with exacerbations of obstructive airways disease: the COPD and Asthma Physiology Score. Respiratory medicine 2007;101:1994-2002.

12. Shorr AF, Sun X, Johannes RS, et al. Validation of a novel risk score for severity of illness in acute exacerbations of COPD. Chest 2011;140:1177-83.

13. Lim WS, van der Eerden MM, Laing R, et al. Defining community acquired pneumonia severity on presentation to hospital: an international derivation and validation study. Thorax 2003;58:377-82.

14. Jacobs S, Chang RW, Lee B. One year's experience with the APACHE II severity of disease classification system in a general intensive care unit. Anaesthesia 1987;42:738-44.

15. Ge L, Tian JH, Li YN, et al. Association between prospective registration and overall reporting and methodological quality of systematic reviews: a meta-epidemiological study. Journal of clinical epidemiology 2018;93:45-55.

16. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. Journal of clinical epidemiology 2009;62:e1-34.

17. Whiting PF, Rutjes AW, Westwood ME, et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. Annals of internal medicine 2011;155:529-36.

18. Kim KW, Lee J, Choi SH, et al. Systematic Review and Meta-Analysis of Studies Evaluating Diagnostic Test Accuracy: A Practical Review for Clinical Researchers-Part I. General Guidance and Tips. Korean J Radiol 2015;16:1175-87.

19. Lee J, Kim KW, Choi SH, et al. Systematic Review and Meta-Analysis of Studies Evaluating Diagnostic Test Accuracy: A Practical Review for Clinical Researchers-Part II. Statistical Methods of Meta-Analysis. Korean J Radiol 2015;16:1188-96.

20. Rutter C M., Gatsonis C A. A hierarchical regression approach to meta-analysis of diagnostic test accuracy evaluations. Stat Med 2001, 20:2865-84.

21. Chu H, Cole SR. Bivariate meta-analysis of sensitivity and specificity with sparse data: a generalized linear mixed model approach. J Clin Epidemiol 2006;59:1331–1332.

22. Memon MA, Faryal S, Brohi N, et al. Role of the DECAF Score in Predicting In-hospital Mortality in Acute Exacerbation of Chronic Obstructive Pulmonary Disease. Cureus 2019;11:e4826.

23. Higgins J, Green S. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0. Cochrane Collaboration; 2008.

24. Deville WL, Buntinx F, Bouter LM, et al. Conducting systematic reviews of diagnostic studies: didactic guidelines. BMC Med Res Methodol 2002;2:9.

25. Deeks JJ, Macaskill P, Irwig L. The performance of tests of publication bias and other sample size effects in systematic reviews of diagnostic test accuracy was assessed. J Clin Ep- idemiol 2005;58:882–893.

26. Echevarria C, Steer J, Bourke SC. Comparison of early warning scores in patients with COPD exacerbation: DECAF and NEWS score. Thorax 2019;74:941-6.

27. Shi QF, Sheng Y, Zhu N, et al. The v-DECAF score can predict 90-day all-cause mortality in patients with COPD exacerbation requiring invasive mechanical ventilation. The clinical respiratory journal 2019.

28. Echevarria C, Steer J, Heslop-Marshall K, et al. Validation of the DECAF score to predict hospital mortality in acute exacerbations of COPD. Thorax 2016;71:133-40.

29. Shi QF, Sheng Y, Wang SY. Comparison of four score modes in prognosis assessment of AECOPD patients with respiratory failure. Journal of Practical Medicine 2017; 33: 242-5

30. Bastidas AR, Hincapie Diaz G, Mantilla Cardozo B, et al. Validity CURB 65, BAP 65, DECAF for predicting outcomes in exacerbation of COPD. American Journal of Respiratory and Critical Care Medicine 2018;197.

31. Shafuddin E, Chang CL, Hancox RJ. Comparing severity scores in exacerbations of chronic obstructive pulmonary disease. The clinical respiratory journal 2018;12:2668-75.

32. Bisquera RR, Cruz BOD. Prognostic utility of the DECAF score to predict in-hospital mortality among patients with acute exacerbation of chronic obstructive pulmonary disease admitted at Chinese general hospital. Respirology 2018;23:128-9.

33. Mantilla BM, Ramírez CA, Valbuena S, et al. Saturación de oxígeno/fracción inspirada de oxígeno como predictor de mortalidad en pacientes con exacerbación de EPOC atendidos en el Hospital Militar Central. Acta Medica Colombiana 2017;42:215-23.

34. Sangwan V, Chaudhry D, Malik R. Dyspnea, Eosinopenia, Consolidation, Acidemia and Atrial Fibrillation Score and BAP-65 Score, Tools for Prediction of Mortality in Acute Exacerbations of Chronic Obstructive Pulmonary Disease: A Comparative Pilot Study. Indian journal of critical care medicine : peer-reviewed, official publication of Indian Society of Critical Care Medicine 2017;21:671-7.

35. Xu MM, Yu SY, Zhang TT. Evaluation of the three scores to assess the severity of chronic obstructive pulmonary disease exacerbation. Journal of Tianjin Medical University 2017; 23:530-3.

36. Parras AMV, Bautista CL, Chica GP, et al. Evaluation of DECAF, CURB-65 and BAP-65 scales as predictor of mortality risk in acute exacerbation of COPD in a retrospective cohort. European Respiratory Journal 2017;50.

37. Yousif M, El Wahsh RA. Predicting in-hospital mortality in acute exacerbation of COPD: Is there a golden score? Egyptian Journal of Chest Diseases and Tuberculosis 2016;65:579-84.

38. Collier L, David T, Craig C, et al. PRACTICAL USE OF THE DECAF SCORE: CAN WE IMPROVE OUTCOMES IN ACUTE EXACERBATION OF COPD ADMISSIONS? Thorax 2015;70:A98-A.

39. Rabbani B, Brammer P. CAN THE DECAF SCORE BE USED TO GUIDE PROGNOSIS AFTER AN ACUTE ADMISSION FOR COPD EXACERBATION? Thorax 2014;69:A139-A40.

40. Nafae R, Embarak S, Gad DM. Value of the DECAF score in predicting hospital mortality in patients with acute exacerbation of chronic obstructive pulmonary disease admitted to Zagazig University Hospitals, Egypt. Egyptian Journal of Chest Diseases and Tuberculosis 2015;64:35-40.

41. Celli BR, Cote CG, Marin JM, et al. The body-mass index, airflow obstruction, dyspnea, and exercise capacity index in chronic obstructive pulmonary disease. The New England journal of medicine 2004;350:1005-12.

42. Steer J, Gibson GJ, Bourke SC. Predicting outcomes following hospitalization for acute exacerbations of COPD. QJM : monthly journal of the Association of Physicians 2010;103:817-29.

43. Shorr AF, Sun X, Johannes RS, et al. Predicting the need for mechanical ventilation in acute exacerbations of chronic obstructive pulmonary disease: comparing the CURB-65 and BAP-65 scores. Journal of critical care 2012;27:564-70.

44. Patil SP, Krishnan JA, Lechtzin N, et al. In-hospital mortality following acute exacerbations of chronic obstructive pulmonary disease. Archives of internal medicine 2003;163:1180-6.

45. Mach K. [Staphylococcus epidermidis infection. Results of three groups evaluated according to APACHE II--severity of disease classification system--with reference to risk, mortality and prognosis]. Wiener klinische Wochenschrift 1992;104:540-2.

46. Akhter S, Warraich UA, Ghazal S, et al. Assessment and comparison of APACHE II (Acute Physiology and Chronic Health Evaluation), SOFA (Sequential Organ Failure

Assessment) score and CURB 65 (Confusion; Urea; Respiratory Rate; Blood Pressure), for prediction of inpatient mortality in Acute Exacerbation of Chronic Obstructive Pulmonary Disease. JPMA The Journal of the Pakistan Medical Association 2019;69:211-5.

47. Costello RW, Cushen B. A risk stratification tool for exacerbations of COPD: time to switch to DECAF. Thorax 2016;71:489-90.

48. Irwig L, Macaskill P, Glasziou P, et al. Meta-analytic methods for diagnostic test accuracy. Journal of clinical epidemiology 1995;48:119-30.

Authors' contributions

The authors Jian Liu, Qiangru Huang, Chengying He, Meng Zhang, Chuchu Zhang, Huaiyu Xiong and Tiankui Shuai participated in the design of the project, conducted the literature review, and participated in the analysis. The authors Qiangru Huang, Yalei Wang wrote this paper. The authors Lei Zhu and Jiaju Lu were responsible for the statistical analysis and participated in data interpretation. The author Jian Liu was the principal investigator for the project. All authors approved the final version of the article.

Table 1. DECAF score

Variables	Score
Dyspnea	1
eMRCD 5a (too breathless to leave the house unassisted but independent in washing and/or dressing)	1
eMRCD 5b (too breathless to leave the house unassisted and requires help with washing and dressing)	2
Eosinopenia (eosinophils <0.05×109/L)	1
Consolidation	1
Moderate or severe acidemia (pH <7.3)	1
Atrial fibrillation (including history of paroxysmal atrial fibrillation)	1
Maximum DECAF score	6

DECAF: dyspnea, eosinopenia, consolidation, acidemia, and atrial fibrillation; eMRCD, extended Medical Research Council dyspnea score

Table 2. Characteristics of included studies

Author/Year	Study Inception (Year)	Country	Study design	Sample size	Male	Age (years)	Mortality (%)	Measured time	Collection of DECAF	DECAF Cutoff value	Early warning scores
Echevarria 2019	NA	UK	PC	2645	1217	73.10	8.62	in-hospital	Pre-specified in the original study protocol	NA	DECAF
Shi 2019	2016.1-2017.12	China	PC	112	73	77.57	33.93	28d	At admission	3	DECAF
Bastidas 2018	NA	Colombia	PC	462	229	79.00	2.38	30d	At admission	2	DECAF, BAP-65 and CURB-65
Shafuddin 2018	2006.7-2007.7 2012.8-2013.7	New Zealand	RC	423	190	71.00	4.49 7.33	in-hospital 30d	Compiled by admission data	NA	DECAF, CURB-65, CRB-65, and BAP-65
Bisquera 2018	NA	Philippines	PC	77	68	72.50	6.49	in-hospital	At admission	3	DECAF
Mantilla 2017	2014.2-2017.1	Colombia	PC	462	233	79.00	2.60 5.84	in-hospital 30d	At admission	2	DECAF, BAP-65 and CURB-65
Sangwan 2017	NA	India	PC	50	43	61.20	18.00	in-hospital	At admission	NA	DECAF and BAP-65
Xu 2017	2014.1-2016.1	China	CC	302	150	75.50	7.95	28d	Within 24h after admission	4	DECAF, BAP-65 and CURB-65
Parras 2017	NA	Spain	RC	164	153	76.14	20.12	in-hospital	Compiled by admission data	3	DECAF
Shi 2016	2014.1-2016.6	China	RC	186	108	66.20	15.59	in-hospital	Compiled by admission data	3	DECAF, m-DECAF, CAPS and APACHE Ⅱ
Yousif 2016	2014.1-2015.9	Egypt	R&PC	264	176	63.61	7.58	in-hospital	Compiled by admission data	4	DECAF, m-DECAF and BAP-65
Echevarria 2016	2012.1-2014.5	UK	R&PC	1725	788	73.10	7.65 28.35	in-hospital 30d	Recorded as routine practice	3	DECAF, CAPS, APACHE Ⅱ, CURB-65 and BAP-65
Zidan 2015	NA	Egypt	PC	100	58	46.46	11.00	in-hospital	At admission	4	DECAF and m-DECAF
Collier 2015	2014.12-2015.3	UK	PC	78	47	72.70	15.38	in-hospital	At admission	2	DECAF
Rabbani 2014	2012.12-2013.1	UK	RC	159	92	72.14	9.43	30d	Compiled by admission data	4	DECAF

Nafae 2014	2010.10-2013.4	Egypt	PC	200	102	68.50	12.50	in-hospital	At admission	3	DECAF, CAPS and APACHE Ⅱ
Steer 2012	2008.12-2010.6	UK	PC	920	424	73.10	10.43	in-hospital	Compiled by admission data	3	DECAF, CAPS and APACHE Ⅱ

Abbreviations: PC, prospective cohort; RC, retrospective cohort; R&PC, retrospective and prospective cohort; CC, case-control; NA, not available.

Table 3 The Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) for included studies

Studies	Patient Selection				Index Test			Reference Standard			Flow and Timing				Scores
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
Echevarria 2019	Y	Y	U	Low	Y	Y	Low	Y	U	Low	Y	Y	Y	Low	12
Shi 2019	Y	Y	Y	Low	Y	U	Unclear	Y	U	Low	U	Y	Y	Low	10
Bastidas 2018	U	Y	U	Unclear	Y	U	Unclear	Y	U	Low	Y	Y	Y	Low	8
Shafuddin 2018	U	Y	Y	Unclear	Y	U	Unclear	Y	U	Low	Y	Y	N	High	7
Bisquera 2018	U	Y	U	Unclear	Y	U	Low	Y	U	Low	Y	Y	U	Unclear	7
Mantilla 2017	U	Y	U	Unclear	Y	U	Low	Y	U	Low	Y	Y	Y	Low	9
Sangwan 2017	Y	Y	Y	Unclear	Y	U	Low	Y	U	Low	Y	Y	U	Unclear	9
Xu 2017	U	N	Y	High	N	U	High	Y	N	High	U	Y	Y	Unclear	4
Parras 2017	U	Y	Y	Unclear	Y	U	Low	Y	U	Low	U	Y	Y	Low	9
Shi 2016	U	Y	Y	Unclear	Y	U	Low	Y	Y	Low	U	Y	Y	Low	10
Yousif 2016	U	Y	Y	Unclear	Y	U	Unclear	Y	U	Low	U	Y	Y	Low	8
Echevarria 2016	Y	Y	Y	Low	Y	U	Low	Y	Y	Low	Y	Y	Y	Low	13
Zidan 2015	Y	Y	Y	Unclear	Y	U	Low	Y	U	Low	Y	Y	Y	Low	12
Collier 2015	U	Y	U	Unclear	Y	U	Low	Y	U	Low	U	Y	U	Unclear	6
Rabbani 2014	U	Y	U	Unclear	U	U	Unclear	Y	U	Low	U	Y	Y	Low	6
Nafae 2014	Y	Y	Y	Low	Y	U	Low	Y	U	Low	Y	Y	Y	Low	12
Steer 2012	Y	Y	Y	Low	Y	U	Unclear	Y	U	Low	Y	Y	Y	Low	11

Y = Yes, represents certain answer for the corresponding question; N = no, represents negative answer for the corresponding question; U = unclear, i.e. the information provided in the individual studies was insufficient to answer the corresponding question. QUADAS-2 criteria: 1. Was a consecutive or random sample of patients enrolled? 2. Was a case-control design avoided? 3. Did the study avoid inappropriate exclusions? 4. Could the selection of patients have introduced bias? 5. Were the index test results interpreted without knowledge of the results of the reference standard? 6. If a threshold was used, was it pre-specified? 7. Could the conduct or interpretation of the index test have introduced bias? 8. Is the reference standards likely to correctly classify the target condition? 9. Were the reference standard results interpreted without knowledge of the results of the index tests? 10. Could the reference standard, its conduct, or its interpretation have introduced bias? 11. Was there an appropriate interval between index test and reference standard? 12. Did all patients receive the same reference standard? 13. Were all patients included in the analysis? 14. Could the patient flow have introduced bias?

Table 4. The Quantitative Analysis of scores in AECOPD mortality

Variables	Studies, No.	Patients, No.	WMD	95%CI	P value
DECAF	3	600	1.87	1.19-2.56	<0.001
CURB-65	2	414	0.69	-0.08-1.45	0.078
BAP-65	2	414	0.75	-0.07-1.56	0.071
Modified DECAF	2	298	1.74	1.36-2.13	0.001
APACHE II	2	298	5.24	4.00-6.47	<0.001

Abbreviations: WMD, weighted mean difference; 95% CI, 95% confidence interval

Table 5. Subgroup analysis of the prognostic value of DECAF based on different variables.

Variables	Studies, No. (Patients, No.)	Sensitivity (95%CI)	Specificity (95%CI)	PLR (95%CI)	NLR (95%CI)	DOR (95%CI)	AUC (95%CI)
Overall	17(8329)	0.76(0.70-0.81)	0.76(0.68-0.83)	3.20(2.40-4.10)	0.32(0.27-0.37)	10(8-13)	0.82(0.78-0.85)
in-hospital	15(7655)	0.77(0.70-0.82)	0.76(0.67-0.84)	3.20(2.40-4.40)	0.31(0.25-0.37)	11(8-15)	0.83(0.79-0.86)
30d	5(3084)	0.71(0.53-0.84)	0.75(0.58-0.86)	2.80(2.00-4.10)	0.39(0.27-0.56)	7(6-9)	0.79(0.76-0.83)
cutoff= 4	5(2550)	0.75(0.69-0.81)	0.80(0.68-0.89)	3.80(2.20-6.60)	0.31(0.23-0.41)	12(6-26)	0.76(0.72-0.80)
cutoff= 3	4(1361)	0.77(0.70-0.82)	0.76(0.67-0.84)	3.20(2.40-4.40)	0.31(0.25-0.37)	11(8-15)	0.83(0.79-0.86)
cutoff= 2	3(1002)	0.84(0.68-0.93)	0.53(0.50-0.56)	1.80(1.50-2.10)	0.31(0.15-0.64)	6(2-14)	0.77(0.73-0.80)

Abbreviations: CI, confidence interval; PLR, positive likelihood ratio; NLR, negative likelihood ratio; DOR, diagnostic odds ratio; AUC, area under the receiver operating characteristic curve.

Table 6. The prognostic value of prognostic scores for predicting in-hospital mortality in patients with AECOPD.

Variables	Studies, No. (Patients, No.)	Sensitivity (95%CI)	Specificity (95%CI)	PLR (95%CI)	NLR (95%CI)	DOR (95%CI)	AUC (95%CI)
DECAF	15(7655)	0.77(0.70-0.82)	0.76(0.67-0.84)	3.20(2.40-4.40)	0.31(0.25-0.37)	11(8-15)	0.83(0.79-0.86)
CURB-65	4(2912)	0.46(0.21-0.72)	0.92(0.63-0.99)	6.00(1.70-21.60)	0.59(0.40-0.86)	10(4-28)	0.73(0.69-0.77)
BAP-65	6(3226)	0.70(0.46-0.87)	0.50(0.31-0.70)	1.40(0.90-2.20)	0.59(0.29-1.20)	2(1-7)	0.64(0.59-0.68)
APACHE II	4(3031)	0.70(0.63-0.76)	0.65(0.58-0.72)	2.00(1.60-2.50)	0.46(0.37-0.57)	4(3-7)	0.72(0.68-0.76)
CAPS	4(3031)	0.77(0.60-0.88)	0.62(0.46-0.76)	2.00(1.50-2.70)	0.37(0.24-0.58)	5(3-9)	0.75(0.71-0.79)
Modified DECAF	3(666)	0.84(0.71-0.91)	0.62(0.46-0.75)	2.20(1.40-3.40)	0.27(0.13-0.55)	8(3-25)	0.84(0.81-0.87)

Abbreviations: CI, confidence interval; PLR, positive likelihood ratio; NLR, negative likelihood ratio; DOR, diagnostic odds ratio; AUC, area under the receiver operating characteristic curve.

Table 7. The prognostic value of prognostic scores for predicting 30-day mortality in patients with AECOPD.

Variables	Studies, No. (Patients, No.)	Sensitivity (95%CI)	Specificity (95%CI)	PLR (95%CI)	NLR (95%CI)	DOR (95%CI)	AUC (95%CI)
DECAF	5(3084)	0.71(0.53-0.84)	0.75(0.58-0.86)	2.80(2.00-4.10)	0.39(0.27-0.56)	7(6-9)	0.79(0.76-0.83)
CURB-65	4(3072)	0.52(0.48-0.56)	0.85(0.56-0.96)	3.50(1.00-12.50)	0.56(0.45-0.71)	6(1-28)	0.53(0.49-0.57)
BAP-65	5(3236)	0.61(0.34-0.82)	0.57(0.23-0.85)	1.40(0.80-2.40)	0.70(0.46-1.06)	2(1-5)	0.62(0.57-0.66)
APACHE II	2(1837)	0.68(0.52-0.80)	0.73(0.66-0.79)	2.50(1.60-3.90)	0.44(0.26-0.74)	6(2-15)	0.77(0.73-0.80)

Abbreviations: CI, confidence interval; PLR, positive likelihood ratio; NLR, negative likelihood ratio; DOR, diagnostic odds ratio; AUC, area under the receiver operating characteristic curve.

Figure Legends

Figure 1 : PRISMA (preferred reporting items for systematic reviews and meta-analyses) flow diagram and exclusion criteria

Figure 2: Forest plot of sensitivity and specificity of DECAF for the prediction of mortality in AECOPD.

Figure 3: Hierarchical summary receiver operating characteristic curve for evaluating prognostic value of mortality of DECAF in AECOPD.

The HSROC curves was conducted which plots sensitivity versus specificity. All studies were presented as a circle and plotted with the HSROC curve. The summary point (red box) indicates that the summary sensitivity was 0.76 and the summary specificity was 0.76. The summary results are displayed as the 95% confidence region and 95% prediction region in the HSROC curve plot. The size of the marker is scaled according to the total number of patients in each study.

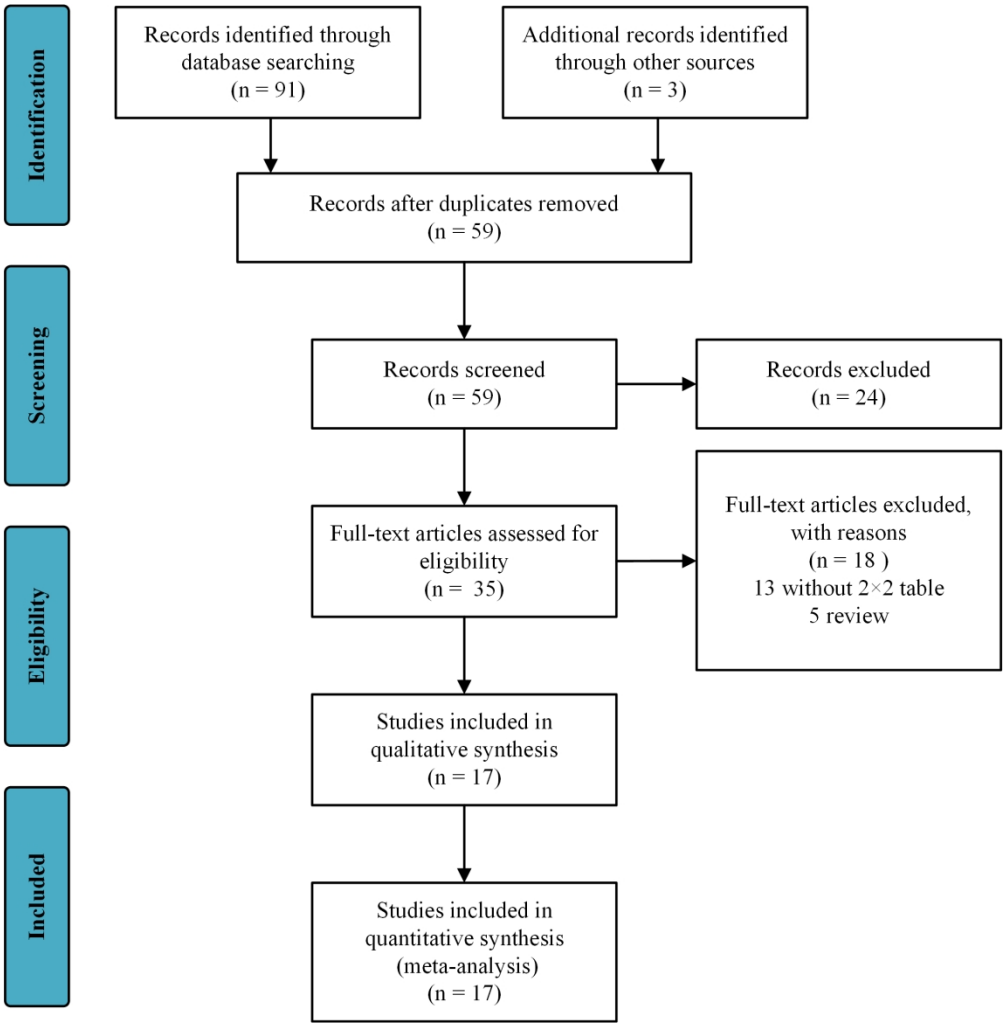

Figure 1 : PRISMA (preferred reporting items for systematic reviews and meta-analyses) flow diagram and exclusion criteria

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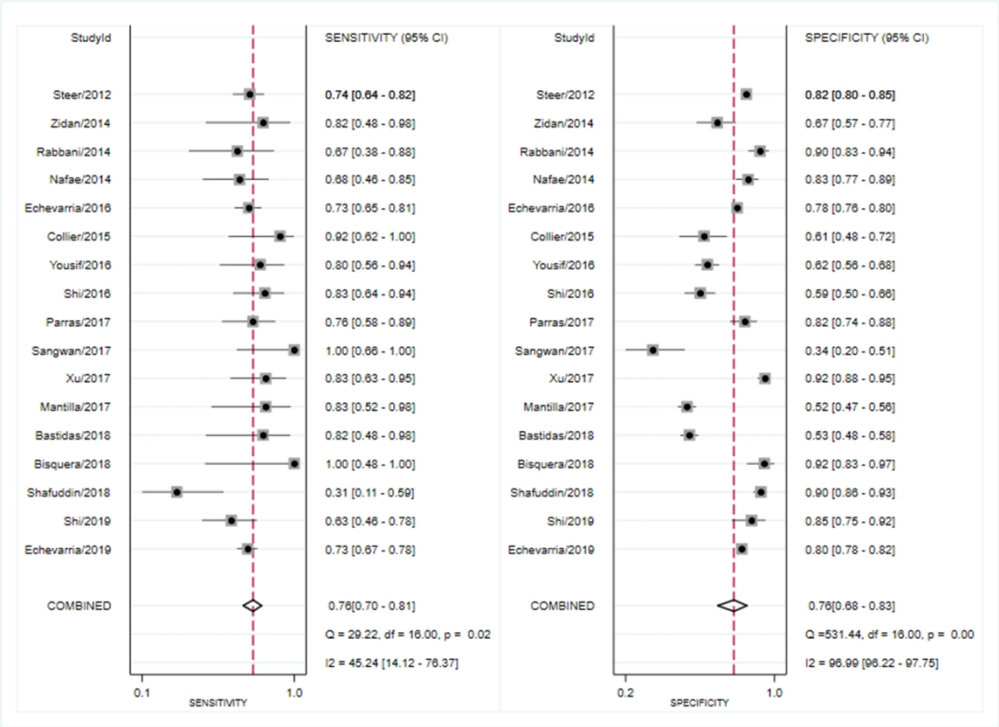

Figure 2: Forest plot of sensitivity and specificity of DECAF for the prediction of mortality in AECOPD.

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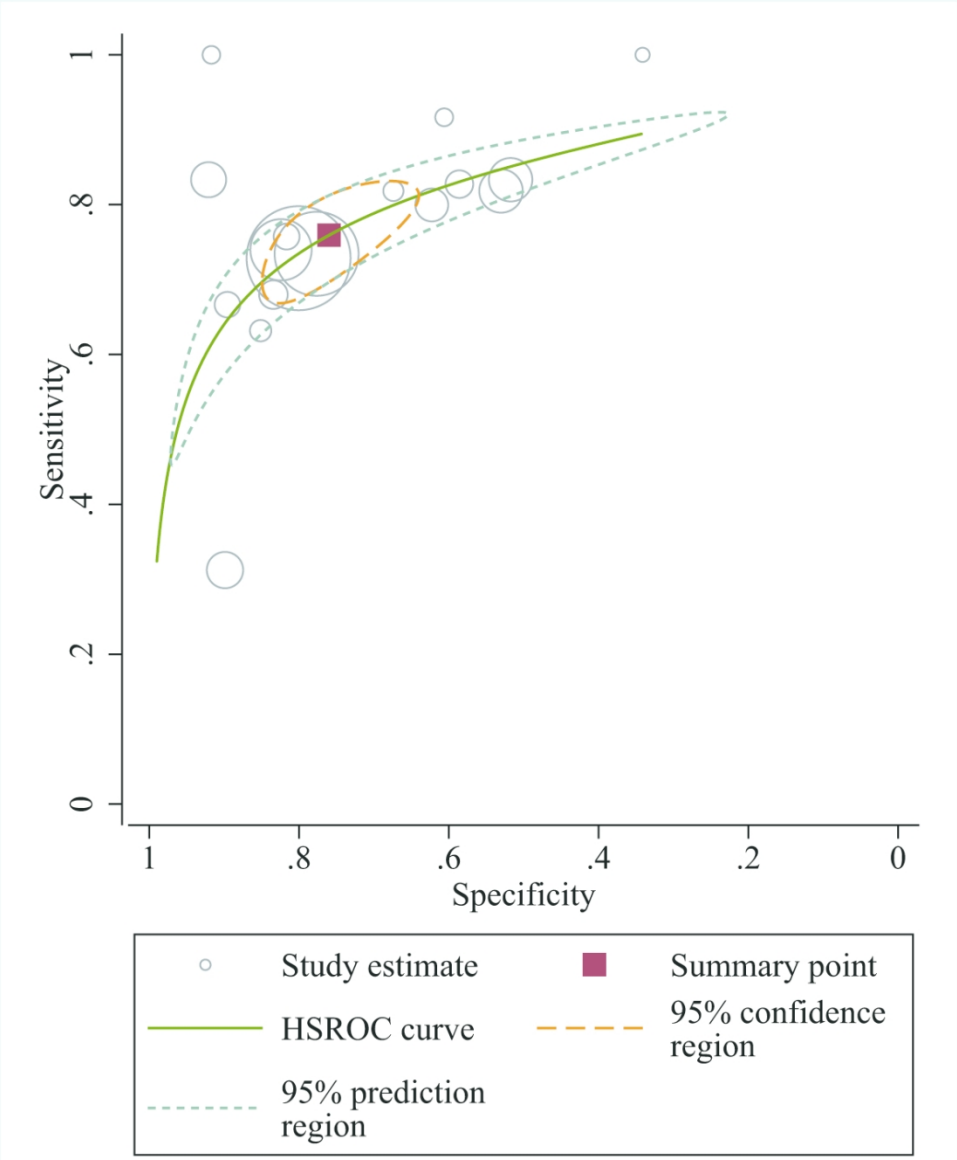

Figure 3: Hierarchical summary receiver operating characteristic curve for evaluating prognostic value of mortality of DECAF in AECOPD.
The HSROC curves was conducted which plots sensitivity versus specificity. All studies were presented as a circle and plotted with the HSROC curve. The summary point (red box) indicates that the summary sensitivity was 0.76 and the summary specificity was 0.76. The summary results are displayed as the 95% confidence region and 95% prediction region in the HSROC curve plot. The size of the marker is scaled according to the total number of patients in each study.

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Supplementary

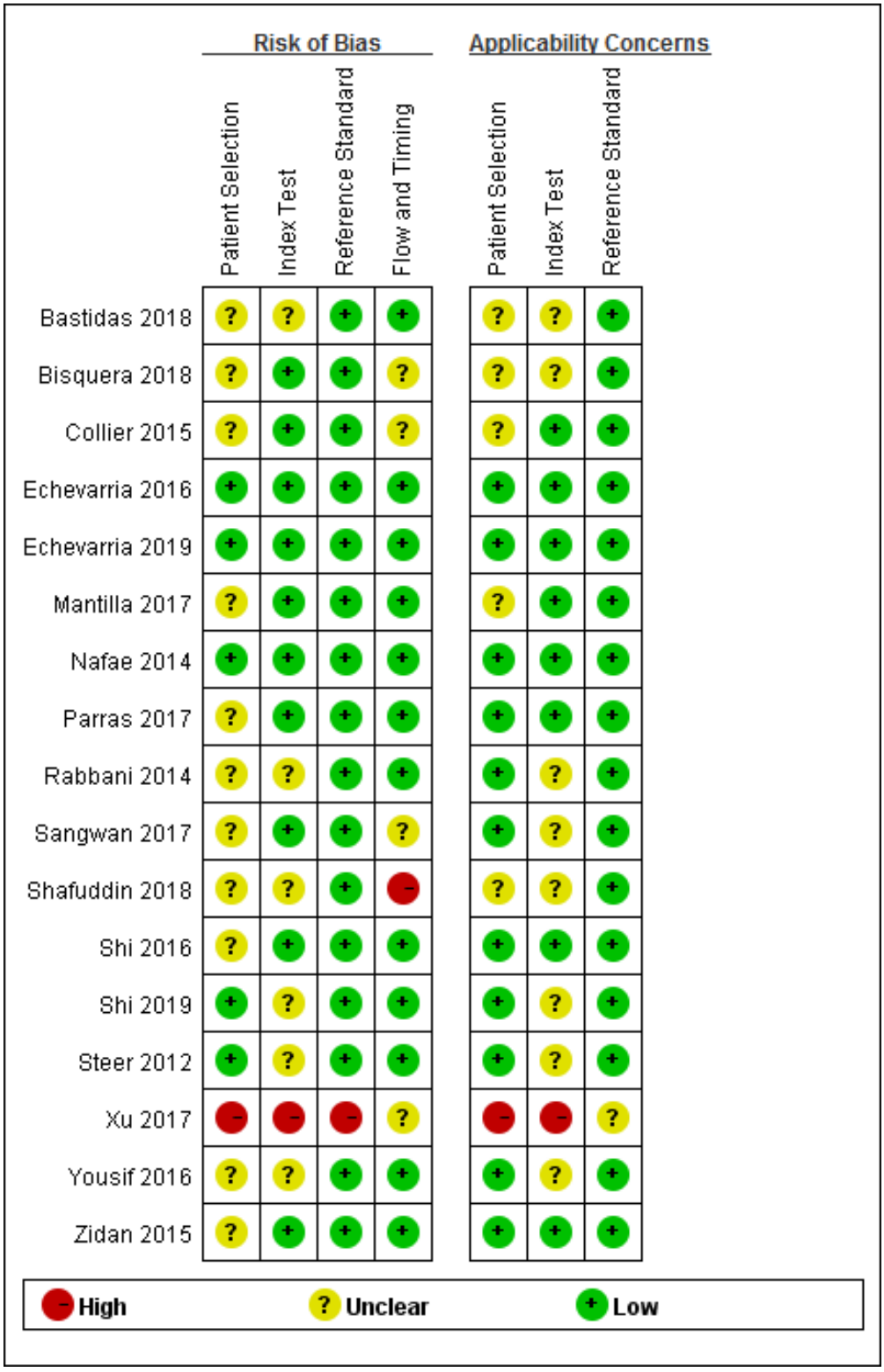

Figure S1: The quality evaluation and risk of bias in included studies.

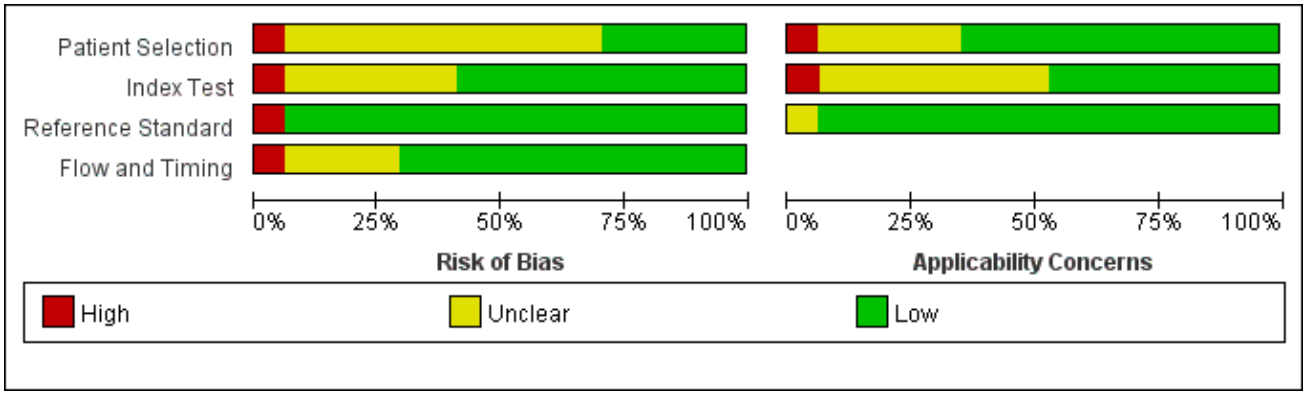

Figure S2: Methodological quality graph in included studies.

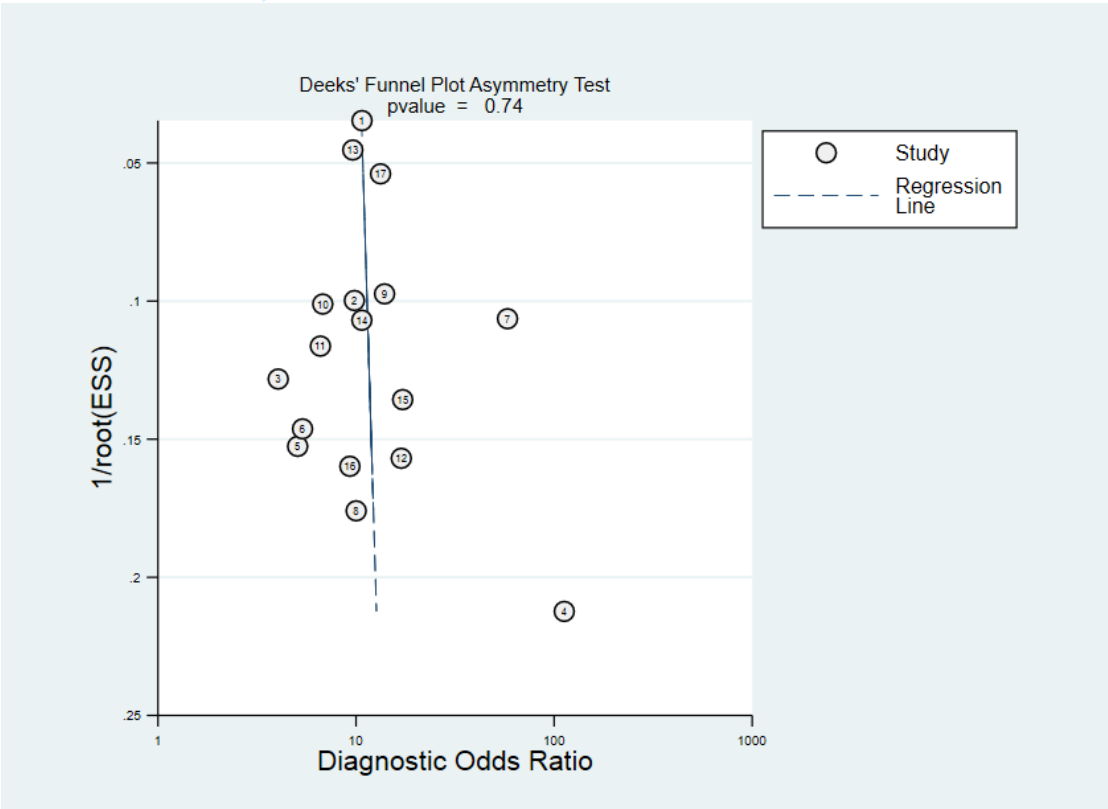

Figure S3: Deek's funnel plot asymmetry test for publication bias of studies evaluating the value of DECAF for the prognosis of AECOPD

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Search Strategies

1. Pubmed

Search ((("Pulmonary Disease, Chronic Obstructive"[Mesh]) OR ((((((((((((COPD[Title/Abstract]) OR Chronic Obstructive Pulmonary Disease[Title/Abstract]) OR Chronic Airflow Obstructions[Title/Abstract]) OR Chronic Airflow Obstruction[Title/Abstract]) OR COAD[Title/Abstract]) OR Chronic Obstructive Airway Disease[Title/Abstract]) OR Airflow Obstruction, Chronic[Title/Abstract]) OR Airflow Obstructions, Chronic[Title/Abstract]) OR Chronic Obstructive Lung Disease[Title/Abstract]) OR Chronic Obstructive Lung Disease[Title/Abstract]) OR airways obstruction[Title/Abstract]) OR obstructive lung disease[Title/Abstract]) OR emphysema[Title/Abstract]) OR bronchitis[Title/Abstract]))) AND ((DECAF score[Title/Abstract]) OR DECAF[Title/Abstract])

2. The Cochrane Library

#1 MeSH descriptor: [undefined] explode all trees
#2 (Chronic Obstructive Lung Disease):ti,ab,kw
#3 (Chronic Obstructive Pulmonary Disease):ti,ab,kw
#4 (COPD):ti,ab,kw
#5 (COAD):ti,ab,kw
#6 (Chronic Obstructive Airway Disease):ti,ab,kw
#7 (Airflow Obstruction, Chronic):ti,ab,kw
#8 (Chronic Airflow Obstruction):ti,ab,kw
#9 (Airflow Obstructions, Chronic):ti,ab,kw
#10 (Chronic Airflow Obstructions):ti,ab,kw
#11 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10
#12 MeSH descriptor: [Lung Diseases, Obstructive] explode all trees
#13 (Pulmonary Disease, Obstructive):ti,ab,kw
#14 (Obstructive Pulmonary Diseases):ti,ab,kw
#15 (Obstructive Lung Diseases):ti,ab,kw
#16 (Obstructive Lung Disease):ti,ab,kw
#17 (Lung Disease, Obstructive):ti,ab,kw
#18 (Pulmonary Diseases, Obstructive):ti,ab,kw
#19 (Obstructive Pulmonary Disease):ti,ab,kw
#20 #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19
#21 MeSH descriptor: [Pulmonary Emphysema] explode all trees
#22 (Emphysema, Centrilobular):ti,ab,kw
#23 (Centrilobular Emphysema):ti,ab,kw
#24 (Emphysemas, Pulmonary):ti,ab,kw
#25 (Emphysema, Pulmonary):ti,ab,kw
#26 (Pulmonary Emphysemas):ti,ab,kw
#27 (Emphysema, Panlobular):ti,ab,kw

#28 (Panlobular Emphysema):ti,ab,kw
#29 (Focal Emphysema):ti,ab,kw
#30 (Emphysema, Focal):ti,ab,kw
#31 #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30
#32 MeSH descriptor: [Bronchitis, Chronic] explode all trees
#33 (Chronic Bronchitis):ti,ab,kw
#34 #32 or #33
#35 #11 or #20 or #31 or #34
#36 MeSH descriptor: [Pulmonary Disease, Chronic Obstructive] explode all trees
#37 #35 or #36
#38 (DECAF):ti,ab,kw
#39 (DECAF score):ti,ab,kw
#40 #38 or #39
#41 #37 and #40

3. Web of Science (WOS)

1 TOPIC: (Pulmonary Disease, Chronic Obstructive) OR TOPIC: (COPD) OR TOPIC: (Chronic Obstructive Pulmonary Disease) OR TOPIC: (COAD) OR TOPIC: (Chronic Obstructive Airway Disease) OR TOPIC: (Chronic Obstructive Lung Disease) OR TOPIC: (Airflow Obstruction, Chronic) OR TOPIC: (Airflow Obstructions, Chronic) OR TOPIC: (Chronic Airflow Obstructions) OR TOPIC: (Chronic Airflow Obstruction) OR TOPIC: (Lung Diseases, Obstructive) OR TOPIC: (Lung Disease, Obstructive) OR TOPIC: (Obstructive Lung Disease) OR TOPIC: (Obstructive Lung Diseases) OR TOPIC: (Obstructive Pulmonary Diseases) OR TOPIC: (Obstructive Pulmonary Disease) OR TOPIC: (Pulmonary Disease, Obstructive) OR TOPIC: (Pulmonary Diseases, Obstructive) OR TOPIC: (Bronchitis, Chronic) OR TOPIC: (Chronic Bronchitis) OR TOPIC: (Pulmonary Emphysema) OR TOPIC: (Emphysema)
2 TOPIC: (DECAF) OR TOPIC: (DECAF score) OR TOPIC: (decaf score)
3 #2 AND #1

4. Embase

#5 #3 AND #4
#4 decaf:ab,ti OR 'decaf score':ab,ti
#3 #1 OR #2
#2 'chronic airflow obstruction':ab,ti OR 'chronic airway obstruction':ab,ti OR 'chronic obstructive bronchitis':ab,ti OR 'chronic obstructive bronchopulmonary disease':ab,ti OR 'chronic obstructive lung disorder':ab,ti OR 'chronic obstructive pulmonary disease':ab,ti OR 'chronic obstructive pulmonary disorder':ab,ti OR 'chronic obstructive respiratory disease':ab,ti OR copd:ab,ti OR 'lung chronic obstructive disease':ab,ti OR 'lung disease, chronic obstructive':ab,ti OR 'lung diseases, obstructive':ab,ti OR 'obstructive lung disease':ab,ti OR 'obstructive lung disease, chronic':ab,ti OR 'obstructive pulmonary disease':ab,ti OR 'obstructive respiratory disease':ab,ti OR 'obstructive respiratory tract disease':ab,ti OR 'pulmonary disease, chronic obstructive':ab,ti OR 'pulmonary disorder, chronic

obstructive':ab,ti
#1 'chronic obstructive lung disease'/exp

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	page1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	page2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	page3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	page 3
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	page 4
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	page 4
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	page 4
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	page 4
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	page 4
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	page 4-5
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	page 5
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	page 5
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	page 5
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	page 5

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	page 5
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	page 5
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	page 5 and Fig. 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	page5, 7, 8
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	page6
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Page9-11
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Page9-11
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Page6 and Fig.S1
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	Page 10-11
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	Page12
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	Page13
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	Page14
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	Page14

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097