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Validation of the DECAF score to predict hospital mortality in acute exacerbations of COPD

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ABSTRACT

Background Hospitalisation due to acute exacerbations of COPD (AECOPD) is common, and subsequent mortality high. The DECAF score was derived for accurate prediction of mortality and risk stratification to inform patient care. We aimed to validate the DECAF score, internally and externally, and to compare its performance to other predictive tools.

Methods The study took place in the two hospitals within the derivation study (internal validation) and in four additional hospitals (external validation) between January 2012 and May 2014. Consecutive admissions were identified by screening admissions and searching coding records. Admission clinical data, including DECAF indices, and mortality were recorded. The prognostic value of DECAF and other scores were assessed by the area under the receiver operator characteristic (AUROC) curve.

Results In the internal and external validation cohorts, 880 and 845 patients were recruited. Mean age was 73.1 (SD 10.3) years, 54.3% were female, and mean (SD) FEV_1 45.5 (18.3) per cent predicted. Overall mortality was 7.7%. The DECAF AUROC curve for inhospital mortality was 0.83 (95% CI 0.78 to 0.87) in the internal cohort and 0.82 (95% CI 0.77 to 0.87) in the external cohort, and was superior to other prognostic scores for inhospital or 30-day mortality.

Conclusions DECAF is a robust predictor of mortality, using indices routinely available on admission. Its generalisability is supported by consistent strong performance; it can identify low-risk patients (DECAF 0–1) potentially suitable for Hospital at Home or early supported discharge services, and high-risk patients (DECAF 3–6) for escalation planning or appropriate early palliation.

Trial registration number UKCRN ID 14214.

Key messages

What is the key question?

- Does the DECAF score predict inhospital mortality in patients admitted to hospital with an acute exacerbation of COPD?

What is the bottom line?

- In both internal and external validation cohorts, DECAF is a robust predictor of inhospital mortality using indices that are routinely available at the time of admission, and can be easily applied at the bedside.

Why read on?

- Accurate risk stratification may be used to inform clinical decision-making, although further research is required to quantify the impact on clinical and financial outcomes.

INTRODUCTION

Acute exacerbations of COPD (AECOPD) account for one in eight hospital admissions,[1] and are associated with worsening symptoms, lung function, health-related quality of life, and mortality risk.[2–6] Inhospital mortality is reported to be between 4.4% and 7.7%.[7–10] Clinicians are unable accurately to predict prognosis in patients hospitalised with AECOPD.[11] A robust prediction tool, which stratifies patients according to mortality risk, may help inform management, including Hospital at Home (HAH) or early supported discharge (ESD) for low-risk groups, and early escalation or appropriate palliation for high-risk groups.

The Dyspnoea, Eosinopenia, Consolidation, Acidaemia, and atrial Fibrillation (DECAF) score was derived in a large cohort of consecutive patients hospitalised with AECOPD, is simple to apply at the bedside and predicts inhospital mortality using indices routinely available on admission.[12] The score comprises five predictors, the strongest of which is stable state dyspnoea, as measured by the extended Medical Research Council Dyspnoea score (eMRCD; table 1).[13]

In the derivation study (the original study, in which the DECAF score was developed), DECAF showed strong performance and was superior to other tools designed or proposed for patients with AECOPD,[12] namely APACHE II,[14] BAP-65,[15] CAPS[16] and CURB-65.[17]

The 2014 UK National COPD audit recommended that the DECAF score be documented on all patients admitted with an AECOPD but noted that validation was required,[7] which is essential to prove the generalisability of a prognostic score.[18] We present temporal and geographical validation of the DECAF score and re-examine its predictive performance for short and medium term mortality in a large multicentre cohort of patients hospitalised with AECOPD. Two cohorts are presented: the internal validation cohort assesses performance of DECAF in both hospitals from the original derivation study, but over a different time period; the external validation study

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Table 1 eMRCD score, guidance note for eMRCD and DECAF score

eMRCD score **'In the past 3 months, when you were feeling at your best, which of the following statements best describes your level of breathlessness?'**	**(Circle)**
Only breathless on strenuous exertion	1
Breathless hurrying on the level or walking up a slight hill	2
Walks slower than contemporaries, or stops after walking on the level for 15 min	3
Stops for breath after walking 100 m, or for a few minutes, on the level	4
Too breathless to leave the house unassisted but independent in washing and/or dressing	5a
Too breathless to leave the house unassisted and requires help with washing and dressing	5b

Guidance notes:
Remember that you are asking the patient about their level of breathlessness *on a good day over the preceding 3 months*, not breathlessness during an exacerbation/on admission.

A patient only achieves a higher grade if they are as breathless as defined in that higher grade.
- eg, if worse than defined in eMRCD 3, but not as bad as eMRCD 4, they remain eMRCD 3.

A key distinction is between eMRCD 4 and eMRCD 5a/5b:
- only score 5a or 5b if the patient cannot leave the house without assistance.
- if a patient can only walk 30 to 40 metres, but can leave the house unassisted, they are eMRCD 4.
- if a patient can walk 5 or 10 metres, perhaps from their front door to a car, but need a wheelchair otherwise, they require assistance: eMRCD 5a or 5b. Simple walking aids do not constitute assistance.

If a patient requires assistance in personal washing and dressing they are eMRCD 5b. If they only require assistance in washing *or* dressing they are eMRCD 5a. Remember to ask about putting on socks and shoes.

If patients are limited for a reason other than breathlessness, score based on their functional limitation.

DECAF Score		**Circle**
D	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
E	Eosinopenia (eosinophils $<0.05\times10^9$/L)	1
C	Consolidation	1
A	Moderate or severe acidaemia (pH <7.3)	1
F	atrial Fibrillation (including history of paroxysmal atrial Fibrillation)	1
Total		

eMRCD, extended Medical Research Council dyspnoea score.

assesses the performance and generalisability of DECAF in four hospitals from different geographical areas. Since the DECAF score could identify low-risk patients (DECAF 0–1) who might benefit from HAH or ESD schemes, we report a detailed analysis of this subgroup.

METHODS

Study design and participation

Six UK hospitals participated between January 2012 and May 2014. Sites A and B formed the internal validation cohort and sites C–F formed the external validation cohort (table 2). The latter were selected to ensure wide variation in structures of care and population characteristics (COPD prevalence, socioeconomic factors and rurality). In participating hospitals, consecutive patients admitted with AECOPD were identified. In the internal validation cohort hospitals, the DECAF indices are recorded as part of routine practice. This allowed the period of the study to be extended retrospectively to enhance recruitment; patients were primarily identified from a broad coding records search (discharge codes). However this was cross-referenced with existing records of patients identified by respiratory specialist nursing and physiotherapy teams. In the external validation cohort to identify consecutive admissions of patients with AECOPD, all medical admissions were screened prospectively. This involved dedicated staff attending the medical admissions unit and base wards. Coding records were also reviewed to maximise patient capture.

Inclusion criteria were: a primary diagnosis of pneumonic or non-pneumonic exacerbation of COPD; preadmission spirometric evidence of airflow obstruction; age ≥35 years and smoking history of ≥10 cigarette pack-years. Exclusion criteria were: previous inclusion in the present study and any illness, other than COPD, likely to limit survival to less than 1 year (principally metastatic malignancy). Spirometry showing airflow obstruction performed at any time point prior to admission was accepted, and both primary and secondary care records were searched.

Treatment was at the discretion of attending clinicians, and not influenced by the research team. Antibiotic therapy was informed by the prescribing policy of individual sites. Ethical approval was granted by the local research ethics committee.

Data collection

Clinical indices on admission, and demographic and survival data were collected.[12] In our derivation study,[12] 118 patients had oxygen saturation (SpO_2) >92% while breathing room air, of whom none had an arterial pH of <7.30 (DECAF acidaemia score=1). In the present study, therefore, if the attending physician deemed that arterial blood gas (ABG) sampling was unnecessary and SpO_2 was >92% without supplementary oxygen, it was presumed that the arterial pH was ≥7.30.[19]

Outcome

The primary outcome was inhospital mortality prediction, with comparison of DECAF risk groups between the derivation and validation cohorts. Secondary outcomes included assessment of

Table 2 Baseline characteristics of patients by site

	Internal validation n=880		External validation n=845					
	Site A n=459	Site B n=421	Site C n=307	Site D n=271	Site E n=171	Site F n=96	All sites N=1725	p Value
Recruitment period	Jan 12-May 13	Jan 12-May 13	Aug 13- May 14	Jul 13-Apr 14	Apr 13-Feb 14	Feb 14-Apr 14	Jan 12-May 14	N/A
Recruitment/day	0.89	0.82	1.07	0.89	0.58	1.12	0.86	N/A
Died inhospital, %	9.8	7.8	7.5	6.6	4.7	5.2	7.7	0.27
DECAF 0–1, %	44.4	46.6	47.6	34.3	44.4	61.5	44.9	0.00018
DECAF 2, %	30.9	26.6	29.6	28.0	32.7	21.9	28.9	0.33
DECAF 3–6, %	24.6	26.8	22.8	37.6	22.8	16.7	26.3	0.00013
Sociodemographics								
Age, years*	73.5 (9.9)	73.9 (10.3)	73.5 (10.4)	72.0 (9.8)	72.4 (10.7)	70.7 (11.4)	73.1 (10.3)	0.025
Female, %	56.4	58.0	56.4	40.6	58.5	53.1	54.3	0.00012
Smoking pack-years, n†	41 (30–58)	40 (30–55)	44 (30–60)	40 (30–56)	45 (30–60)	40 (30–59)	40 (30–59)	0.71
Current smoking, %	38.2	40.9	39.7	36.2	36.1	47.4	39.1	0.41
Institutional care, %	8.9	5.0	2.9	2.6	4.1	5.2	5.2	0.0018
Markers of disease severity								
eMRCD score 1–4, %	44.7	49.2	49.5	35.1	44.4	68.8	46.4	<0.0001
eMRCD score 5a, %	39.7	36.6	30.3	24.7	42.1	24.0	34.3	<0.0001
eMRCD score 5b, %	15.7	14.3	20.2	40.2	13.5	7.3	19.3	<0.0001
Hospital admissions in previous year, n†	0 (0–1)	0 (0–1)	1 (0–1)	1 (0–2)	1 (0–2)	1.5 (0–3)	0 (0–1)	<0.0001
FEV_1% predicted*	47.8 (19.4)	48.5 (18.5)	44.8 (18.2)	40.6 (14.9)	40.5 (15.4)	46.6 (20.4)	45.5 (18.3)	<0.0001
LTOT, %	15.7	16.2	13.4	17.7	26.8	17.7	16.9	0.014
Cor pulmonale, %	5.9	7.4	10.4	8.5	8.9	2.1	7.5	0.052
LT prednisolone, %	8.1	6.7	5.5	10.0	9.0	7.3	7.6	0.38
Comorbidity								
IHD, %	27.5	32.3	31.9	27.7	26.6	27.1	29.4	0.46
CVD, %	13.3	12.4	13.1	13.7	5.9	11.5	12.3	0.14
Diabetes, %	11.3	11.9	15.0	13.0	14.8	17.7	13.1	0.40
Atrial fibrillation, %	14.8	20.7	16.9	17.7	16.4	14.6	17.2	0.33
LVD, %	8.1	9.3	18.2	10.0	4.7	3.2	9.9	<0.0001
Cognitive impairment, %	5.0	5.0	6.8	8.5	3.6	1.0	5.5	0.049
Anxiety, %	13.9	13.3	37.6	20.3	7.1	9.4	18.1	<0.0001
Depression, %	23.3	18.3	33.6	25.5	19.4	9.4	23.1	<0.0001
Admission clinical data								
Acute confusion, %	12.9	12.9	8.7	8.9	6.6	6.3	10.6	0.060
Respiratory rate, n*	26.5 (6.8)	25.7 (6.0)	21.8 (4.5)	24.1 (6.2)	23.9 (6.2)	23.5 (6.3)	24.7 (6.3)	<0.0001
Pulse rate, n*	104.9 (21.0)	102.8 (22.8)	97.1 (18.3)	102.2 (20.5)	104.7 (21.6)	99.7 (18.4)	102.3 (21.0)	<0.0001
sBP, mm Hg*	136.5 (30.3)	145.2 (26.6)	130.8 (22.0)	135.0 (26.5)	134.5 (22.9)	133.6 (24.2)	137.1 (26.9)	<0.0001
dBP, mm Hg*	74.6 (17.0)	80.0 (19.0)	71.6 (15.8)	77.2 (18.5)	77.3 (19.6)	73.2 (13.7)	76.0 (17.9)	<0.0001
Temperature, °C†	36.9 (36.3–37.6)	36.5 (36.0–37.2)	36.8 (36.4–37.3)	36.5 (36.0–37.1)	36.5 (35.9–37.0)	36.7 (36.0–37.0)	36.7 (36.2–37.3)	<0.0001
Oxygen saturation†	92 (87–94)	93 (88–95)	94 (91–95)	93 (90–95)	93 (90–95)	92 (91–95)	93 (89–95)	<0.0001
Pedal oedema, %	25.8	21.6	26.8	27.0	32.7	5.3	24.9	<0.0001
BMI, kg/m^2*	25.1 (6.8)	24.9 (6.8)	24.5 (6.4)	25.4 (6.4)	24.1 (6.5)	N/A	24.9 (6.6)	0.28

Continued

Table 2 Continued

	Internal validation n=880		External validation n=845					
	Site A n=459	Site B n=421	Site C n=307	Site D n=271	Site E n=171	Site F n=96	All sites N=1725	p Value
Weight loss >5%, %	14.2	10.6	21.2	24.7	12.9	2.4	15.3	<0.0001
CXR consolidation, %	30.5	34.4	22.8	30.6	18.7	19.8	28.3	<0.0001
Arterial blood gas values								
pH†	7.42 (7.37–7.46)	7.42 (7.37–7.46)	7.43 (7.38–7.46)	7.40 (7.35–7.44)	7.45 (7.38–7.48)	7.39 (7.35–7.43)	7.42 (7.37–7.46)	<0.0001
PaO_2, kPa†	8.0 (6.9–9.3)	8.0 (6.9–9.3)	8.6 (7.7–9.8)	8.4 (7.3–10)	9.4 (7.8–9.4)	8.3 (7.5–9.4)	8.3 (7.2–9.7)	<0.0001
$PaCO_2$, kPa†	5.6 (4.8–7.1)	5.7 (4.8–7.3)	5.2 (4.4–6.2)	6.1 (5.3–7.5)	5.6 (4.8–7.6)	6.1 (5.1–7.1)	5.7 (4.8–7.1)	<0.0001
HCO_3, mmol/L*	28.1 (6.0)	28.7 (6.8)	26.5 (5.5)	28.7 (5.4)	30.2 (8.9)	27.8 (5.0)	28.3 (6.4)	<0.0001
pH <7.35, %	17.8	19.2	15.1	24.3	17.9	20.8	18.9	0.19

Sites compared by Fisher's (proportions), ANOVA or Welch (means), or Kruskal–Wallis (median) tests.
*Mean (SD).
†Median (IQR).
BMI, body mass index; CVD, cerebrovascular disease; CXR, chest radiograph; dBP and sBP, diastolic and systolic blood pressure; HCO_3, bicarbonate; IHD, ischaemic heart disease; LT, long term; LTOT, long-term oxygen therapy; LVD, left ventricular dysfunction.

the optimal thresholds for pH and eosinopenia, prediction of 30-day mortality by DECAF and comparison with other prognostic scores (APACHE II,[14] BAP-65,[15] CAPS[16] and CURB-65[17]). Length of stay (LOS) was compared across DECAF scores.

Statistical methods

Based on an expected sensitivity of 70%, an SE of the estimate of sensitivity of 5% required a minimum of 840 patients in both the internal and external validation cohorts.[20] For indices with <20% missing values, data were imputed using the Markov Chain Monte Carlo method on IBM SPSS Statistics 22, with linear and logistic regression for continuous and categorical variables.[21] A large number of variables (n=67) were used as predictors for variables with missing data to create five datasets.

Baseline population characteristics and outcome were described using proportions, means with SDs or medians with IQRs, and compared using Fisher's exact test, analysis of variance or Welch, and Kruskal–Wallis test. Clinical scores' performance was assessed by the area under the receiver operator characteristic (AUROC) curve and compared with each other by the method of DeLong with and without multiple imputation;[22] results were pooled using Rubin's method.[21] Logistic regression was used to model DECAF indices to provide ORs, 95% CIs and coefficients to assess the weighting of indices. Calibration was assessed with the Hosmer–Lemeshow statistic.[23] The optimal thresholds for pH and eosinophil count were reassessed by visual inspection of the ROC curve. Subgroup analyses assessed outcome in patients at low risk according to DECAF, with (a) coexisting consolidation or (b) acidaemia.

RESULTS

Patient characteristics

Data were obtained for 880 and 845 patients in the internal and external validation cohorts, respectively. Across both cohorts, mean (SD) age was 73.1 (10.3) years, 54.3% were female and most had severe airflow limitation; mean (SD) FEV_1 45.5 (18.3) per cent predicted. The median DECAF score was 2 (IQR 1–3), 28.3% had radiographic consolidation and 18.9% had an acidaemic exacerbation (pH<7.35). In keeping with the UK national audit,[7] rates of comorbidity were high, notably ischaemic heart disease and diabetes (table 2).

Significant differences between sites included: the proportion requiring institutional care, radiographic consolidation, age, gender, DECAF score, severity of airflow limitation, the number of previous hospital admissions and the proportion with significant weight loss. Sites were broadly similar for comorbidity, though the proportions with left ventricular dysfunction, anxiety or depression differed. All of these factors were also significantly different between internal and external validation cohorts, except for DECAF score and left ventricular dysfunction.

Missing data

There were no missing mortality or DECAF data. The percentage of complete data for each risk score was: BAP-65 97.2%, CURB-65 96.5%, CAPS 85.9% and APACHE II 73.2%. For individual variables, missing data were P_aO_2 12.6%, albumin 12.2%, pH 12.1%, GCS 11.7%, potassium 3.3%, confusion 2.6%, temperature 2.6%, mean arterial blood pressure 1.8%, respiratory rate 1.8%, systolic BP 1.7%, diastolic BP 1.7%, heart rate 1.4%, haematocrit 1.2%, creatinine 0.5%, white blood cell count 0.2%, urea 0.1% and sodium 0.1%.

Table 3 Comparison of AUROC curves for DECAF and other scores (with imputation)

Prognostic score	AUROC curve (95% CI) Inhospital death	Comparison with DECAF, p value	AUROC curve (95% CI) 30-day death	Comparison with DECAF, p value
DECAF	0.82 (0.79 to 0.85)	N/A	0.79 (0.75 to 0.83)	N/A
CURB-65	0.76 (0.72 to 0.80)	0.0057	0.73 (0.69 to 0.77)	0.0051
CAPS	0.77 (0.73 to 0.81)	0.038	0.73 (0.69 to 0.77)	0.0083
APACHE II	0.78 (0.74 to 0.82)	0.083	0.72 (0.68 to 0.77)	0.0039
BAP-65	0.77 (0.73 to 0.81)	0.038	0.72 (0.68 to 0.76)	0.0021

AUROC curves of each prognostic score compared with DECAF by method of DeLong.[22]
AUROC, area under the receiver operator characteristic.

Validation of the DECAF score

The $AUROC_{DECAF}$ curve for inhospital mortality was: internal validation=0.83 (95% CI 0.78 to 0.87), external validation=0.82 (95% CI 0.77 to 0.87) and overall=0.82 (95% CI 0.79 to 0.85). The discrimination of the DECAF score was significantly stronger than CURB-65, CAPS, APACHE II and BAP-65 for 30-day mortality. For inhospital mortality, the DECAF score was again superior, except in comparison with APACHE II where the higher discriminatory strength of DECAF was not significant (table 3 and figure 1).

In a complete case analysis (without imputation), the conclusions were unchanged for 30-day mortality; for inhospital mortality, $AUROC_{DECAF}$ curve was again the highest, but was not statistically superior to CAPS (p=0.068) or BAP-65 (p=0.060).

Table 4 shows mortality rates, sensitivity and specificity by DECAF score in the overall validation cohort, and mortality by DECAF risk group compared with our derivation cohort.[12]

Compared with the derivation study, mortality overall and in the high-risk group was lower. Higher DECAF scores were again associated with higher mortality, though absolute numbers were small for DECAF 5 and 6 groups. The model was a satisfactory fit to the data (Hosmer–Lemeshow statistic=0.48, Nagelkerke R^2=24%). The previously assigned weightings of the DECAF score were confirmed on logistic regression (see online supplementary table S1), and eMRCD score remained the strongest predictor.

Compared with the traditional MRCD scale,[24] eMRCD had superior prognostic strength for inhospital mortality: $AUROC_{eMRCD}$=0.74 (95% CI 0.70 to 0.78) versus $AUROC_{traditional\ MRCD}$=0.68 (95% CI 0.64 to 0.72); p<0.0001. In the subpopulation with a pneumonic exacerbation (n=485), eMRCD was again superior to the MRCD scale: $AUROC_{eMRCD}$=0.67 (95% CI 0.60 to 0.73) versus $AUROC_{MRCD}$=0.62 (95% CI 0.56 to 0.69); p=0.0070.

CURB-65 predicts 30-day mortality in patients with community acquired pneumonia, and is commonly applied to patients with a pneumonic exacerbation of COPD (pAECOPD). In the validation cohort, for the subgroup of patients with pAECOPD (n=489), the DECAF score was a non-significantly stronger predictor of 30-day mortality than CURB-65: $AUROC_{DECAF}$=0.76 (95% CI 0.70 to 0.81) versus $AUROC_{CURB\text{-}65}$=0.68 (95% CI 0.62 to 0.74); p=0.057 (figure 2; online supplementary table S2 shows sensitivity and specificity for DECAF scores).

When patients with pAECOPD were pooled across the derivation and validation cohort (n=788), DECAF was superior for 30-day ($AUROC_{DECAF}$=0.75 (95% CI 0.71 to 0.79) vs $AUROC_{CURB\text{-}65}$=0.66 (95% CI 0.62 to 0.71); p<0.0001) and inpatient mortality ($AUROC_{DECAF}$=0.76 (95% CI 0.71 to 0.80) vs $AUROC_{CURB\text{-}65}$=0.70 (95% CI 0.65 to 0.75); p=0.024). The superior performance of DECAF is of particular importance for patients deemed at low risk by each score, who may be considered suitable for home treatment. Patients with a low-risk DECAF score had a lower inhospital mortality compared with those with a low-risk CURB-65 score: DECAF=1.6% (2/122) versus CURB-65=7.2% (17/237); p=0.026. There were similar differences for 30-day mortality: DECAF 0–1=3.3% (4/122) versus CURB-65 0–1=10.1% (24/237); p=0.022 (see online supplementary table S3).

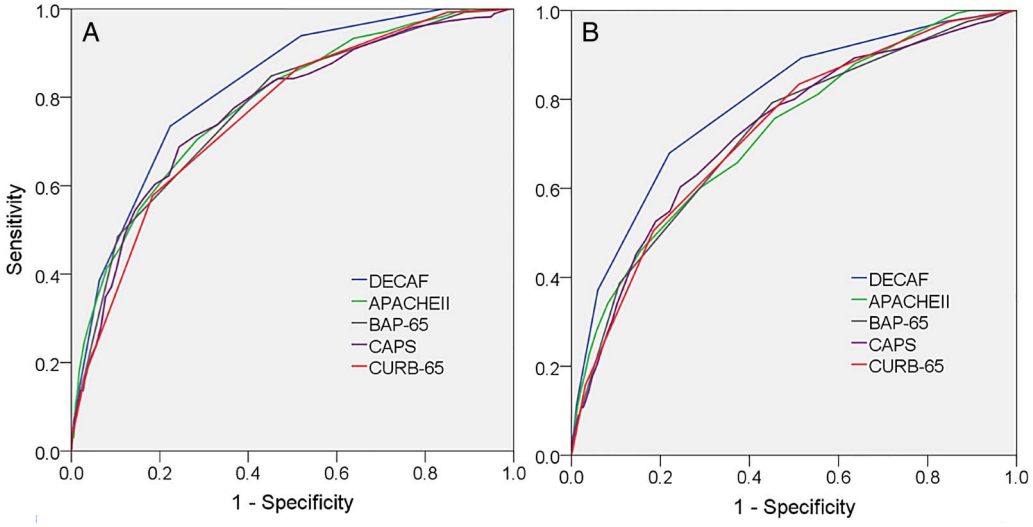

Figure 1 Receiver operator characteristic curves of prognostic scores for inhospital (A) and 30-day mortality (B).

Table 4 DECAF score, inhospital mortality, sensitivity and specificity

DECAF score	n	Died inhospital, n (%)	Sensitivity	Specificity	Mortality by risk group*, %		p Value
					Validation	Derivation	
0	255	0 (0)	1.00	0	1.0	1.4	0.60
1	519	8 (1.5)	1.00	0.16			
2	498	27 (5.4)	0.94	0.48	5.4	8.4	0.14
3	301	46 (15.3)	0.73	0.78	21.4	34.7	0.00046
4	113	35 (31.0)	0.39	0.94			
5	37	15 (40.5)	0.12	0.99			
6	2	1 (50.0)	0.0076	1.00			
Total	1725	132 (7.7)	N/A	N/A	7.7	10.4	0.016

*Risk groups: low=DECAF 0–1; intermediate=DECAF 2; high=DECAF 3–6.
Proportions of patients who died by risk group for validation and derivation cohort compared with Fisher's exact test.

The optimal thresholds for eosinophil count and pH were reassessed. On visual inspection of the ROC curve, the optimal cut-off for eosinopenia was unchanged (0.05×10^9/L).[12] For pH threshold, both 7.30 and 7.35 offered similar discrimination. The 7.30 threshold identified in the derivation study was retained for consistency, and because no deaths occurred among 58 patients with a low-risk DECAF score and non-scoring acidaemia (7.30-7.34). Only three patients had a DECAF score of 1 due to a pH<7.30, all of whom survived.

Patients with SpO_2 >92% without supplemental oxygen in whom ABG sampling was deemed unnecessary were assigned a score of 0 for the pH component of DECAF. Of the 209 such patients overall, only 6 died (2.9%); this total included 0/52 with a DECAF score of 0 and 2/67 with a DECAF score of 1.

Time to death in those who died during the index admission and LOS in those who survived to discharge, by DECAF score, are shown in table 5. Among survivors, higher DECAF scores were associated with longer LOS.

DISCUSSION

In a large, multicentre study of patients admitted with AECOPD, we have confirmed that the DECAF score is a robust predictor of mortality that can be easily scored at the bedside using indices routinely available on admission. As in our earlier study, DECAF was superior to other scores (BAP-65, CAPS, APACHE II, CURB-65) sometimes used to predict short-term mortality of patients with AECOPD.

We went to considerable lengths to capture consecutive patients, but a small number of patients who died or who were discharged shortly after admission may have been missed. In order to minimise any resulting bias and to maximise capture of all eligible patients, admission units were screened and a broad coding records search was performed. In the 2014 UK national audit,[7] mean site recruitment of patients with spirometric confirmation of COPD was 0.36 per day. In our study, recruitment was substantially higher at all sites (table 2), which supports high case ascertainment rates. Investigators in site E reported problems obtaining spirometry results, which may in part explain their comparatively lower recruitment rate.

The CHARMS checklist provides guidance on the appraisal of prediction model studies (see online supplementary material).[18] The main limitation of this study is that the internal validation study was, in part, performed retrospectively. Although retrospective collection of data may bias results, this risk was mitigated as the DECAF indices were collected as part of routine clinical practice in the participating hospitals, the researchers extracting data were blinded to outcome and case ascertainment and outcome were similar to the prospective external cohort. Of importance, the latter was individually adequately powered.

Data were only regarded as 'missing' once all data sources had been checked and rates of missing data were low. For key outcomes, analyses were repeated with and without multiple imputation. To improve data completeness for DECAF, patients with SaO_2 >92% breathing room air, and judged by a clinician not to require ABG analysis, scored 0 for the acidaemia component of DECAF; this was justified by the low mortality in this group, and supports a similar pragmatic approach in the clinical application of the score, reducing burden for both patients and clinicians.

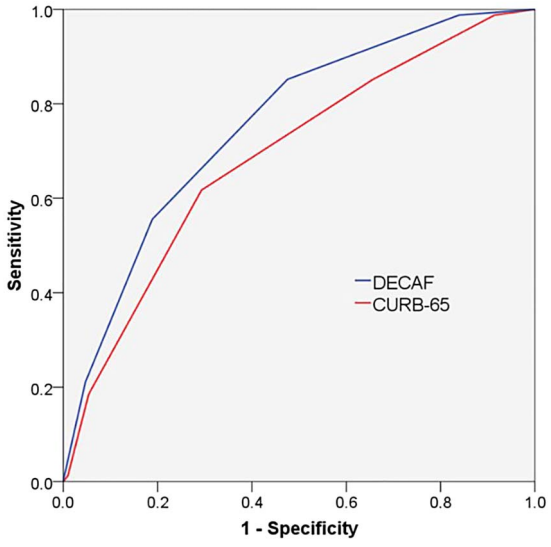

Figure 2 Receiver operator characteristic curves of prognostic scores for 30-day mortality in patients with pneumonic exacerbations (n=489).

Table 5 Time to death in patients who died during the index admission and median length of stay in those who survived to discharge, by DECAF score

DECAF score	Median time to death, days (IQR)	Median length of stay, days (IQR)
0	N/A	3 (1–5)
1	4.5 (4–12.5)	4 (2–7)
2	9 (5–16)	5 (3–10)
3	10 (3.75–23.25)	7 (3–13)
4	5 (1–11)	7.5 (5–18)
5	2 (1–9)	10 (6–19.5)
6	2 (2–2)	22 (22–22)

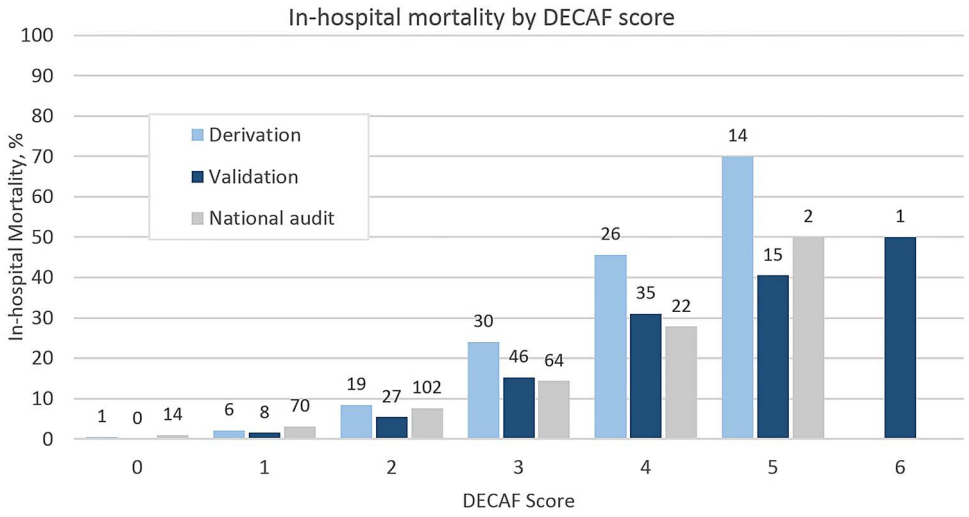

Figure 3 Inhospital mortality (percentage and absolute number) in the DECAF derivation and validation study, and 'DECAF light' (see discussion) from the 2014 UK National COPD Audit.

However, we do not advise that this assumption is used to lower clinician's threshold for performing ABG sampling.

There were important differences between site populations, in particular the receipt of institutional care, coexistent consolidation, degree of airflow obstruction and severity of DECAF score. This may in part reflect our efforts to select diverse sites for participation in the study, and the strong and consistent performance of DECAF, despite such differences in baseline characteristics, emphasises the external validity of the score.

Mortality varied between sites (from 4.7% to 9.8%) and between cohorts (internal validation=8.9% vs external validation=6.4%; p=0.057). This largely reflects differences in baseline characteristics, notably the proportion of patients admitted from institutional care and with coexistent pneumonia. When these two subgroups were excluded, mortality was 4.8% in both cohorts. Overall mortality was 7.7%, which is in keeping with the 2003 (7.7%) and 2008 (7.8%) UK national audits. In the 2014 UK audit, mortality was 4.3% though the reason for the lower mortality rate is reported as unknown. In our study, case ascertainment, comorbidity and the proportion of patients with consolidation or an MRCD score of 5 was higher than in the 2014 UK national audit.

Since our 2012 DECAF derivation study, two further prognostic scores have been published.[25 26] In one,[25] patients with acute ECG features of ischaemia and radiographic pulmonary congestion were included. Such patients are unlikely to have met our inclusion criterion of a primary diagnosis of AECOPD.

In the second study, the derived score showed good discrimination, and validation is awaited.[26] However, the score included subjective recognition of 'use of inspiratory accessory muscles or paradoxical breathing', reducing generalisability, especially in healthcare settings which lack specialist review within 24 h of admission.[7 27] Recruitment was lower than equivalent audit data,[27] because written patient consent was required, which disproportionately excludes the lowest and highest risk patients. Our methodology mirrored UK national audits; only routine data were collected, so patient consent was not required.

LOS for AECOPD is falling, and early discharge, both supported and unsupported, is commonplace, with patient selection based largely on clinical judgement. However, clinical judgement of prognosis is poor[11] while the DECAF score has consistently shown a high sensitivity for identifying low-risk patients. ESD and HAH services for patients with AECOPD are expanding.[7] National Institute for Health and Care Excellence (NICE) recommend that patient selection for these services be based on mortality risk,[28] and also highlight the (previous) lack of a robust prognostic score to guide decision-making. In the present study, DECAF 0–1 patients (including those with pneumonia or acidaemia) had an acceptably low mortality risk and comprised 45% of patients. The effect of treating this group with HAH or ESD requires a randomised controlled trial (RCT) to assess clinical outcomes and associated costs. We are currently undertaking an RCT to address this question (ISRCTN 29082260). In our experience, the CURB-65 score is commonly applied in patients with pneumonic exacerbations of COPD to inform discharge planning and choice of antibiotics. Evidence from both the derivation and validation studies shows that clinicians should not be reassured by 'low risk' CURB-65 scores in patients with pneumonic AECOPD as the associated mortality is unacceptably high. We advise against its use in this population.

A high-risk DECAF score is associated with both a high risk of death and, in those who die, a short time to death. The latter is particularly true of patients scoring DECAF 5 or 6, in whom the median time to death was only 2 days. Such patients may be suitable for early escalation in care, or alternative palliative care, but the window for intervention is short. Among patients who survive to discharge, LOS increases incrementally with DECAF score.

In both the derivation and present study, dyspnoea severity measured by the eMRCD score was the strongest single predictor of mortality and a superior predictor to the traditional MRCD scale. In the 2014 UK national audit, 'DECAF light' was scored retrospectively using the traditional MRCD scale (see figure 3). However, 'DECAF light', as opposed to the full DECAF score, was calculated only because eMRCD data was unavailable. We support the recommendation of the UK national audit that DECAF indices, including the eMRCD score, be collected on all patients admitted with AECOPD. To allow hospitals to meet this recommendation, we have included a figure of the DECAF score which can be downloaded and incorporated into COPD bundles and admission documentation (online supplementary figure 1). Various versions of the traditional MRCD scale exist,[24 29 30] which may lead to differences in scoring. We caution against such modifications to the eMRCD score unless supported by empirical evidence.

In conclusion, we have shown that DECAF can be used in a variety of hospital settings in order accurately to stratify mortality risk in patients with AECOPD. Further research is required to quantify its impact on clinical practice, for example, in the identification of patients for HAH or ESD services.

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Contributors SCB designed and obtained funding for the study. CE, GJG and JS contributed to trial design. CE collated the data, performed the statistical analysis and drafted the manuscript. Data analysis and interpretation was supported by SCB, GJG, JS and NS. The manuscript was redrafted by SCB, GJG, JS, AJS and CE. All authors reviewed the manuscript.

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Data sharing statement The corresponding author should be contacted if anyone wishes to access unpublished data from the study.

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Online Supplementary Material

Online supplementary table 1: DECAF indices as predictors of inhospital mortality

Index	B	OR (95%CI)	P value	Score
Dyspnoea				
eMRCD 1-4		1	<0.0001	0
eMRCD 5a	1.13	3.10 (1.78- 5.40)	<0.0001	1
eMRCD 5b	2.17	8.79 (5.13-15.03)	<0.0001	2
Eosinopenia (<0.05 x10^9/L)	0.90	2.45 (1.61-3.72)	<0.0001	1
Consolidation	0.90	2.45 (1.66-3.62)	<0.0001	1
Acidaemia (pH <7.3)	1.35	3.87 (2.38-6.31)	<0.0001	1
Atrial Fibrillation	0.85	2.35 (1.53-3.60)	<0.0001	1

Online supplementary table 2: Sensitivity and specificity of DECAF in pneumonic exacerbations of COPD.

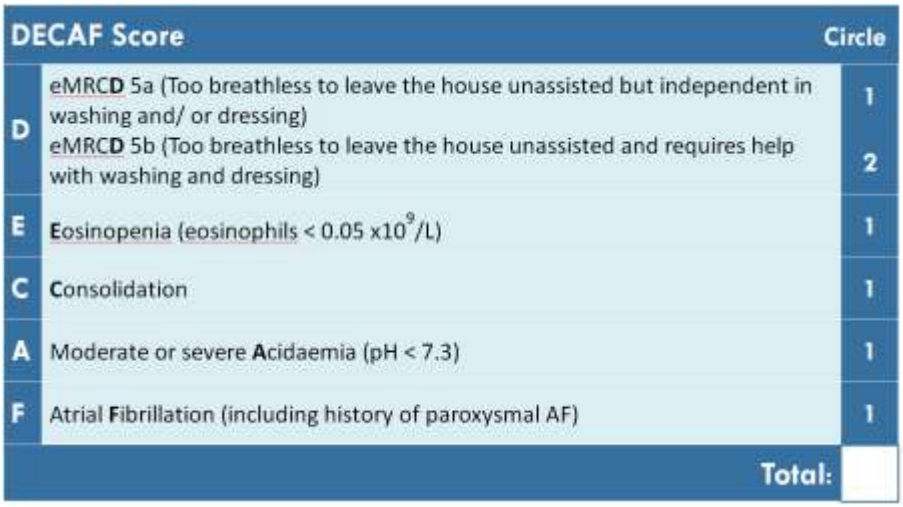
	Validation cohorts		Derivation and validation cohorts	
DECAF score	Sensitivity	1 - Specificity	Sensitivity	1 - Specificity
0	N/A	N/A	N/A	N/A
1	1.00	0.84	0.98	0.82
2	0.87	0.48	0.82	0.44
3	0.55	0.20	0.54	0.17
4	0.20	0.052	0.21	0.043
5	0.014	0.0024	0.0078	0.0015
6	0	0	N/A	N/A

Online supplementary table 3: Inpatient and 30-day mortality by DECAF and CURB-65 score in those with pAECOPD, derivation and validation cohorts.

	Inpatient death, n (%)		30-day death, n (%)	
Score	DECAF	CURB-65	DECAF	CURB-65
0	N/A*	3/55 (5.5)	N/A*	4/55 (7.3)
1	2/122 (1.6)	14/182 (7.7)	4/122 (3.3)	20/182 (11.0)
2	21/267 (7.9)	31/264 (11.7)	25/267 (9.4)	39/264 (14.8)
3	36/215 (16.7)	50/219 (22.8)	42/215 (19.5)	57/219 (26.0)
4	43/129 (33.3)	24/57 (42.1)	48/129 (37.2)	24/57 (42.1)
5	26/53 (49.1)	7/11 (63.3)	29/53 (54.7)	5/11 (45.5)
6	1/2 (50)	N/A	1/2 (50)	N/A
Total	129/788 (16.3)		149/ 744 (18.9)	

*The lowest possible DECAF score in those with pAECOPD is 1.

Online supplementary figure 1: The DECAF score



DECAF Score		Circle
D	eMRC**D** 5a (Too breathless to leave the house unassisted but independent in washing and/ or dressing)	1
	eMRC**D** 5b (Too breathless to leave the house unassisted and requires help with washing and dressing)	2
E	**E**osinopenia (eosinophils < 0.05 x10^9/L)	1
C	**C**onsolidation	1
A	Moderate or severe **A**cidaemia (pH < 7.3)	1
F	Atrial **F**ibrillation (including history of paroxysmal AF)	1
	Total:	

CHARMS CHECKLIST

Source of Data

1) Source of data (e.g. cohort, case-control, randomised trial participants, or registry data)

- The external validation cohort was prospective, and individually adequately powered. The internal validation cohort was partially prospective, with retrospective extension.

Participants

1) Participant eligibility and recruitment method (consecutive participants, location, number of centres, setting, inclusion and exclusion criteria)

Eligible patients analysis

- All eligible patients were included in the validation cohorts, except those that did not have complete data for all DECAF indices. This was approximately 1% of the population, and mainly comprised of patients with SpO2 92% or less in whom arterial blood gas analysis was not performed

Eligible patients excluded

- Exclusion criteria were few. For the internal validation study, patients were excluded for the following reasons: survival <1 year n=27 (12 lung cancer, 3 end stage dementia, 3 metastatic cancer, 2 metastatic bladder cancer, 2 idiopathic pulmonary fibrosis, 1 metastatic renal cancer, 1 metastatic bower cancer, 1 metastatic rectal cancer, 1 oesophageal cancer, and 1 mesenteric cancer), less than ten pack year smoking history n=24, spirometry not obstructive= 42. Ten patients had no ABG results, but had supplemental oxygen or oxygen saturations that were too low to assume a DECAF acidaemia score of 0. One patient had no eosinophil count. Robust data is not available for the external validation cohort.

Consecutive patients

- Extensive efforts were made to capture consecutive patients, including a broad coding search. Patients were captured by daily screening (Monday to Friday) on admission units and medical wards (external validation cohort) by a dedicated team.
- In the internal validation cohort, patients were mainly identified retrospectively using a broad coding search, with cross referencing to patients identified by clinical staff who routinely review patients admitted with AECOPD. This methodology was compared to prospective screening over three months, showing superior capture overall, and only one eligible patient was identified by prospective screening alone.

Location, centres, setting, and inclusion and exclusion criteria

- Six UK centres were involved: the two sites included in the derivation study took part in the internal validation cohort, and four geographically distinct hospitals took part in the external validation. All patients in the study were recruited from secondary care. Inclusion and exclusion criteria are described.

2) Participant description

- Detailed description of participants by different sites in table 2

3) Details of treatments received, if relevant

- Medical treatment for acute exacerbations of COPD included antibiotics, steroids, nebulised bronchodilators, and non-invasive ventilation. In creating a score that is intended for use to guide management, it is not appropriate to include acute treatments as predictors. The research team did not influence clinical treatment.

4) Study dates

- Given for each site in table 2

Outcome to be predicted

1) Definition and method for measurement of outcome

- Outcome clearly defined- Inpatient death

2) Was the same outcome definition (and method for measurement) in all patients?

- Yes

3) Type of outcome single or combined endpoints?

- Single endpoint

4) Was the outcome assessed without knowledge of the candidate predictors (I.e., blinded)?

- The DECAF indices were apparent to the team reporting in-hospital death, however in-hospital death is inherently objective, therefore the risk of bias is minimal / absent.

5) Were candidate predictors part of the outcome (e.g., in panel or consensus diagnosis)?

- No

6) Time of outcome occurrence or summary of follow-up

- Inpatient death. Presence or absence of outcome captured in all patients.

Candidate predictors

1) Number and type of predictors (e.g. Demographics, patient history, physical examination, additional testing, disease characteristics)

- Candidate predictors refers to indices for the derivation study, not the validation study, so the number of predictors is not relevant here. The analysis of inpatient mortality was only performed with the five DECAF indices.

2) Definition and methods for measurement of candidate predictors

- Candidate predictors were described in the derivation study. In the validation study, definitions and methods of measurement are provided. Each research site was provided with a data collection guide which included definitions of terms and diseases. eMRCD score as per table 1, eosinophil count cut-off provided, presence of chest radiograph based on assessment from consultant post-take ward round, acidaemia based on arterial blood gas analysis, and atrial fibrillation based on electrocardiogram and/ or history of (paroxysmal) atrial fibrillation.

3) Timing of predictor measurement of candidate predictors (e.g. at patients presentation, at diagnosis, at treatment initiation)

- DECAF indices were assessed on admission (see table 1).

4) Were predictors assessed blinded for outcome, and for each other (if relevant)?

- Predictors were assessed blinded from the outcome. The external validation cohort was identified prospectively, so variables were collected prior to the outcome. The internal validation study was performed retrospectively. Three DECAF variables, eosinopenia, acidaemia and atrial fibrillation, are objective. Potentially, there may be a degree of inter-observer variation in the reporting of chest radiograph consolidation and the eMRCD score, however the research team relied on the observations of the attending clinicians. For patients identified retrospectively, the researcher

obtaining the information from the notes was blinded to the outcome. Collection of individual predictors was not blinded from other DECAF indices, although the consequent risk of bias is low.

5) Handling of predictors in the modelling (e.g. continuous, linear, non-linear transformations or categorised)

- The DECAF variables were applied as per the derivation study. eMRCD score is categorised, eosinophil score and pH are dichotomised, and AF and chest x-ray consolidation are binary. Dichotomising variables can cause a loss of discrimination, depending on their relationship with the outcome. This was not an issue as the continuous variables related to DECAF show a non-linear relationship to mortality, and the pre-define thresholds were optimal. Discrimination of DECAF was very good, and similar to that of the derivation study, in both validation cohorts.

Sample size

1) Number of participants and number of outcomes/events

- The internal and external cohorts were individually adequately powered. Internal cohort: 880 participants, 78 events; external cohort 845 participants, 54 events.

2) Number of outcomes/events in relation to the number of candidate predictors (events per variable)

- This approach to sample size calculation is only relevant to the derivation study.

Missing data

1) Number of participants with any missing value (include predictors and outcomes)
2) Number of participants with missing data for each predictor

- 1+2) Number of missing values and number of participants with missing data provided.

3) Handling of missing data (e.g. complete-case analysis, imputation, or other methods)

- 3) Low rates of missing data. Multiple imputation used; complete-case analysis also performed.

Model development

1) Modeling method (e.g. logistic. survival, neural networks, or machine learning techniques)
2) Modeling assumptions satisfied
3) Methods for selection of predictors for inclusion in multivariable modelling (e.g. all candidate predictors, pre-selection based on unadjusted association with the outcome)
4) Method for selection of predictors during multivariable modeling (e.g. full model approach, backward or forward selection) and criteria used (e.g. p-value, Akaike Information Criterion)

- 1-4) The DECAF model was developed in the DECAF derivation study; these aspects do not apply to the validation study.

5) Shrinkage of predictor weights or regression coefficients (e.g. no shrinkage, uniform Shrinkage, penalized estimation)

- 5) Shrinkage refers to adjusting coefficients to protect against overfitting and loss of discrimination in validation studies. In developing the DECAF score, the prognostic indices were weighted based on their coefficients. The same weighting was used for both validation cohorts, and discrimination remained good in both validation cohorts.

Model performance

1) Calibration (calibration plot, calibration slope, Hosmer-Lemeshow test) and discrimination (C-statistic, D-statistic, log rank) measures with confidence intervals

- Hosmer-Lemeshow test is provided, and observed risk from derivation and validation cohorts described and compared. The validation study showed good calibration. Although the absolute risk differed between the derivation and validation study for high risk patients, this reflects differences in overall mortality rates and a large and stepwise increase in mortality is seen between different risk groups.

2) Classification measures (e.g. sensitivity, specificity, predictive values, net reclassification improvement) and whether a priori cut points were used

- 2) Sensitivity and specificity are provided. Reclassification measures, such as net reclassification improvement, look at the value in adding a single predictor to a prediction model. Due to the very strong performance of the DECAF score, no reclassification measures were performed or required.

Model evaluation

1) Methods used for testing model performance: development dataset only (random split of data, resampling methods, e.g. bootstrap or cross-validation, none) separate external validation (e.g. temporal, geographical, different setting, different investigators)

- Internal validation: involved the same hospitals as the derivation study, but at a different time period (a form of temporal validation) and additional investigators.
- External validation was performed in hospitals that are geographically distinct. Hospitals were chosen to ensure variation in population characteristics (rurality and socioeconomic factors) and structures of care to maximise generalisability. The research staff within external sites were not involved in the derivation study.

2) In case of poor validation, whether model was adjusted or updated (e.g., intercept recalibrated, predictor effects adjusted, or new predictors added)

- Not applicable

Results

1) Final and other multivariable models (e.g. basic, extended, simplified) presented, including predictor weights or regression coefficients, intercept, baseline survival, model performance measures (with standard or confidence Intervals)
2) Any alternative presentation of the prediction models, e.g., sum score, nomogram, score chart, predictions for specific risk subgroups with performance
3) Comparison of the distribution of predictors (including missing data) for development and validation datasets

- 1+2+3) Predictor weights and regression coefficients are given for the DECAF score. All models have AUROC calculated with confidence intervals. Subgroup with pneumonia presented. As with the original DECAF study, missing data rates for both validation cohorts was low.

Interpretation and discussion

1) Interpretation of presented models (confirmatory, if model useful for practice versus exploratory, is more research needed)

- The performance of DECAF is excellent in two separate, and individually adequately powered, validation cohorts. This confirms that DECAF can risk stratify patients effectively. The value of using DECAF to inform clinical practice, such as to identify patients for Hospital at Home, requires further research.

2) Comparison with other studies, discussion of generalisability strengths and limitations.

- DECAF is compared to other prognostic scores, with discussion of the strengths and limitations.