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Relevance of prediction scores derived from the SARS-CoV-2 first wave, in the evolving UK COVID-19 second wave, for safe early discharge and mortality: a PREDICT COVID-19 UK prospective observational cohort study

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ABSTRACT

Objective Prospectively validate prognostication scores, SOARS and 4C Mortality Score, derived from the COVID-19 first wave, for mortality and safe early discharge in the evolving pandemic with SARS-CoV-2 variants (B.1.1.7 replacing D614) and healthcare responses altering patient demographic and mortality.

Design Protocol-based prospective observational cohort study.

Setting Single site PREDICT and multisite ISARIC (International Severe Acute Respiratory and Emerging Infections Consortium) cohorts in UK COVID-19 second wave, October 2020 to January 2021.

Participants 1383 PREDICT and 20 595 ISARIC SARS-CoV-2 patients.

Primary outcome measures Relevance of SOARS and 4C Mortality Score determining in-hospital mortality and safe early discharge in the evolving UK COVID-19 second wave.

Results 1383 (median age 67 years, IQR 52–82; mortality 24.7%) PREDICT and 20 595 (mortality 19.4%) ISARIC patient cohorts showed SOARS had area under the curve (AUC) of 0.8 and 0.74, while 4C Mortality Score had AUC of 0.83 and 0.91 for hospital mortality, in the PREDICT and ISARIC cohorts respectively, therefore, effective in evaluating safe discharge and in-hospital mortality. 19.3% (231/1195, PREDICT cohort) and 16.7% (2550/14992, ISARIC cohort) with SOARS of 0–1 were candidates for safe discharge to a virtual hospital (VH) model. SOARS implementation in the VH pathway resulted in low readmission, 11.8% (27/229) and low mortality, 0.9% (2/229). Use to prevent admission is still suboptimal, as 8.1% in the PREDICT cohort and 9.5% in the ISARIC cohort were admitted despite SOARS score of 0–1.

Conclusions SOARS and 4C Mortality Score remains valid, transforming complex clinical presentations into tangible numbers, aiding objective decision making, despite SARS-CoV-2 variants and healthcare responses altering patient demographic and mortality. Both scores, easily implemented within urgent care pathways for safe early discharge, allocate hospital resources appropriately to the pandemic's needs while enabling normal healthcare services resumption.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ COVID-19 prognostication scores are all derived from the first wave of the pandemic, and this is the first study to prospectively validate relevance of existing scores in the evolving pandemic (UK COVID-19 second wave) due to SARS-CoV-2 variants (prevalent B.1.1.7 replacing parent D614), healthcare responses and/or different host-viral interactions, altering patient demographic and mortality.

⇒ This study prospectively validates two widely used COVID-19 prognostication scores, SOARS, a clinical assessment-based score and 4C Mortality Score, a clinical and blood investigation-based score, in a large single site cohort (PREDICT) and multisite cohort (International Severe Acute Respiratory and Emerging Infections Consortium).

⇒ This study is also the first to address safety of COVID-19 scores, SOARS and 4C Mortality Score prospectively, in triaging for safe early home discharge and to the virtual hospital model enabling appropriate allocation of hospital resources to the pandemic's needs in tandem with resuming normal healthcare services.

⇒ A limitation of this study is the absence of SARS-CoV-2 serotyping of individual patients, which would help assess the contribution of B.1.1.7 variant in presentations and outcomes.

⇒ Effects of vaccination did not contribute significantly to the UK COVID-19 second wave, a limitation that requires further review in future.

INTRODUCTION

The overwhelming burden of the SARS-CoV-2 pandemic on global healthcare is well

reported with severe ongoing impact in lower resource healthcare systems.[1–4] Over 160 million people have been infected with global mortality exceeding 3.5 million.[5] Infections continue to escalate when restrictions are lifted, with a mutating virus adapting to ensure infectivity, evading both vaccination and host adaptive immunity.[6 7] The pandemic is evolving, documented by heterogeneity in outcomes between the first and second waves. Differing unadjusted mortality and case fatality rate are recorded, higher in South Africa, Belarus and Russia but contrastingly lower in Japan, Italy, UK, USA, Spain and Sweden in the second wave.[8–14] India and Nepal, affected severely in the lethal second wave, exemplify this variation where the first wave was more sanguine.[15]

The UK variant, B.1.1.7, accounted for 58% to 83% of all second wave UK hospitalised cases with increased infectivity but reduced mortality compared with the parent D614G.[16 17] This started in early September 2020, peaking on1 January 2021 and prior to any significant vaccination effort.[18] A younger (60 years vs 62 years), less frail (12.8% vs 22.8%), more obese (29.1% vs 24.6%) and more female (47.3% vs 41.8%) case population in the second wave was noted in a small London study.[17] Spain and Japan noted similar demographic changes with reduced mortality but without documented SARS-CoV-2 variants.[11 13] Age, the most significant predictor of mortality in early reports, was less strongly predictive of case fatality with substantial reduction in nursing home mortality in many first world countries, although it remained the same in Denmark and Norway but increased in Australia.[12] South Africa noted a higher mortality in the second wave thought to be due to a combination of an overloaded healthcare system, less restrictive public health measures, under-reported mortality in the first wave and the B.1.351 subtype.[9 19]

The changing behaviour noted in COVID-19 is considered due to evolving SARS-CoV-2 subtypes, socioeconomic healthcare responses and/or varying host-viral interactions, suggests difficulties in prognostication.[4 6 7 20–22] An early scramble to produce COVID-19 severity scores to help transform complex clinical pictures into objective decision aids resulted in a plethora with varying efficacy.[23] Of these, the 4C Mortality Score, a clinical assessment and blood investigation-based score, validated in a large multisite UK cohort using International Severe Acute Respiratory and Emerging Infections Consortium WHO Clinical Characterisation Protocol UK (ISARIC) data from first wave hospitalised SARS-CoV-2 patients, is widely used.[24] SOARS, a rapid clinical assessment only score with multisite validation including the ISARIC cohort, is a peer-reviewed model that enables safe, reliable and expedient discharge on presentation to any urgent care area, making it invaluable during peak pressures.[25] Scores stratifying mortality and deterioration are all based on the first wave of the pandemic without updates advocated by the evolving pandemic.

As the COVID-19 pandemic evolves, should prognostications scores evolve with it or does existing scores remain relevant? This study updates the performance of both the 4C Mortality Score and SOARS scores in the UK COVID-19 second wave, characterised by the predominant B.1.1.7 variant, in both the derivation and multisite cohorts: PREDICT and ISARIC. Although both scores have been validated during the first wave for in-hospital mortality, neither score has been prospectively validated in the subsequent wave, especially for safe early discharge. Prospective validation particularly of the early discharge score (SOARS,) which is a low resource tool is vital for rapid and reliable healthcare resource planning, enabling resumption of usual services.[1 2] We predict that subsequent waves will infect lower-risk patients, who will benefit most from safe triage for home discharge or to the supportive virtual hospital (VH).[26 27] Safe and rapid triage to home care cannot be overemphasised as the pandemic threatens the developing world with a huge scarcity of hospital beds.[4]

METHODS

Study design and characteristics of cohorts

Adults 18 years and older who tested positive for SARS-CoV-2 nucleic acid by real-time reverse transcriptase PCR (rRT-PCR) between 1 October 2020 and 25 January 2021 (defined as the UK COVID-19 second wave) after presenting to the emergency department (ED) at West Hertfordshire Hospitals NHS Trust, were prospectively recruited (PREDICT second wave cohort). Comparison data representing the first wave (March–May 2020) with similar inclusion criteria was previously collected (online supplemental file 1).[25] Baseline clinical characteristics and investigations in the ED were collected according to a prespecified protocol (online supplemental file 1) in a National Health Service Health Research Authority (NHS HRA).[25] Patients were either discharged, referred to the VH for outpatient monitoring or admitted to the hospital.[27] As per the previously published protocol (online supplemental file 1) there was a minimum of 30-day follow-up for all patients recruited, including patients deemed safe for early discharge. In-hospital mortality of patients recruited was determined if the primary cause for mortality was due to COVID-19 infection. Patients who did not have this minimum follow-up or data were excluded. We also received an additional 20 595 UK COVID-19 second wave data collected on presentation to ED from ISARIC (ISARIC second wave cohort) to determine the performance of SOARS and 4C Mortality Score in the UK COVID-19 second wave.

Laboratory, physiological and radiographic data

All laboratory tests were performed as part of routine clinical care. Nasopharyngeal mucosal swabs for rRT-PCR were tested in a recognised UK Public Health England laboratory. Recorded baseline vital observations included all the parameters recommended by the previously described scores: SOARS and 4C Mortality Score.[24 25] Chest X-ray (CXR) acquired in ED were collated and scored at the end of the recruitment period by two independent

respiratory physicians and verified if discordant by a respiratory radiologist. Each lung field was divided into upper, middle and lower zones, and one point was scored for each zone affected.

Location and level of care

After presentation to the ED at West Hertfordshire Hospitals NHS Trust, the clinical course was protocol and pathway driven as per NHS HRA and REC 20/HRA/2344, IRAS ID 283888 (online supplemental file 1).[25] Patients who were clinically judged to have mild infection were referred to the VH for subsequent monitoring. Patients who were admitted but did not require additional respiratory support beyond supplemental oxygen were managed on designated medical wards. Where clinically indicated, high-flow nasal oxygen (HFNO) or continuous positive airway pressure were provided on respiratory level-2 wards supported by respiratory physicians or in the intensive care unit (ICU). Intubation and mechanical ventilation were undertaken in the ICU. All hospital admitted patients were treated with dexamethasone as per the National Institute for Health and Care Excellence (NICE) guidance. Remdesivir and tocilizumab were offered where clinically indicated, according to current available evidence.[28]

Patient and public involvement

As this study was initiated early in the pandemic (March 2020), it was neither feasible nor appropriate to involve patient or public participation in the design, recruitment, conduct, writing or dissemination of this study. This contrasted with the VH care design in the previous prespecified protocol used for this study with patient engagement.[25 27] However, for admitted patients, as per the local hospital protocol for escalation of care management plans, a religious advisor and a non-executive non-clinical director were consulted during multidisciplinary meetings.

Validation of scores derived from the first wave in the second wave cohorts

The primary outcome of the study was in-hospital mortality, a measure used to prospectively evaluate published COVID-19 scores.[24 25] Variables considered relevant in the SOARS and 4C Mortality Score studies with numerically relevant OR or a p<0.05 were included in the final analysis. All variables required for the 4C Mortality Score (8 variables: sex, age, number of comorbidities, Glasgow Coma Scale, respiratory rate (RR), oxygen saturation (SpO2), urea and C reactive protein (CRP)) and SOARS (five variables: SpO2, obesity, age, RR and history of stroke) were collected and prospectively evaluated in the time period defined previously.[24 25] The ability to discriminate for in-hospital mortality was assessed by the area under the curve (AUC). We then externally validated scores with the additional 20 595 UK COVID-19 second wave data received from ISARIC.

Statistical analysis

Categorical variables were expressed as frequency (%), with significance determined by the Pearson's χ^2 test. Continuous variables were expressed as median (IQR) or mean (SD) and analysed by the t-test, Kruskal-Wallis or Mann-Whitney U test, as appropriate. P values were adjusted by Bonferroni correction. A p<0.05 was considered statistically significant. Receiving operating characteristics curves for SOARS and 4C Mortality Score were constructed by multiple linear regression of the variables included in the respective score. This was done both in our population (PREDICT) and in the ISARIC dataset comprising 20 595 patients. Patients with missing values in one or more of the variables included in the regression model have been excluded from the calculation. All statistical analyses including risk modelling calculations were performed using GraphPad PRISM statistics software (GraphPad, San Diego, USA) and R statistical language.

RESULTS

Comparison of characteristics between waves

A total of 1383 patients (53.4% male) confirmed as SARS-CoV-2 rRT-PCR-positive were prospectively recruited over the 14-week study period (from 1 October 2020 to 25 January 2021) from West Hertfordshire Hospitals NHS Trust, UK (PREDICT second wave cohort). The baseline characteristics of the patients in both waves are compared in table 1.

When comparing the first wave (March–May 2020) and second wave (October 2021–Jan 2021), there was a significant decrease in median age, 70.3 years (IQR: 53.9–83.2) vs 67.5 years (IQR: 52.3–82.4), with no difference in male sex (53% vs 53%) and ethnicity, (77% white, 16% Asian, 4% black vs 78% white, 16% Asian, 3% black). The second wave noted increased patients with smoking history (19% vs 43%) and body mass index (BMI) >30 (25% vs 39%). Patients were significantly less frail, with reduced number of Clinical Frailty Score (CFS) >5 (40% vs 28%), less likely to have dementia (15.9% vs 9.8%) and care home residence patients halved (21% vs 10%) in the second wave. A lower prevalence of cardiovascular, respiratory and renal diseases was noted in the second wave, with significantly lower number of patients with ischaemic heart disease (20% vs 12%, p<0.001) and chronic obstructive pulmonary disease (13% vs 9.8%, p=0.03). There was similar prevalence of diabetes (24% vs 26%), cancer (12% vs 12%) and asthma (11% vs 13%)

Presenting symptoms of fever were less prevalent but gastrointestinal symptoms (diarrhoea and vomiting) and headache were more prevalent in the second wave. No differences were noted in respiratory or haemodynamic observations on presentation: respiratory rate, oxygen saturation, SF ratio, blood pressure and heart rate. Blood investigations in ED noted reduced patients with CRP >50 mg/L (65% vs 58%) and white cell count >11×10^9/L (20% vs 16%), but no difference in lymphopenia in the second wave. CXR was more severe in the first wave with

Table 1 Baseline characteristic of first and second wave (PREDICT cohort)

All patients	Wave 1 (N=983)	Wave 2 (N=1383)	P value
Age—median (IQR)	70.3 (53.9–83.2)	67.5 (52.3–82.4)	**0.015**
Age-range—no. (%)			
18–49	176 (18)	293 (21)	0.13
50–59	160 (16)	250 (18)	–
60–69	151 (15)	208 (15)	–
70–79	181 (18)	226 (16)	–
≥ 80	315 (32)	406 (29)	–
Age—median (IQR) by level of care			**0.005**
Virtual hospital	53 (43–65)	50 (39–60)	–
Ward	77 (61–87)	73 (56–85)	–
Ward+received CPAP	61 (54–72)	70 (66.00–72)	–
Intensive care unit	63 (57–74)	62 (53–72)	–
Male sex—no. (%)	531 (53)	738 (53)	0.68
Ethnic background (%)			0.8
White	758 (77)	926 (78)	–
Asian	159 (16)	191 (16)	–
Black	39 (4)	39 (3)	–
Other	27 (3)	37 (3)	–
Smoking history—no. (%)			
Former or current smoker	186 (19)	597 (43)	**<0.001**
BMI >30 no. (%)	243 (25)	529 (39)	**<0.001**
Care Home residency—no. (%)	210 (21)	140 (10)	**<0.001**
Clinical Frailty Score—no./total (%)			
1–4	250 (25)	795 (71)	**<0.001**
5–6	268 (27)	230 (20)	–
7–8	126 (13)	98 (8)	–
Symptoms at presentation—no. (%)			
Fever	508 (52)	539 (39)	**<0.001**
Breathlessness	482 (49)	713 (52)	0.24
Cough	345 (39)	507 (40)	0.75
Myalgia	181 (18)	300 (22)	0.55
Headache	62 (6)	125 (9)	**0.02**
Diarrhoea and vomiting	134 (14)	268 (19)	**<0.001**
Symptom onset to ED—median (IQR)	4.9 (1–10)	4.7 (2–8)	0.61
Baseline observations—no./total (%)			
Respiratory rate >24/min	295 (36)	408 (34)	0.32
Sp02 ≤92%	359 (43)	545 (45)	0.59
Systolic blood pressure <90	23 (2.8)	23 (1.9)	0.17
Pulse rate >120/min	81 (10)	119 (9.8)	0.94
Laboratory findings—no./total (%)			
C reactive protein >50 mg/L	526 (65)	631 (58)	**0.006**
Total white cell count >11×10^9/L	175 (20)	202 (16)	**0.04**
Lymphocyte count <0.7×10^9/L	297 (33)	420 (34)	0.89
Chronic kidney disease—no./total (%)			**<0.001**
Stage 1	118 (14)	68 (6.2)	–

Continued

Table 1 Continued

All patients	Wave 1 (N=983)	Wave 2 (N=1383)	P value
Stage 2	380 (46)	557 (51)	–
Stage 3	237 (28)	368 (34)	–
Stage 4	65 (8)	76 (7)	–
Stage 5	32 (4)	21 (1.9)	–
≥ 4 abnormal CXR zones—no./total (%)	336 (49)	332 (27)	**<0.001**
Comorbid conditions—no. (%)			
Hypertension	475 (48)	610 (45)	0.14
Ischaemic heart disease	194 (20)	169 (12)	**<0.001**
Cardiac failure	32 (3.3)	71 (5.1)	**0.025**
Cardiac arrhythmias	34 (3.5)	196 (14)	**<0.001**
Diabetes mellitus	232 (24)	347 (26)	0.24
Cancer	124 (12)	168 (12)	0.85
Respiratory disease	293 (30)	368 (27)	0.09
Chronic obstructive pulmonary disease	125 (13)	135 (9.8)	**0.03**
Asthma	113 (11)	185 (13)	0.19
Chronic kidney disease	196 (20)	200 (15)	**0.001**
Cerebrovascular disease	107 (11)	145 (10.5)	0.79
Mental health/behavioural disorders			
Dementia	156 (15.9)	135 (9.8)	**<0.001**
Anxiety—depression or both	155 (16)	184 (13)	0.1
Median length of stay—days (IQR)	7.6 (3.4–14)	6.6 (3.2–11.9)	**0.04**
Mortality %	292 (29.7)	342 (24.7)	**0.007**

Bold text in the P value column show p values of less than 0.05
BMI, body mass index; CPAP, continuous positive airway pressure; CXR, chest X-ray; ED, emergency department.

significantly higher number of patients with severe CXR scores of >4 zones (49% vs 27%).

Dexamethasone was only given to all admissions in the second wave as per updated NICE guideline in comparison to the first wave where dexamethasone was not prescribed. Remdesivir and tocilizumab, 10.7% and 2%, respectively, were given only in the second wave according to current available recommendation28. Mortality and intubation in patients on tocilizumab and/or remdesivir compared with age matched second wave patients did not show any change in outcomes. The two waves noted similar time from symptom onset to presentation, but reduced length of stay in hospital and mortality from 29.7%–24.7%.

Prospective validation of SOARS and 4C Mortality Score in PREDICT second wave cohort

SOARS achieved an AUC for hospital mortality of 0.80 (figure 1) in the PREDICT second wave cohort (95% CI 0.77 to 0.83, p<0.0001) and demonstrated negative predictive power of 83%, with positive predictive power of 60.4%. ORs of predicting mortality using SOARS were the greatest for age (between 1.98 and 23.19), followed by low oxygen saturations (2.48, 95% CI 1.77 to 3.49), BMI (1.70, 95% CI 1.23 to 2.36) and respiratory rate (1.72, 95% CI 1.23 to 2.40). Presence of cerebrovascular disease was not significant (OR 0.78, 95% CI 0.55 to 1.36). Figure 2 shows SOARS score OR predicting mortality in PREDICT second wave cohort.

SOARS applied to the PREDICT second wave cohort had a linear relationship between score severity and

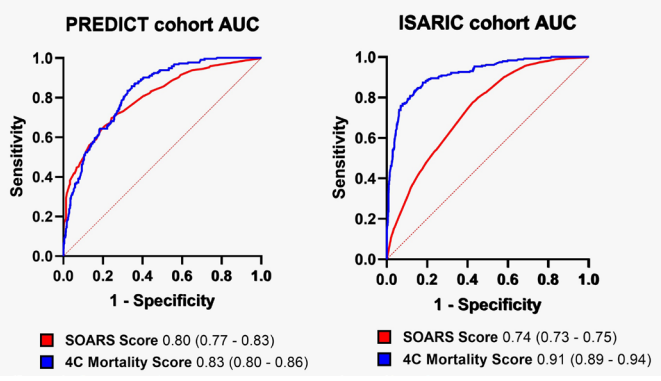

Figure 1 AUC for hospital mortality of prediction scores in PREDICT and ISARIC second wave cohorts. AUC, area under the curve; ISARIC, International Severe Acute Respiratory and Emerging Infections Consortium; SOARS, SpO2, obesity, age, RR and history of stroke.

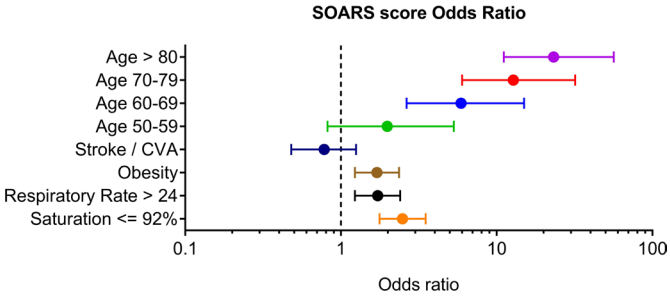

Figure 2 SOARS OR predicting mortality in PREDICT second wave cohort. SOARS, SpO2, obesity, age, RR and history of stroke (cerebrovascular accident (CVA)).

in-hospital mortality (figure 3). Of note, no deaths were noted in the subgroup who scored 0 (n=101). Compared with the first wave, mortality significantly reduced in the second wave especially in the more severe disease, scores between 3 and 8, with a mortality reduction between 10% and 21%. Performance of the 4C Mortality Score in the PREDICT second wave cohort also showed increasing mortality with score severity, but less linearly as seen in SOARS (figure 3).

External validation of SOARS and 4C Mortality Score on ISARIC second wave data

We looked at performance of scores derived from the first wave in an additional 20595 UK second wave data provided by ISARIC (figure 4). Again, the SOARS score showed a linear relationship with mortality until a score

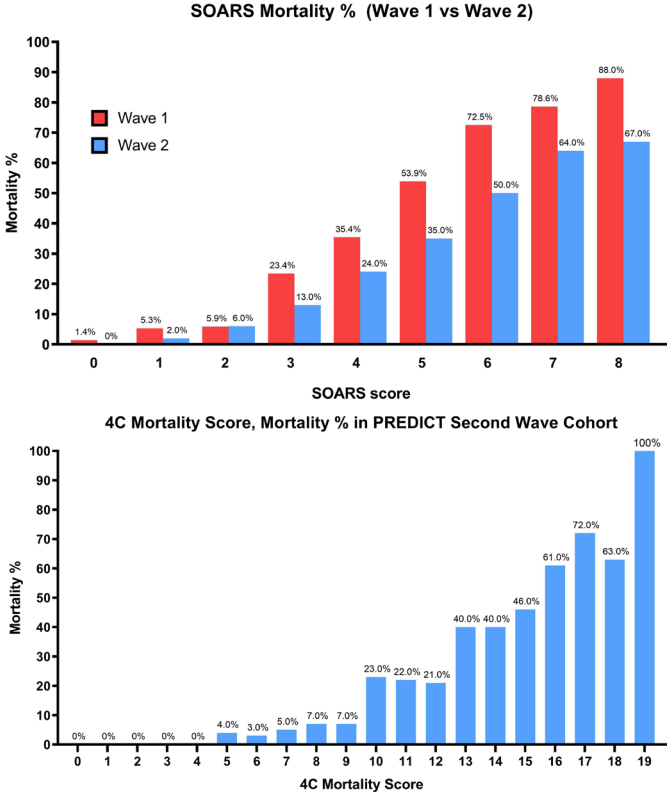

Figure 3 SOARS and 4C Mortality Score mortality in first and second wave PREDICT cohort. SOARS, SpO2, obesity, age, RR and history of stroke.

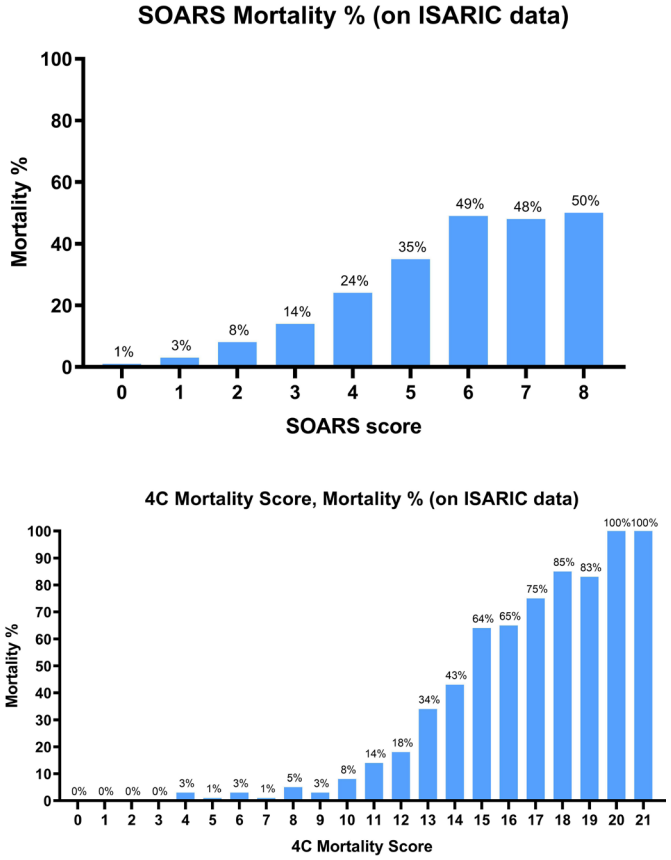

Figure 4 SOARS and 4C mortality score in the ISARIC second wave cohort. ISARIC, International Severe Acute Respiratory and Emerging Infections Consortium.

of 6 which then tapers in the higher scores. The 4C Mortality Score showed score severity correlating with mortality in the ISARIC second wave cohort, with similar safety to SOARS for the low risk (less than a score of 7). AUC of SOARS and 4C Mortality Score looking at sensitivity and specificity of scores in both the PREDICT and ISARIC second wave cohorts predicting mortality is shown in figure 1.

Virtual hospital

16.6% (n=229/1383) of patients in the PREDICT second wave cohort with SOARS scores of 0 or 1 on presentation were discharged to the VH, where only 11.8% (27/229) of these patients required subsequently hospital admission and 0.9% (2/229) mortality. 8.1% (113/1383) of the PREDICT second wave cohort were admitted despite scoring SOARS 0 or 1, with mortality of 2.6%. 9.5% (309/3257) of patients in the ISARIC second wave cohort were admitted with SOARS of 0 or 1, with a mortality of 2%. Outcomes of patients in different treatment pathways are compared between waves 1 and 2 in table 2.

DISCUSSION

The COVID-19 pandemic continues to escalate and evolve globally with lethal consequences, especially in South Asia and Latin America, despite remarkable

Table 2 SOARS and outcomes of patients in various treatment pathways utilised in waves 1 and 2: VH, ward, ward CPAP and ICU

Care setting	Wave 1	%	Wave 2	%
VH and discharged (n)	230/983	23.4%	229/1383	16.6%
SOARS (median (IQR))	3 (1–5)		2 (0–2)	
Readmission	25	10.9%	27	11.8%
Mortality	2	0.8%	2	0.9%
Ward (n)	632/983	64.3%	958/1383	69.3%
SOARS (median (IQR))	4 (2–5)		4 (2–5)	
0–1	116		113	
2	75		99	
3	86		115	
Mortality	212/632	33.5%	223/958	23.3%
Ward with CPAP (n)	41/983	4.2%	17/1383	1.2%
SOARS (median (IQR))	2 (1–4)		3 (3–6)	
Mortality	20		2	
ICU (n)	87/983	8.8%	179/1383	12.9%
SOARS (median (IQR))	3 (2–5)		4 (3–5)	
Mortality	54/87	62.1%	77/179	43%

% in Table 2 shows percentage of patients in different care settings per total number of COVID-19 admission in Wave 1 and 2 respectfully
CPAP, continuous positive airway pressure; ICU, intensive care unit; SOARS, SpO2, obesity, age, RR and history of stroke; VH, virtual hospital.

advances in treatment, vaccination and public health measures.[22 28–30] This may reflect increased infectivity and virulence of SARS-CoV-2 variants and inadequate healthcare response.[4 6 7 15 20 21] Infection may in time be adequately managed by vaccination and prudent public health measures, but this needs to be considered in tandem with the more urgent priority of ensuring appropriate hospital resource allocation for the acutely unwell while providing normal healthcare to the rest of the population.[1 2 31–33] We report prospective validation of two published scores derived from the COVID-19 first wave, in the evolving pandemic: SOARS, a clinical assessment-based triage score, and 4C Mortality Score, a hospital-based mortality score which is dependent on both clinical and investigation results.[24 25] We confirm the ongoing utility of SOARS for discharge in a multi-site UK study for score 0 and 1. The 4C Mortality Score retains utility for hospitalised patients for safe discharge below a score of 7.

As lockdown is lifted and routine life resumes in the United Kingdom, with high vaccination rates in the over 50s, preparation for a new rise of SARS-CoV-2 cases in a less comorbid population is paramount.[26] Learning from the pandemic, taught us that preserving limited healthcare resources is crucial to enable continued normal services in tandem with the needs of the pandemic.[1] The older and comorbid population have accrued morbidity, both from the pandemic itself and the absence of regular complex care needs, therefore, stressing the importance of resuming regular healthcare services.[1 31 32] The prospective validation of the SOARS score, based only on clinical assessment as a mortality and discharge score, permits risk-assessed discharges to both the VH and community care, reducing burden on hospitals. More importantly, the SOARS score without diagnostic investigations, is as valid prospectively in the second wave as resource intensive scores, making it a valuable tool for study and use in pandemic peaks in low resource systems.

The accelerated use of telemedicine in many countries for the pandemic enabled low-risk patients to be followed up in a VH in the community. VH has successfully been used by Atrium Health, a US integrated healthcare organisation where low-risk patients were defined by the modified DSCRB-65 of less than 2.[34] Of the 1293 patients they followed-up in VH, only 40 (3%) required hospitalisation, where in the readmitted cohort 18% required ventilator support and 5% mortality during their hospital admission.[34] Our experience using a VH model with integrated distant monitoring during the first wave, where 900 low-risk patients (defined by a NEWS score <2 and CRP<50) were followed up, resulted in 8.1% readmission and 2% mortality.[27] The initial success of the VH model stimulated the need for a safe discharge scoring system, where the SOARS score was developed. SOARS scores of 0 and 1 were used to discharge and follow-up patients in the VH in a reliable, safe and easy to use pathway, with integrated mortality at the various scores enabling educated decision making between clinician and patient (online supplemental file 2). Using the SOARS in triaging discharge during the second wave, 16.6% (229/1383) of patients were discharged home or to the VH, where

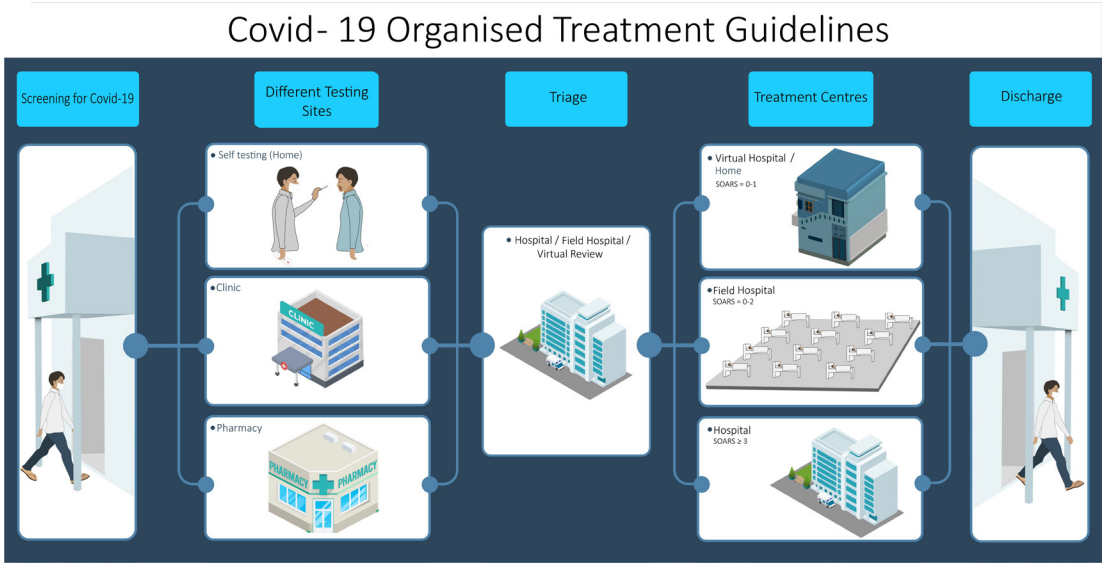

Figure 5 Using SOARS in COVID-19 management. SOARS, SpO2, obesity, age, RR and history of stroke.

11.8% (27/229) of those discharged were readmitted and 0.9% mortality. However, the use of SOARS score is still suboptimal as 8.1% (113/1383) were still admitted despite having scores of 0 or 1. Applying the SOARS score nationally in the ISARIC second wave cohort could have potentially avoided admission in an additional 9.5% (309/3257) of patients. We, therefore, recommend using the SOARS score as an integral part of managing SARS-CoV-2 cases, as shown in figure 5.

Improved public health measures and lower virulence of SARS-CoV-2 may account for the reduced admissions from care homes with frailty, dementia and stroke (cerebrovascular accident (CVA)) in the PREDICT second wave cohort. It is unlikely to reflect treatment advances, as these patients were less seen or admitted and mortality reducing treatments were only provided to those hospitalised. Vaccinations were unlikely to play a role as were only started in the older population in Hertfordshire at the end of December 2020 and beginning of January 2021. The improvement in mortality in the VH population who did not receive Dexamethasone suggests some reduction in SARS-CoV-2 virulence in the second wave. It is of interest to note the loss in significance of some variables that accounted for mortality in the first wave, including smoking, obesity, CVA and lymphopenia. A number of these comorbidities are associated with inflammation, particularly smoking, which may have been attenuated with the early use of dexamethasone.

One of the main limitations of the SOARS score is its dependance on age. Older patients automatically trigger a higher mortality score regardless of their comorbidities and clinical presentation, a limitation in all COVID-19 severity scores due to high weighting for age. This may change with vaccination and will require review in post-vaccination waves. If viral subtypes evade vaccination or boosters are delayed, age may still be relevant to scoring.[7] Additionally, multivariate analysis from the second wave revealed that pre-morbid CVA (OR 0.78), despite affecting a similar proportion of SARS-CoV-2 cases in both waves (table 1), was no longer associated with mortality, an observation difficult to explain.

A major limitation of this study is the absence of SARS-CoV-2 serotyping of individual patients, which would help assess the contribution of B.1.1.7 variant in presentations and outcomes. This may have provided some clarity to the differential contribution of the variant to treatment, public health measures and host characteristics resulting in the reduced mortality in the second wave. Another limitation in this study was that unlike the PREDICT cohort where we had fully characterised all the patients, we did not have this information for the ISARIC cohort. Although we did not have this information in the ISARIC cohort, our objective was not to characterise the demographic of the second wave, but this information would have given more insight to why some variables of the prediction scores lost their significance to determine mortality in COVID-19 infections. We also did not know if patients in the ISARIC cohort who were discharged home early were followed up in a VH model like in the PREDICT cohort. The VH model was not implemented throughout the UK and this could have potentially affect readmission and mortality rates. The contribution of remdesivir and tocilizumab were also not discussed in view of the small number of patients treated with these agents and as it was not the primary objective of this study. Effects of vaccination did not contribute significantly to the second wave, a limitation that requires further review in future.

SOARS, a clinical score developed to enable safe discharge to the community and VH, now prospectively validated in both the derivation and multisite UK cohorts, remains relevant to its purpose despite the evolution of the virus and the pandemic. This score developed in the parent variant remains relevant despite significant displacement by the B.1.1.7 variant, a prominent subtype in the second wave.[16 17] The relevance of this score in overwhelmed healthcare systems allows expedient, safe

and reliable decision making. Utility of the SOARS score in the South African (B.1.351), Brazilian (Gamma), Delta and now Omicron SARS-CoV-2 variants warrants further study. Further studies in future waves should continue to be performed to ensure the tool's validity in purpose and safety in SARS-CoV-2 infection.

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