The performance of the National Early Warning Score and National Early Warning Score 2 in hospitalised patients infected by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)

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ABSTRACT

Introduction: Since the introduction of the UK's National Early Warning Score (NEWS) and its modification, NEWS2, Coronavirus disease 2019 (COVID-19), has caused a worldwide pandemic. NEWS and NEWS2 have good predictive abilities in patients with other infections and sepsis, however there is little evidence of their performance in COVID-19.

Methods: Using receiver-operating characteristics analyses, we used the area under the receiver operating characteristic (AUROC) curve to evaluate the performance of NEWS or NEWS2 to discriminate the combined outcome of either death or intensive care unit (ICU) admission within 24 h of a vital sign set in five cohorts (COVID-19 POSITIVE, n=405; COVID-19 NOT DETECTED, n=1716; COVID-19 NOT TESTED, n=2686; CONTROL 2018, n=6273; CONTROL 2019, n=6523).

Results:
The AUROC values for NEWS or NEWS2 for the combined outcome were: COVID-19 POSITIVE, 0.882 (0.868-0.895); COVID-19 NOT DETECTED, 0.875 (0.861-0.89); COVID-19 NOT TESTED, 0.876 (0.85-0.902); CONTROL 2018, 0.894 (0.884-0.904); CONTROL 2019, 0.842 (0.829-0.855).

Conclusions:
The finding that NEWS or NEWS2 performance was good and similar in all five cohorts (range = 0.842-0.894) suggests that amendments to NEWS or NEWS2, such as the addition of new covariates or the need to change the weighting of existing parameters, are unnecessary when evaluating patients with COVID-19. Our results support the national and international recommendations for the use of NEWS or NEWS2 for the assessment of acute-illness severity in patients with COVID-19.

Keywords: Early warning scores; Adverse events; Rapid Response Systems; mortality; Intensive care unit admission

INTRODUCTION

The National Early Warning Score[1] (NEWS) and its modification, NEWS2[2], are validated for the identification of patient deterioration in a range of clinical conditions and settings.[3-10] Both scores are advocated as screening tools for sepsis,[2, 11-13] performing better than the quick Sequential (Sepsis-Related) Organ Failure Assessment (qSOFA) score[14-17] - a bedside prompt for identifying patients with suspected infection and a high risk of poor outcomes.[18] However, since the introduction of NEWS and NEWS2 in 2012 and 2017, respectively, the world has experienced an ongoing pandemic

of a new infectious disease, coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). NEWS2 is currently recommended for use in patients with COVID-19 by the Royal College of Physicians of London (RCP) and the World Health Organisation (WHO),[19,20] whilst the National Institute for Health Care and Excellence (NICE) states that it may be useful for predicting the risk of clinical deterioration in COVID-19 pneumonia in the community.[21]

COVID-19 has a variable clinical presentation on a spectrum from asymptomatic carriage to life-threatening organ dysfunction.[22] Many of its clinical features appear to be similar to those seen in other infections, e.g. increased respiratory rate, raised temperature and low systolic blood pressure,[23, 24] making the use of either NEWS or NEWS2 appear attractive for screening or monitoring in COVID-19.

The aim of this study was to evaluate the ability of NEWS or NEWS2 to discriminate the combined outcome of either death or intensive care unit (ICU) admission within 24 h of a vital sign set in five patient cohorts – a COVID-19 positive cohort and four control cohorts (one from 2018, one from 2019 and two from 2020).

METHODS

The study took place in a large NHS acute general hospital that provides acute services to approximately 640,000 people. It has approximately 7,900 staff and delivers all acute clinical services except for the management of burns, spinal injury, and neurosurgical and cardiothoracic surgery. The study was performed under existing Isle of Wight, Portsmouth and South East Hampshire Research Ethics Committee approval (ref 08/02/1394).

In the study hospital, all routine patient vital signs measured at the bedside are documented and charted in real-time in commercially available, electronic software (Vitalpac, The Learning Clinic, London, United Kingdom)[25] running in handheld devices. (Note: The Learning Clinic was acquired by System C Healthcare Limited in 2015 and the Vitalpac product is now marketed within CareFlow Vitals). The software demands that each dataset contains the following: date/time of observation set (automatically recorded by Vitalpac); pulse rate (HR); breathing rate (RR); systolic blood pressure (sBP), body temperature (T); neurological status using either the Alert-Verbal-Painful-Unresponsive (AVPU) scale; and peripheral oxygen saturation (S_pO_2). A record of the inspired gas (i.e., air or oxygen) being breathed by the patient at the time of S_pO_2 measurement was also recorded in Vitalpac, as was the patient's target S_pO_2 range, which established the correct NEWS2 S_pO_2 weighting scale for the patient.[2] The Vitalpac software has embedded upper/lower limit rules to ensure that highly or extremely abnormal physiological values (out-of-range values) are only accepted after staff have been advised to check the validity of the submitted data and have been given the opportunity to modify the data originally entered. Vitalpac is used throughout the hospital's general wards but not in the maternity unit or intensive care unit.

Up until 05/02/19, the original version of NEWS[1] was deployed within Vitalpac. Thereafter, the 2017 modification of NEWS, NEWS2,[2] was implemented as handheld devices were updated. NEWS or NEWS2 values were calculated automatically by Vitalpac in accordance with the original guidance from the Royal College of Physicians (RCP) (Supplementary Figures 1 and 2).[1,2] The structure of NEWS2 differs from that of NEWS by the inclusion of a specific scale for use in patients with hypercapnic respiratory failure (S_pO_2 Scale 2) and the addition of 'new confusion' (C) to the AVPU scale, which becomes ACVPU. However, for most patients, NEWS and NEWS2 are effectively

identical. The NEWS or NEWS2 values used in our analyses were those calculated and displayed by the Vitalpac software.

On 04/05/2020, we extracted a database of vital sign sets for consecutive adults (>16 years) admitted to Portsmouth Hospitals University NHS Trust (PHT) between 01/01/18 and 04/05/20, inclusive. The following were excluded: (a) data from patients discharged alive from hospital before midnight on the day of admission, (b) vital sign sets where measurements were outside the following limits: S_pO_2 50-100%; temperature 30-42^{o}C; pulse/heart rate 30-200 bpm; sBP 0-300 mmHg; respiratory rate 0-70 bpm, and (c) vital sign sets for which one or more parameter measurements were missing (because a full set of data is required to calculate NEWS and NEWS2 values). Additionally, in the current analysis, patients transferred directly at admission to a critical care area and those with no vital sign sets within the last 24 h before the primary outcome were also excluded.

We studied five admission cohorts, based on the finding that the first reverse-transcriptase–polymerase-chain-reaction (RT-PCR) test that was positive for SARS-CoV-2 for an inpatient in the study hospital was sampled on 11/03/2020:

- COVID-19 POSITIVE: Inpatients with vital sign sets between 11/03/2020 and 30/4/2020 who had a positive RT-PCR test. For the purposes of this study, only vital signs on or after the date of the patient's first positive RT-PCR test were used.
- COVID-19 NOT DETECTED: Inpatients with vital sign sets between 11/03/2020 and 30/4/2020 who had a negative RT-PCR test and never had a positive or indeterminate one.
- COVID-19 NOT TESTED: Inpatients with vital sign sets between 11/03/2020 and 30/4/2020 who never had a RT-PCR test.
- CONTROL 2018: Inpatients with vital sign sets measured between 11/03/2018 and 30/4/2018.
- CONTROL 2019: Inpatients with vital sign sets measured between 11/03/2019 and 30/4/2019.

We did not include those patients who only had an indeterminate test result, or where there were sampling or other technical failures (n=53).

The primary outcome studied was the combination of death or intensive care unit (ICU) admission within 24 h of a vital sign set. These were identified from the hospital's patient administration system (PAS) and the ICU admission database, respectively.

Data storage and analysis

All data were stored in Microsoft SQL Server 2019, and analysed using R v3.6.0 statistical computing and graphics software.[26]

Descriptive statistics were calculated including counts, means (+ SD), medians (IQR, Q_1-Q_3) and proportions. Proportions were compared using the chi squared test with Bonferroni correction for multiple comparisons. Mean values were compared with one-way ANOVA and Scheffe's test, and median values were compared using Kruskal-Wallis and Dunn's test (Bonferroni correction).

Analyses were undertaken using either NEWS or NEWS2 values, whichever was provided by Vitalpac. Using the area under the receiver-operating characteristics (AUROC) curve,[27] we evaluated the ability of NEWS or NEWS2 to discriminate the combination of death or ICU admission within 24 h of a vital sign set in the each of the five cohorts previously described. We considered AUROC values of 0.700 to 0.800 to represent 'reasonable' discrimination; AUROC values exceeding 0.800 were considered to represent 'good' discrimination.

RESULTS

After exclusions, the main data extract for the period 01/01/2018 to 04/05/20 contained 2867313 vital sign sets from 97669 admissions (60436 discrete patients). Figure 1 shows the development of the datasets for each of the five study cohorts (COVID-19 POSITIVE, COVID-19 NOT DETECTED, COVID-19 NOT TESTED, CONTROL 2018 and CONTROL 2019) and Table 1 presents the details of the admissions and vital sign sets. The categorisation of admissions to medical, surgical and other groups is shown in Supplementary Table 1. Admissions in the COVID-19 POSITIVE and COVID-19 NOT DETECTED cohorts were older than in the others (<0.001). Those in the COVID-19 POSITIVE cohort were also more likely to be male (<0.001). There were also significant differences in some of the vital signs (notably, higher median RR and mean temperature, and lower median S_pO_2) and a higher median EWS during the stay. More patients in the COVID-19 POSITIVE cohort received supplemental oxygen whilst in-hospital (<0.001).

Figure 2 shows the distribution of NEWS or NEWS2 values for patients in the five cohorts and Figure 3 demonstrates an increasing risk of the combined outcome with increasing NEWS/NEWS2 value in all five cohorts. Confidence intervals are not shown on Figure 3 to improve clarity; however, these are available in Supplementary Figure 3 and Supplementary Table 2.

The AUROC values for NEWS or NEWS2 for the combined outcome were: COVID-19 POSITIVE, 0.882 (0.868-0.895); COVID-19 NOT DETECTED, 0.875 (0.861-0.89); COVID-19 NOT TESTED, 0.876 (0.85-0.902); CONTROL 2018, 0.894 (0.884-0.904); CONTROL 2019, 0.842 (0.829-0.855).

Figure 4 shows the AUROC values for NEWS or NEWS2 for the discrimination of the combined outcome plotted through time on a monthly basis from 01/01/18 to 31/12/2019. Across the two years there was clear seasonal variation but all monthly AUROC values were within the range 0.830 – 0.895.

DISCUSSION

The study demonstrates that NEWS or NEWS2 are good discriminators of the combined outcome of either death or ICU admission within 24 h of a vital sign set in patients with a RT-PCR test result that is positive for SARS-CoV-2. Indeed, there was very little difference between the AUROC values for admissions in the COVID-19 POSITIVE cohort compared to any of our other study cohorts, with values ranging from 0.842-0.894.

The results also demonstrate that admissions in the COVID-19 POSITIVE cohort were older than in the other groups and more likely to be male, which appear to be common findings in COVID-19.[22] Vital sign values were also more abnormal in this cohort, the EWS quartiles were higher and more patients received oxygen therapy.

In the CONTROL 2019 cohort we found an AUROC value of 0.842 (0.829-0.855), which is significantly lower than all other cohorts except the COVID-19 NOT TESTED cohort. Given the limited demographic data available to us and the pattern of the AUROC values across the period 01/01/18 – 31/12/19 (Figure 4), we believe that this could reflect the influence of differing pressures on clinical services. However, it is also possible that the change from NEWS to NEWS2 from 06/02/19 onwards may have contributed, as particular elements of implementing NEWS2, including the use of a specific scale for use in patients with hypercapnic respiratory failure, have proven challenging.[28]

Interestingly, the AUROC value for the COVID-19 NOT DETECTED cohort was the same as that for the COVID-19 POSITIVE group of admissions. However, the percentage of observation sets followed by the combined outcome in the COVID-19 NOT DETECTED cohort was half that in the COVID-19 POSITIVE cohort. In most cases in the COVID-19 NOT DETECTED cohort, the RT-PCR test was performed on the basis of symptoms and signs, and a presumed diagnosis of COVID-19 infection. However, the high false negative rate observed for RT-PCR tests for SARS-CoV-2[29] could mean that many of the patients in the COVID-19 NOT DETECTED cohort were actually positive for COVID-19 infection. Perhaps a lower viral load in the COVID-19 NOT DETECTED cohort leads to a lower chance of SARS-CoV-2 detection and a lower risk of the combined outcome.[30]

Major strengths of this study are that it considers all patient admissions to the study hospital during the first two months of the COVID-19 outbreak. It draws upon a large dataset of vital signs collected simultaneously in a standardized manner during clinical care using an electronic data collecting system. It also considers a repeatable, clinically and operationally useful, objective combined outcome, for which data were easily retrievable from the hospital's electronic records.

However, there are also weaknesses. The RT-PCR test for SARS-CoV-2 is not 100% accurate and negative results need to be interpreted with caution.[22,29] Therefore, as mentioned earlier, there is a risk that the COVID-19 NOT DETECTED cohort may have been contaminated by false-negative test results. In addition, there is also a chance, albeit much smaller, that the COVID-19 POSITIVE cohort includes false-positive results. On the basis that the first known UK case of COVID-19 occurred on 29/01/20, we used control groups from 2018 and 2019 to permit comparisons with the COVID-19 era. However, uncertainty still exists about the location and date of the index case of COVID-19 and this may have relevance to our use of the control group from 2019 for comparisons with the COVID-19 POSITIVE cohort.

We excluded admissions that were admitted directly to critical care areas of the hospital. Our logically necessary exclusion of all those with no vital sign sets in the last 24 h also had the effect of removing any patient on an End-of-Life (EoL) pathway where vital sign monitoring had ceased. We obtained the patient's date and time of death and/or ICU admission from the hospital's PAS and ICU admission database, respectively. These data are likely to be systematically late, implying that the number of observations followed by the combined outcome may be an underestimate.

This is a single centre study such that the results are not necessarily transferrable and require external validation. We used repeated observation sets from the same patient episode in the analysis, making the assumption that the observation sets are independent based on previous work by our group.[31] The conclusions of our work are also based on the assumption that all patients were treated optimally and equitably. A further weakness is that the study was conducted in a single site, where the precursor of NEWS – ViEWS[32] - was developed. Prediction models are almost always more accurate in the population in which they were derived. Finally, this is a statistical evaluation of NEWS or

NEWS2 during the COVID-19 pandemic and there is no guarantee that similar results would be generated operationally.

As SARS-CoV-2 emerged relatively recently, there are only currently a small number of publications regarding the performance of NEWS and NEWS2 in patients with COVID-19. Gidari et al. showed that the predictive value of admission NEWS2 values for ICU admission in 68 patients with severe COVID-19 was good (AUROC = 0.90 (CI, 0.82–0.97)).[33] Peng et al. showed similar AUROC values for predicting 'serious events' of 0.837 (0.748 - 0.943) for admission NEWS and 0.846 (0.735 - 0.939) for admission NEWS modified by age, where 'serious events' were defined as any of the following during hospitalisation: death, unplanned transfer to an ICU or initiation of non-invasive ventilation.[34] Covino et al. reported that NEWS was the most accurate predictor of ICU admission within 48 h (AUROC = 0.802 (0.756-0.844)) and 7 days (AUROC 0.783 (0.735-0.826)) of emergency department arrival.[35] Liu et al. found that NEWS 0.882 (0.847–0.916) and NEWS2 0.880 (0.845–0.914) had the highest AUROC values for predicting in-hospital death.[36] However, Knight et al. showed an AUROC of 0.654 (0.645 to 0.662) for NEWS with in-hospital mortality as an outcome.[37]

Our study provides data from a large cohort of unselected hospital admissions and focuses on an outcome measure that is both clinically relevant and has the potential to be averted with the appropriate and timely clinical intervention. Unlike other journal publications,[33-37] it uses NEWS and NEWS2 values from the whole hospital admission and compares the performance of the scores in patients who had a positive RT-PCR test result for SARS-CoV-2 with several other patient groups in the same hospital that were, as far as can be determined, not suffering from a COVID-19 illness. This has permitted an assessment of the need for any amendment to NEWS or NEWS2, such as the addition of age[34,38] or other covariates or a change in the weighting of existing parameters,[39] when evaluating patients with COVID-19. The finding that NEWS or NEWS2 performance was good and similar in all five cohorts (range = 0.842-0.894) suggests that such changes are unnecessary and supports the continued use of NEWS or NEWS2 role as systems for the assessment of acute-illness severity in hospitalised patients *irrespective of the underlying condition*.[3-10] In addition, the results demonstrate that NEWS and NEWS2 remain highly relevant for illness severity assessment, even for

patients suffering a completely novel disease that has emerged some years after the two scoring systems were developed. Previous research into the performance of NEWS or NEWS2 for 24 h outcomes shows similar AUROC values to those found in the current study.[2-6,13,15] Consequently, our results support the continued adherence to the national and international guidance on the use of the systems in patients with COVID-19.[20-22] Of course, demonstration that NEWS and NEWS2 discriminate adverse outcomes well does not imply that the important, but separate, issues of when and how care is escalated may not require modification.[40]

The results of our study require validation, if possible, in a larger population. In addition, future research could investigate the hypothesis that, because both NEWS and NEWS2 use a binary weighting for oxygen supplementation [air = 0, oxygen = 2 points], they might not detect sudden and rapid respiratory decompensation if a patient who is already receiving supplemental oxygen develops a rapid increase in oxygen requirement *without additional changes in other physiological parameters*.[19]

CONCLUSIONS

The finding that NEWS or NEWS2 performance was good and similar in all five cohorts (range = 0.842-0.894) suggests that amendments to NEWS or NEWS2, such as the addition of new covariates or the need to change the weighting of existing parameters, are unnecessary when evaluating patients with COVID-19. Our results support the national and international recommendations for the use of NEWS or NEWS2 for the assessment of acute-illness severity in patients with COVID-19.

CRediT author statement

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LEGENDS FOR FIGURES:

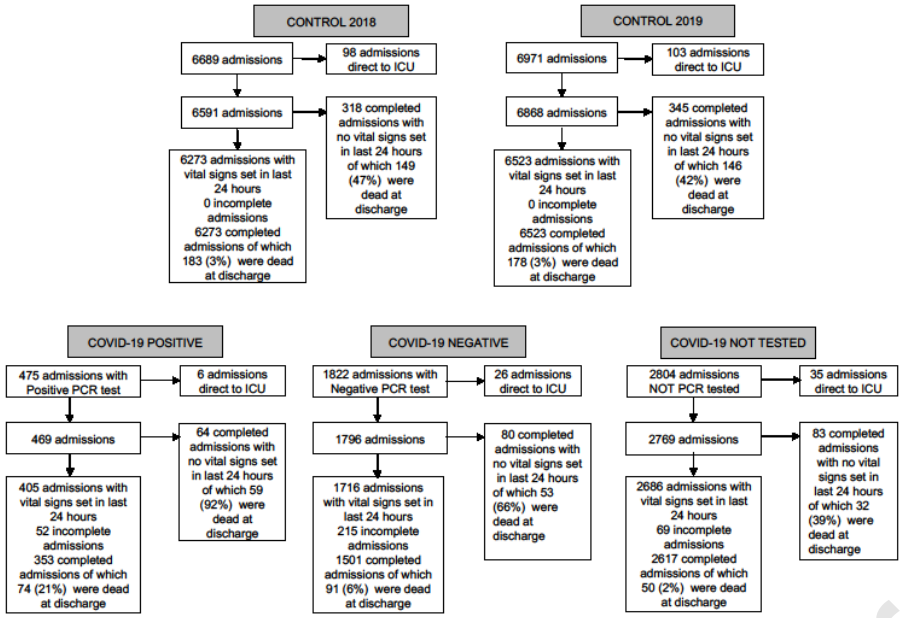

Figure 1. Development of the datasets for each of the five study cohorts

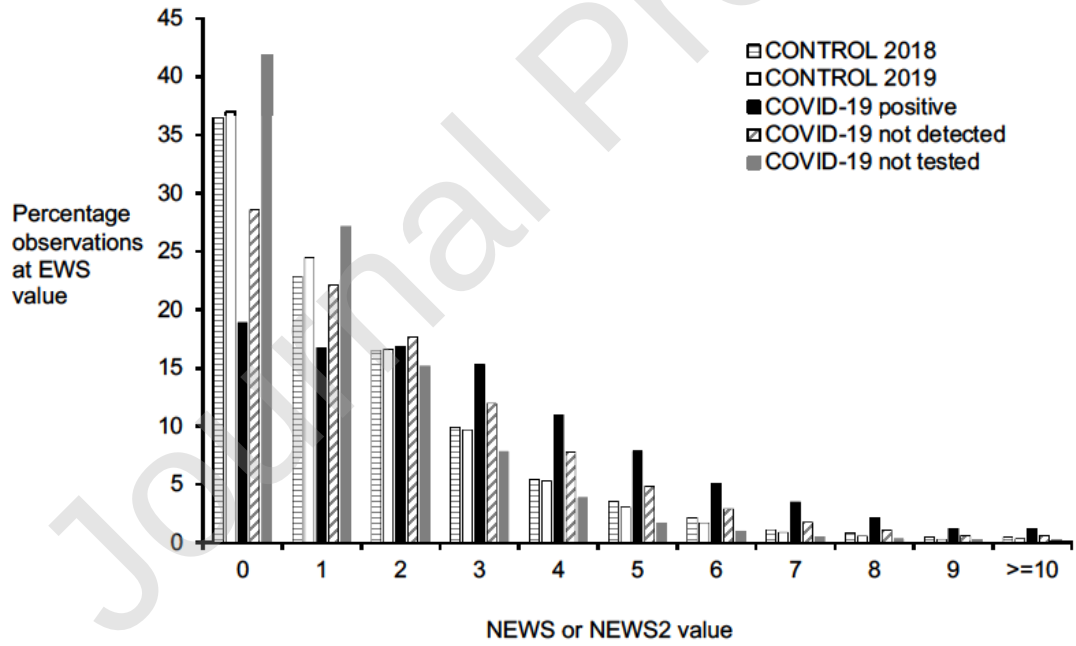

Figure 2

Distribution of NEWS or NEWS2 values for the five admission cohorts

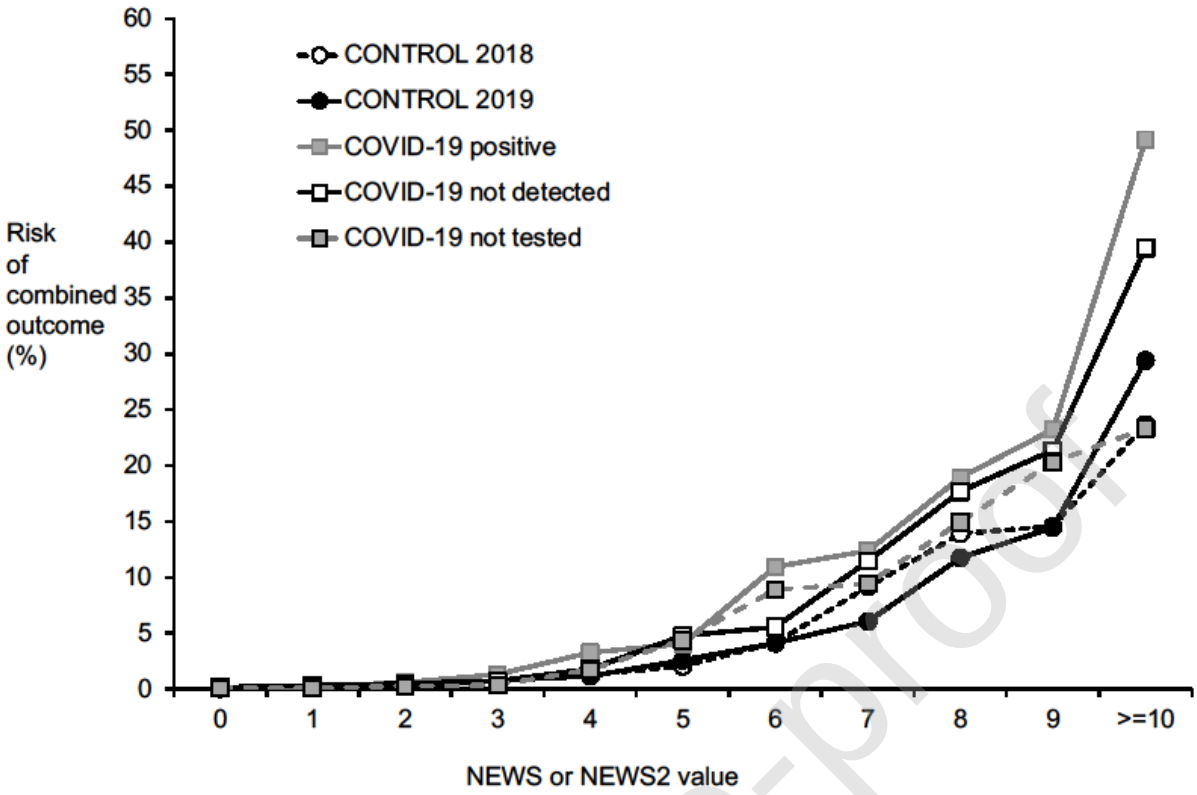

Figure 3. The relationship between NEWS or NEWS2 value and the risk of the combined outcome in all five cohorts.

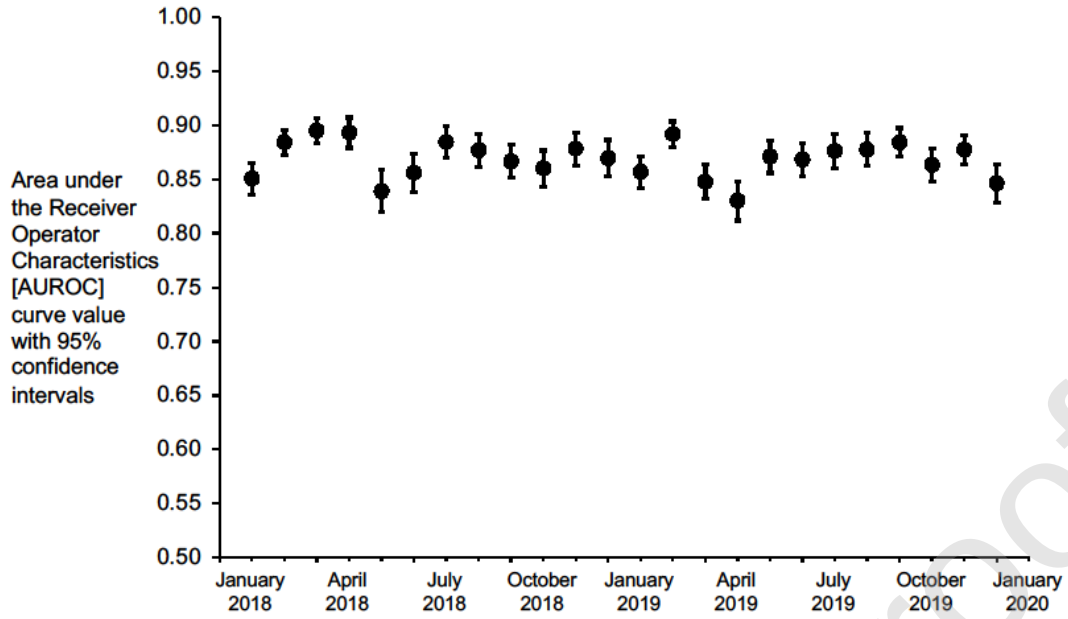

Figure 4. Monthly area under the receiver operating characteristic (AUROC) curve values from 01/01/18-31/12/19 for NEWS or NEWS2 and the combined outcome

Table 1: Demographics data for admissions in the five study cohorts

	CONTROL 2018 (a)	CONTROL 2019 (b)	COVID-19 POSITIVE (c)	COVID-19 NOT DETECTED (d)	COVID-19 NOT TESTED (e)	p-value all groups	post-hoc tests p value			
							(c) v (a)	(c) v (b)	(c) v (d)	(c) v (e)
Admissions										
Admissions, N	6273	6523	405	1716	2686					
Patients, N	5658	5883	400	1619	2505					
Admissions to Medical specialties, N (%)	4,088 (65.2%)	4,142 (63.5%)	380 (93.8%)	1,435 (83.6%)	1,712 (63.7%)	<0.001	<0.001	<0.001	<0.001	<0.001
Admissions to Surgical specialties, N (%)	1,847 (29.4%)	2,000 (30.7%)	22 (5.4%)	260 (15.2%)	877 (32.7%)	<0.001	<0.001	<0.001	<0.001	<0.001
Admissions to Other specialties, N (%)	338 (5.4%)	381 (5.8%)	3 (0.7%)	21 (1.2%)	97 (3.6%)	<0.001	<0.001	<0.001	1.000	0.008
Emergency admissions, N (%)	5,290 (84.3%)	5,476 (83.9%)	400 (98.8%)	1,681 (98%)	2,316 (86.2%)	<0.001	<0.001	<0.001	1.000	<0.001
Elective admissions, N (%)	983 (15.7%)	1,047 (16.1%)	5 (1.2%)	35 (2%)	370 (13.8%)	<0.001	<0.001	<0.001	1.000	<0.001
Age at admission [years], median (IQR)	71 (55-82)	72 (55-83)	75 (62-85)	74 (58-84)	71 (55-82)	<0.001	<0.001	<0.001	<0.001	<0.001
Males, N (%)	2,945 (46.9%)	3,045 (46.7%)	234 (57.8%)	837 (48.8%)	1,277 (47.5%)	0.001	<0.001	<0.001	0.011	0.001
Patients receiving oxygen during stay, N (%)	1,928 (34.1%)	1,856 (31.5%)	261 (65.3%)	665 (41.1%)	485 (19.4%)	<0.001	<0.001	<0.001	<0.001	<0.001
Patients scored using NEWS2, N (%)	0 (0)%	5814 (98.8%)	400 (100%)	1619 (100%)	2505 (100%)	<0.001	<0.001	0.217	1.000	1.000
Patients scored using Scale 2 of NEWS2, N (%)	n/a	106 (1.8%)	12 (3.0%)	39 (2.4%)	20 (0.8%)	<0.001	n/a	0.748	1.000	0.004
All observations										
No of observations, N	150581	163641	14703	44967	47042					
HR [bpm], mean (SD)	79.9 (15.3)	79.8 (15.1)	81 (14.7)	81.8 (15.5)	78.1 (14.4)	<0.001	<0.001	<0.001	<0.001	<0.001

RR [1/min], median (IQR)	17 (16-18)	17 (16-18)	18 (17-20)	18 (16-19)	17 (16-18)	<0.001	<0.001	<0.001	<0.001	<0.001
sBP [mmHg], mean (SD)	126.2 (22.6)	126.4 (22.1)	127.2 (22.2)	126.7 (22.1)	126.8 (21.5)	<0.001	<0.001	0.006	0.303	0.589
Temperature [^{o}C], mean (SD)	36.8 (0.5)	36.7 (0.4)	36.9 (0.6)	36.8 (0.5)	36.7 (0.4)	<0.001	<0.001	<0.001	<0.001	<0.001
S_pO_2 [%], median (IQR)	96 (95-98)	96 (95-98)	95 (94-97)	96 (95-97)	96 (95-98)	<0.001	<0.001	<0.001	<0.001	<0.001
Supplemental O2, N (%)	25,313 (17%)	25,018 (15%)	6,347 (43%)	11,191 (25%)	4,889 (10%)	<0.001	<0.001	<0.001	<0.001	<0.001
AVPU										
Alert, N (%)	149,787 (99.5%)	162,707 (99.4%)	14,599 (99.3%)	44,588 (99.2%)	46,947 (99.8%)	<0.001	0.067	0.414	1.000	<0.001
Responds to voice, N (%)	541 (0.4%)	496 (0.3%)	80 (0.5%)	219 (0.5%)	64 (0.1%)	<0.001	0.009	<0.001	1.000	<0.001
Responds to pain, N (%)	132 (0.1%)	148 (0.1%)	10 (0.1%)	73 (0.2%)	9 (0%)	<0.001	1.000	1.000	0.069	0.062
Unresponsive, N (%)	92 (0.1%)	82 (0.1%)	4 (0%)	43 (0.1%)	3 (0%)	<0.001	1.000	1.000	0.099	0.601
NEWS/NEWS2, median (IQR)	1 (0-2)	1 (0-2)	2 (1-4)	1 (0-3)	1 (0-2)	<0.001	<0.001	<0.001	<0.001	<0.001
Observation sets followed by combined outcome, N (%)	1,240 (0.8%)	1,194 (0.7%)	492 (3.3%)	724 (1.6%)	279 (0.6%)	<0.001	<0.001	<0.001	<0.001	<0.001

HR = heart/pulse rate; RR= respiratory rate; sBP = systolic blood pressure SpO2 = peripheral oxygen saturation; NEWS, National Early Warning Score; NEWS2, National Early Warning Score 2.
Count data has been tested for significance using Fisher's exact test with Bonferroni correction for pairwise comparison.
Percentages were compared using the chi squared test with Bonferroni correction.
Mean values were compared with one-way ANOVA and Scheffe's test
Median values were compared using Kruskal-Wallis and Dunn's test (Bonferroni correction).
IQR = Interquartile range (Q_1-Q_3)