

This is a repository copy of Do Not Attempt Resuscitation (DNAR) status in people with suspected COVID-19 : secondary analysis of the PRIEST observational cohort study.

White Rose Research Online URL for this paper: http://eprints.whiterose.ac.uk/172005/

Version: Submitted Version

Article:

Sutton, L., Goodacre, S. orcid.org/0000-0003-0803-8444, Thomas, B. et al. (1 more author) (Submitted: 2021) Do Not Attempt Resuscitation (DNAR) status in people with suspected COVID-19 : secondary analysis of the PRIEST observational cohort study. mecRxiv. (Submitted)

https://doi.org/10.1101/2021.01.23.21249978

Reuse

This article is distributed under the terms of the Creative Commons Attribution (CC BY) licence. This licence allows you to distribute, remix, tweak, and build upon the work, even commercially, as long as you credit the authors for the original work. More information and the full terms of the licence here: https://creativecommons.org/licenses/

Takedown

If you consider content in White Rose Research Online to be in breach of UK law, please notify us by emailing eprints@whiterose.ac.uk including the URL of the record and the reason for the withdrawal request.



Do Not Attempt Resuscitation (DNAR) status in people with suspected COVID-19: Secondary analysis of the PRIEST observational cohort study

Laura Sutton, Statistician/Research Associate, University of Sheffield, UK, l.j.sutton@sheffield.ac.uk

Steve Goodacre, Professor of Emergency Medicine, University of Sheffield, UK, s.goodacre@sheffield.ac.uk

Ben Thomas, Study Manager, University of Sheffield, UK, <u>b.d.thomas@sheffield.ac.uk</u>

Sarah Connelly, Research Assistant, University of Sheffield, UK, s.l.connelly@sheffield.ac.uk

Corresponding author:

Steve Goodacre, School of Health and Related Research (ScHARR), University of Sheffield, Regent Court, Regent Street, Sheffield, S10 1UL

s.goodacre@sheffield.ac.uk

ORCID ID: 0000-0003-0803-8444

Word count: 2378

Abstract

Background

Cardiac arrest is common in people admitted with suspected COVID-19 and has a poor prognosis. Do Not Attempt Resuscitation (DNAR) orders can reduce the risk of futile resuscitation attempts but have raised ethical concerns.

Objectives

We aimed to describe the characteristics and outcomes of adults admitted to hospital with suspected COVID-19 according to their DNAR status and identify factors associated with an early DNAR decision.

Methods

We undertook a secondary analysis of 13977 adults admitted to hospital with suspected COVID-19 and included in the Pandemic Respiratory Infection Emergency System Triage (PRIEST) study. We recorded presenting characteristics and outcomes (death or organ support) up to 30 days. We categorised patients as early DNAR (occurring before or on the day of admission) or late/no DNAR (no DNAR or occurring after the day of admission). We undertook descriptive analysis comparing these groups and multivariable analysis to identify independent predictors of early DNAR.

Results

We excluded 1249 with missing DNAR data, and identified 3929/12748 (31%) with an early DNAR decision. They had higher mortality (40.7% v 13.1%) and lower use of any organ support (11.6% v 15.7%), but received a range of organ support interventions, with some being used at rates comparable to those with late or no DNAR (e.g. non-invasive ventilation 4.4% v 3.5%). On multivariable analysis, older age (p<0.001), active malignancy (p<0.001), chronic lung disease (p<0.001), limited performance status (p<0.001), and abnormal physiological variables were associated with increased recording of early DNAR. Asian ethnicity was associated with reduced recording of early DNAR (p=0.001).

Conclusions

Early DNAR decisions were associated with recognised predictors of adverse outcome, and were inversely associated with Asian ethnicity. Most people with an early DNAR decision survived to 30 days and many received potentially life-saving interventions.

Registration

ISRCTN registry, ISRCTN28342533, http://www.isrctn.com/ISRCTN28342533

Introduction

In-hospital cardiac arrest is relatively common in patients with COVID-19 and often results in poor outcome. A multicentre cohort study from the United States [1] reported that 701/5019 (14.0%) critically ill patients with COVID-19 had in-hospital cardiac arrest, with 400/701 (57.1%) receiving CPR, and only 7% of these surviving to hospital discharge with normal or mildly impaired neurological status. Management of cardiac arrest in COVID-19 is further complicated by concerns about infection risk associated with aerosol-generating procedures and consequent risks to staff. [2]

These concerns have raised awareness about the need to consider do not attempt resuscitation (DNAR) decisions when patients are admitted to hospital with suspected COVID-19. An appropriately implemented DNAR decision can ensure that the patient's wishes and best interests are addressed, while avoiding futile medical intervention.[3] However, concerns have been raised about inappropriate use of DNAR orders during the pandemic, [4] leading to the Care Quality Commission being asked to review their use in the United Kingdom (UK). [5]

Previous studies have estimated the prevalence of DNAR orders in patients admitted to hospital with community-acquired pneumonia [6-10] and sepsis,[11-14] and have attempted to identify factors associated with DNAR use, but we currently know very little about how DNAR orders have been used in people admitted with suspected COVID-19. The Pandemic Respiratory Infection Emergency System Triage (PRIEST) study was established to develop and evaluate triage tools for people presenting to hospital emergency departments with suspected COVID-19.[15] DNAR status was recorded to facilitate evaluation of triage tools in pre-specified subgroups. We present a post hoc secondary analysis of patients admitted with suspected COVID-19 that aims to describe their characteristics and outcomes according to their DNAR status and identify factors associated with recording of a DNAR decision.

Methods

PRIEST was an observational cohort study of patients attending an emergency department (ED) in the UK with suspected COVID-19 infection during the first wave of the pandemic. We included patients if the assessing clinician recorded that the patient had suspected COVID-19 in the ED records or completed a standardised assessment form for suspected COVID-19 patients. The clinical diagnostic criteria for COVID-19 during the study were of fever ($\geq 37.8^{\circ}$ C) and at least one of the following respiratory symptoms, which must be of acute onset: persistent cough (with or without sputum), hoarseness, nasal discharge or congestion, shortness of breath, sore throat, wheezing, sneezing. We did not seek consent to collect data but information about the study was provided in the ED and patients could withdraw their data at their request. Patients with multiple presentations to hospital were only included once, using data from the first presentation identified by research staff.

We only included patients who were admitted to hospital after ED assessment because DNAR planning was considered unlikely to be routinely undertaken for discharged patients and would be limited to a minority of highly selected cases. We also only included adults (age \geq 16 years) because previous analysis [15] showed that children with suspected COVID-19 had very low rates of confirmed COVID-19 or adverse outcome.

Baseline characteristics at presentation to the ED were recorded prospectively, using a standardised assessment form that doubled as a clinical record (Appendix 1: Standardised Data Collection Form), or retrospectively, through research staff extracting data onto the standardised form using the clinical records. Research staff collected follow-up data onto a standardised follow-up form (Appendix 2: Follow-up Form) using clinical records up to 30 days after presentation. This included recording whether a DNAR decision made at any time between initial presentation and follow-up, and if so, the date of the decision.

Patients who died or required respiratory, cardiovascular, or renal support were classified as having an adverse outcome. Patients who survived to 30 days without requiring respiratory, cardiovascular or renal support were classified as having no adverse outcome. Respiratory support was defined as any intervention to protect the patient's airway or assist their ventilation, including non-invasive ventilation, or acute administration of continuous positive airway pressure. It did not include supplemental oxygen alone or nebulised bronchodilators. Cardiovascular support was defined as any intervention to maintain organ perfusion, such as inotropic drugs, or invasively monitor cardiovascular status, such as central venous pressure or pulmonary artery pressure monitoring, or arterial blood pressure monitoring. It did not include peripheral intravenous cannulation, or fluid administration. Renal support was defined as any intervention to assist renal function, such as haemofiltration, haemodialysis, or peritoneal dialysis. It did not include intravenous fluid administration.

We compared the characteristics and outcomes of those with a DNAR decision recorded on or before the day of ED assessment (early DNAR) to those with no DNAR recorded or a DNAR decision

recorded at a later date (late/no DNAR). We categorised patients in this way on the assumption that patients with a late DNAR decision were likely to be systematically different from those with an early decision, with implementation of a late DNAR decision reflecting the response to intervention. Our categorisation was therefore based on a theoretical framework in which patient characteristics at admission could determine whether a DNAR decision was recorded at hospital admission, and recording of a DNAR decision at admission could then determine subsequent use of interventions.

We calculated a National Early Warning Score (2nd version, NEWS2) for adults, [16] to provide an overall assessment of acute illness severity on a score from zero to 20, based on respiratory rate, oxygen saturation, systolic blood pressure, heart rate, level of consciousness and temperature. We calculated a PRIEST COVID-19 clinical severity score, to provide an overall prediction of the risk of adverse outcome on a score from zero to 29, based on NEWS2, age, sex and performance status [17].

We also undertook multivariable logistic regression modelling to identify independent predictors of DNAR status. Variables were selected on the basis of clinical interest. Collinearity was observed between Glasgow Coma Scale (GCS) scores and consciousness, recorded as alert, responsive to verbal stimuli, responsive to pain or unconscious (AVPU). Missing AVPU data were imputed using GCS as follows, and GCS dropped from the list of predictors: GCS 15 = Alert, GCS 9-14 = Verbal, GCS 7-8 = Pain, and GCS 3-6 = Unresponsive. Continuous physiological predictors were categorised in accordance with NEWS2 risk categories [16] where the reference category denotes normal range and increasing category levels indicate increasing deviation from the norm. Data were analysed using SAS v9.4.

Ethical approval

The North West - Haydock Research Ethics Committee (REC) gave a favourable opinion on the PAINTED study on 25 June 2012 (reference 12/NW/0303) and on the updated PRIEST study on 23rd March 2020. The Confidentiality Advisory Group of the Health Research Authority granted approval to collect data without patient consent in line with Section 251 of the National Health Service Act 2006. The REC approved a substantial amendment to undertake this secondary analysis on 7 January 2021.

Results

The PRIEST study recruited 22484 patients from 70 EDs across 53 sites between 26 March 2020 and 28 May 2020, including 13997 adults admitted following ED assessment. Of these, 1249 had

unknown DNAR status or timing, and were excluded from the analysis. The remaining 12748 were grouped into those with DNAR decisions made on or before the day of initial ED assessment (N=3929, 31%) and those with no DNAR or DNAR decisions made at a later date (N=8819).

Table 1 shows presenting characteristics for both groups. Patients with a DNAR decision recorded on or before their day of attendance tended to be older and have a higher prevalence of comorbidities, limited activity or self-care. They also tended to have a slightly higher respiratory rate, lower oxygen saturation, and lower Glasgow Coma Scale (GCS), and were less likely to be alert.

Table 1. Presenting characteristics for admitted adults with DNAR decisions in place by the end of ED assessment (N=3929) and adults with no DNAR or DNAR decision made later (N=8819)

Characteristic	Statistic/level	Early DNAR	No/late DNAR
Age (years)	N	3929	8819
	Mean (SD)	79.4 (10.9)	63.9 (17.6)
	Median (IQR)	81 (73,87)	65 (52,78)
Sex	Missing	42	78
	Male	2027 (52.1%)	4704 (53.8%)
	Female	1860 (47.9%)	4037 (46.2%)
Ethnicity	Missing/prefer not to say	601	1746
	UK/Irish/other white	3102 (93.2%)	6027 (85.2%)
	Asian	83 (2.5%)	468 (6.6%)
	Black/African/Caribbean	75 (2.3%)	289 (4.1%)
	Mixed/multiple ethnic groups	27 (0.8%)	102 (1.4%)
	Other	41 (1.2%)	187 (2.6%)
Presenting features	Cough	2117 (53.9%)	5514 (62.5%)
	Shortness of breath	2955 (75.2%)	6678 (75.7%)
	Fever	1777 (45.2%)	4688 (53.2%)
Comorbidities	No Chronic disease	323 (8.2%)	2012 (22.8%)
	Heart Disease	1620 (41.2%)	2036 (23.1%)
	Renal impairment	739 (18.8%)	843 (9.6%)
	Steroid therapy	160 (4.1%)	258 (2.9%)
	Asthma	450 (11.5%)	1446 (16.4%)

Characteristic	Statistic/level	Early DNAR	No/late DNAR
	Diabetes	1123 (28.6%)	2034 (23.1%)
	Active malignancy	370 (9.4%)	508 (5.8%)
	Immunosuppression	126 (3.2%)	326 (3.7%)
	Other chronic lung disease	1219 (31%)	1685 (19.1%)
	Hypertension	1721 (43.8%)	3039 (34.5%)
Symptom duration (days)	N	3396	7986
	Mean (SD)	5.7 (6.8)	7.5 (8.4)
	Median (IQR)	3 (1,7)	5 (2,10)
Heart rate (beats/min)	N	3867	8664
	Mean (SD)	95.5 (23)	97.4 (22)
	Median (IQR)	93 (80,109)	96 (82,111)
Respiratory rate (breaths/min)	N	3867	8625
	Mean (SD)	25.5 (7.5)	23.9 (6.9)
	Median (IQR)	24 (20,29)	22 (19,28)
Systolic BP (mmHg)	N	3834	8629
	Mean (SD)	131.8 (27.8)	134.1 (25.6)
	Median (IQR)	130 (112,149)	132 (117,149)
Diastolic BP (mmHg)	N	3813	8587
	Mean (SD)	73.5 (17.1)	77.4 (16.3)
	Median (IQR)	72 (62,84)	77 (67,87)
Temperature (°C)	N	3803	8576
	Mean (SD)	37.1 (1.2)	37.3 (1.2)
	Median (IQR)	37 (36.4,37.9)	37.2 (36.5,38.1)
Oxygen saturation (%)	N	3893	8741
	Mean (SD)	92.6 (8)	94.1 (6.8)
	Median (IQR)	95 (91,97)	96 (93,98)
Glasgow Coma Scale	N	2985	6643
	Mean (SD)	13.9 (2.1)	14.7 (1.3)
	Median (IQR)	15 (14,15)	15 (15,15)
AVPU	Missing	610	1009
	Alert	2877 (86.7%)	7486 (95.9%)
	Verbal	291 (8.8%)	229 (2.9%)

Characteristic	Statistic/level	Early DNAR	No/late DNAR
	Pain	97 (2.9%)	50 (0.6%)
	Unresponsive	54 (1.6%)	45 (0.6%)
Performance status	Missing	222	455
	Unrestricted normal activity	453 (12.2%)	4341 (51.9%)
	Limited strenuous activity, can do		
	light activity	448 (12.1%)	1160 (13.9%)
	Limited activity, can self care	923 (24.9%)	1351 (16.2%)
	Limited self care	1153 (31.1%)	993 (11.9%)
	Bed/chair bound, no self care	730 (19.7%)	519 (6.2%)
NEWS2 score	N	3911	8723
	Mean (SD)	6.4 (3.3)	5.1 (3.1)
	Median (IQR)	6 (4,9)	5 (3,7)
PRIEST score	N	3870	8645
	Mean (SD)	12.5 (3.9)	8.9 (4.1)
	Median (IQR)	12 (10,15)	9 (6,12)

Figures 1 compares the NEWS2 scores for the two groups and shows that those with early DNAR decisions tended to be more acutely unwell (median score 6 versus 5). Figure 2 compares the PRIEST COVID-19 clinical severity scores for the two groups and shows that those with early DNAR decisions were at a higher risk of adverse outcome (median score 12 versus 9, respectively indicating 38% versus 26% expected risk of a 30-day adverse outcome) [17].

Table 2 gives location of admission, pathogen confirmation and adverse outcome data for the two groups. Patients with an early DNAR decision had a higher mortality rate but most (59.4%) survived to 30 days. They also had lower use of critical care and organ support, but a significant proportion (11.6%) received organ support. Table 2 shows the highest level of organ support received, according to a predefined hierarchy (corresponding to the order presented in the table). Patients with early DNAR decisions received a wide range of interventions, some at comparable rates to those with no or a late DNAR decision (e.g. non-invasive ventilation and high flow nasal oxygen).

Table 2. Outcome data for admitted adults with DNAR decisions in place by the end of ED assessment (N=3929) and adults with no DNAR or DNAR decision made later (N=8819)

Outcome	Level	Early DNAR	No/late DNAR
Location of first admission	Missing	98	194
	Ward	3717 (97%)	7802 (90.5%)
	ITU	57 (1.5%)	667 (7.7%)
	HDU	57 (1.5%)	156 (1.8%)
Respiratory pathogen	COVID-19	1791 (45.6%)	3367 (38.2%)
	Influenza (pandemic or seasonal)	6 (0.2%)	14 (0.2%)
	Other	235 (6%)	701 (7.9%)
	None identified	1897 (48.3%)	4737 (53.7%)
Mortality status	Missing	0	0
,	Alive	2328 (59.3%)	7668 (86.9%)
	Dead	57 (1.5%) 57 (1.5%) 1791 (45.6%) 6 (0.2%) 235 (6%) 1897 (48.3%) 0	1151 (13.1%)
	Death with organ support	251 (15.7%)	373 (32.4%)
	Death without organ support	1350 (84.3%)	778 (67.6%)
Organ support	Respiratory	423 (10.8%)	1313 (14.9%)
Organ support	Mechanical ventilation	51 (1.3%)	509 (5.8%)
	Non-invasive ventilation	173 (4.4%)	292 (3.3%)
	Continuous positive airway pressure	125 (3.2%)	386 (4.4%)
	High-flow nasal oxygen	74 (1.9%)	126 (1.4%)
	Cardiovascular	47 (1.2%)	426 (4.8%)
	Extracorporeal membrane oxygenation	0 (0%)	13 (0.1%)
	Inotropic/vasopressor drugs	29 (0.7%)	283 (3.2%)
	Central venous pressure measurement	2 (0.1%)	25 (0.3%)
	Intra-arterial BP measurement	16 (0.4%)	105 (1.2%)
	Renal	29 (0.7%)	172 (2%)
	Haemofiltration	7 (0.2%)	93 (1.1%)
	Haemodialysis	22 (0.6%)	75 (0.9%)
	Peritoneal dialysis	0 (0%)	4 (0%)
	Any	455 (11.6%)	1386 (15.7%)

Table 3 shows the results of the multivariable logistic regression model. Older age, active malignancy, chronic lung disease, limited performance status, abnormal heart rate, abnormal respiratory rate, lower oxygen saturation, and lower alertness were all associated with increased use of early DNAR. Asian ethnicity was associated with a lower use of early DNAR.

Effect	Odds ratio	95% Cl	p-value
Age	1.054	(1.049, 1.060)	<0.001
Male sex	1.010	(0.905, 1.128)	0.859
Ethnicity (ref=UK/Irish/other white)			
Asian	0.571	(0.416, 0.783)	0.001
Black/African/Caribbean	0.730	(0.524, 1.017)	0.063
Mixed/multiple ethnic groups	0.993	(0.568, 1.737)	0.982
Other	0.647	(0.410, 1.020)	0.061
Shortness of breath	1.150	(1.005, 1.316)	0.042
Cough	1.012	(0.903, 1.133)	0.841
Fever	0.954	(0.851, 1.069)	0.415
No chronic disease	0.753	(0.609, 0.931)	0.009
Heart disease	1.182	(1.048, 1.333)	0.006
Renal impairment	1.241	(1.067, 1.445)	0.005
Steroid therapy	1.268	(0.971, 1.657)	0.082
Asthma	0.900	(0.765, 1.060)	0.209
Diabetes	1.120	(0.987, 1.271)	0.080
Active malignancy	1.604	(1.319, 1.951)	<0.001
Immunosuppression	1.117	(0.835, 1.494)	0.455
Other chronic lung disease	1.456	(1.280, 1.656)	<0.001
Hypertension	0.883	(0.786, 0.993)	0.038
Symptom duration (days)	0.993	(0.986, 1.001)	0.076
Pulse rate (beats/min; ref=51-90)			
41-50 or 91-110	1.121	(0.987, 1.274)	0.079
111-130	1.095	(0.929, 1.290)	0.280
≤40 or ≥131	1.030	(0.816, 1.300)	0.802
Respiratory rate (breaths/min; ref=12-20)			

Table 3. Multivariable analysis of predictors of early DNAR use

Effect	Odds ratio	95% Cl	p-value
9-11	0.772	(0.115, 5.173)	0.790
21-24	1.175	(1.019, 1.355)	0.027
≤8 or ≥25	1.361	(1.187, 1.560)	<0.001
Systolic BP (mmHg; ref=111-219)			
101-110	1.164	(0.968, 1.400)	0.107
91-100	1.347	(1.066, 1.703)	0.013
≤90 or ≥220	1.177	(0.891, 1.555)	0.251
Temperature (°C; ref=36.1-38.0)			
35.1-36.0 or 38.1-39.0	0.916	(0.807, 1.039)	0.173
≥39.1	0.885	(0.693, 1.131)	0.330
≤35.0	1.085	(0.764, 1.540)	0.650
Oxygen saturation (%; ref=≥96)			
94-95	1.041	(0.898, 1.206)	0.595
92-93	1.127	(0.938, 1.354)	0.203
≤91	1.329	(1.153, 1.532)	<0.001
AVPU (ref=Alert)			
Verbal	1.905	(1.563, 2.323)	<0.001
Pain	2.651	(1.644, 4.272)	<0.001
Unresponsive	2.620	(1.429, 4.803)	0.002
Performance status (ref=Unrestricted normal activity)			
Limited strenuous activity, can do light activity	1.885	(1.565, 2.269)	<0.001
Limited activity, can self care	2.629	(2.222, 3.110)	<0.001
Limited self care	4.100	(3.448, 4.876)	<0.001
Bed/chair bound, no self care	5.437	(4.438, 6.660)	<0.001

Discussion

We found that 31% of adults admitted to hospital with suspected COVID-19 during the first phase of the pandemic had a DNAR decision recorded on or before their day of attendance, after excluding those who could not be classified. Most patients (59.4%) with an early DNAR decision survived to 30 days and 11.6% received some form of organ support. These findings show that potentially life-saving treatments were provided to a significant proportion of people, potentially addressing concerns that DNAR decisions may be conflated with 'do not provide active treatment'.[18] The use of invasive intervention, particularly mechanical ventilation, in people with a DNAR decision was an

unexpected finding. Contact with participating site investigators suggested that this could be explained by use of the ReSPECT process in discussions about resuscitation, in which the patient is encouraged to explicitly indicate which treatments they want in a future situation where they are unable to make or express choices.[19] The ReSPECT process therefore allows patients to consent to mechanical ventilation but decline cardiopulmonary resuscitation if it is subsequently required.

Older age, active malignancy, chronic lung disease (excluding asthma), and lower performance status were associated with increased use of early DNAR, whereas Asian ethnicity was associated with decreased use. Patients with early DNAR status tended to be more acutely ill, with higher NEWS2 scores. Abnormal respiratory rate, lower oxygen saturation, and lower alertness were associated with increased use of early DNAR.

Our findings suggest a higher rate of DNAR use (31%) than identified in previous studies of similar conditions. Studies of patients admitted with community-acquired pneumonia reported rates of DNAR use ranging from 13% to 29%, [6-10] while studies in severe sepsis or septic shock reported rates ranging from 9% to 20%. [11-14] DNAR decisions in these studies were associated with older age, but conflicting findings were reported around the use of invasive procedures. Sakari *et al* [11] and Bradford *et al* [12] reported that DNAR orders were associated with lower rates of invasive procedures, while Powell *et al* [13] reported no difference, and Huang *et al* [14] reported a higher rate of arterial or central venous cannulation in those with a DNAR order.

We found an association between Asian ethnicity and decreased use of early DNAR status compared to White ethnicity. The odds ratio for Black/African/Caribbean ethnicity also suggested decreased use but was not significant. Previous studies from the United States have shown less use of DNAR decisions among African-American, Asian, and Hispanic patients, [20,21,22] and Black patients tend to receive more life-prolonging treatment at end of life care. [23] A systematic review of end of life decisions for people from ethnic minority groups suggested that Hispanic and African American people had advance care plans documented less often, citing religious coping and spirituality as factors. [24] A scoping review of culturally- and spiritually-sensitive end-of-life care highlighted a multitude of factors influencing end-of-life care and subsequent experiences by culturally- and spiritually-diverse groups. [25] Further research of DNAR decisions in relation to ethnicity is clearly required.

Studies of DNAR use in COVID-19 are currently limited. Alhatem *et al* [26] analysed 1270 patients admitted across two hospitals with COVID-19, of whom 750/1270 (59%) had a DNAR order at admission, and 570/750 (76%) of these died. Age over 60, male sex, and comorbidities were associated with DNAR at admission. Coleman *et al* [27] examined records of DNAR decisions at a single centre from 2017 to 2020 and showed an increased rate of DNAR use during pandemic, with patients tending to be younger and have fewer comorbidities. It is unclear whether these findings reflect an increased overall need for DNAR decisions during the pandemic or increased willingness to use DNAR decisions in COVID-19. Our findings suggest that a relatively high rate of DNAR use in suspected COVID-19 may contribute to an increased rate of DNAR use during the pandemic.

This study was based on a large representative sample of adults admitted with suspected COVID-19, but has a number of limitations. DNAR decisions were recorded to facilitate subgroup analyses addressing the primary purpose of the study rather than addressing the aims of this secondary analysis. We were unable to include 1249/13997 (9%) cases because data were missing or uncertain regarding the use or timing for DNAR. Our categorisation on the basis of timing of DNAR decision and assumption that later DNAR decisions are qualitatively different to early decisions could be challenged. We did not collect any detailed data to allow us to explore the reasons behind DNAR decisions, so we are unable to offer explanations for the associations identified in our analysis. Our suggestion that the ReSPECT process could explain the use of invasive interventions in people with a DNAR decision is based on informal contacts and requires further research. The use of the ReSPECT process could also undermine our rationale for categorising DNAR decisions as early versus late or no decision, and suggests a complex relationship between DNAR decisions and subsequent interventions.

In conclusion, we found that many patients with an early DNAR decision went on to receive lifesaving interventions and most survived to 30 days. Early DNAR decisions were associated with older age, lower performance status, active malignancy, chronic lung disease and severe illness, as indicated by physiological parameters. We found some evidence of an association between ethnicity and DNAR status that requires further research.

Competing interests

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: grant funding to their employing institutions from the National Institute for Health Research; no financial relationships with any organisations that might have an interest in the

submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

Contributor and guarantor information

SG conceived and designed the study. BT oversaw data acquisition. LS analysed the data. SC undertook literature searches. SG, LS, BT and SC interpreted the data. All authors contributed to drafting the manuscript. SG is the guarantor of the paper. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

Acknowledgements

We thank Katie Ridsdale for clerical assistance with the study, Erica Wallis (Sponsor representative), all members of the PRIEST Research Team, (Appendix 3), all members of the Study Steering Committee (Appendix 4) and the site research teams who delivered the data for the study (Appendix 5), and the research team at the University of Sheffield past and present (Appendix 6).

Data sharing

Anonymised data are available from the corresponding author upon reasonable request (contact details on first page).

Role of the funding source

The PRIEST study was funded by the United Kingdom National Institute for Health Research Health Technology Assessment (HTA) programme (project reference 11/46/07). The funder played no role in the study design; in the collection, analysis, and interpretation of data; in the writing of the report; and in the decision to submit the article for publication. The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health and Social Care.

References

 Hayek Salim S, Brenner Samantha K, Azam Tariq U, Shadid Husam R, Anderson Elizabeth, Berlin Hanna et al. In-hospital cardiac arrest in critically ill patients with covid-19: multicenter cohort study BMJ 2020; 371 :m3513

- Perkins GD, Morley PT, Nolan JP, Soar J, Berg K, Olasveengen T, Wyckoff M, Greif R, Singletary N, Castren M, de Caen A, Wang T, Escalante R, Merchant RM, Hazinski M, Kloeck D, Heriot G, Couper K, Neumar R. International Liaison Committee on Resuscitation: COVID-19 consensus on science, treatment recommendations and task force insights. Resuscitation. 2020; 151: 145-147.
- Curtis JR, Kross EK, Stapleton RD. The Importance of Addressing Advance Care Planning and Decisions About Do-Not-Resuscitate Orders During Novel Coronavirus 2019 (COVID-19). JAMA 2020; 323(18): 1771-1772.
- 4. Dyer Clare. Covid-19: Campaigner calls for national guidance to stop DNR orders being made without discussion with patients and families BMJ 2020; 369 :m1856
- Care Quality Commission. Reviewing the use of do not resuscitate decisions during COVID-19, 17/11/2020. <u>https://www.cqc.org.uk/news/stories/reviewing-use-do-not-resuscitate-</u> <u>decisions-during-covid-19</u> (accessed 11/12/2020)
- 6. Egelund GB, Jensen AV, Petersen PT, et al. Do-not-resuscitate orders in patients with community-acquired pneumonia: a retrospective study. BMC Pulm Med 2020; 20(1): 201.
- 7. Marrie TJ, Fine MJ, Kapoor WN, Coley CM, Singer DE, Obrosky DS. Community-acquired pneumonia and do not resuscitate orders. J Am Geriatr Soc 2002; 50(2): 290–299.
- 8. Oshitani Y, Nagai H, Matsui H. Rationale for physicians to propose do-not-resuscitate orders in elderly community-acquired pneumonia cases. Geriatr Gerontol Int 2014; 14(1): 54–61.
- Walkey AJ, Weinberg J, Wiener RS, Cooke CR, Lindenauer PK. Association of do-not-Resuscitate Orders and Hospital Mortality Rate among Patients with Pneumonia. JAMA Intern Med 2016; 176(1): 97–104.
- 10. Mulder T, van Werkhoven CH, Huijts SM, Bonten MJ, Postma DF, Oosterheert JJ. Treatment restrictions and empirical antibiotic treatment of community-acquired pneumonia in elderly patients. Neth J Med 2016; 74(1): 56.
- 11. Sarkari NN, Perman SM, Ginde AA. Impact of early do-not-attempt-resuscitation orders on procedures and outcomes of severe sepsis. J Crit Care 2016; 36: 134-139.
- 12. Bradford MA, Lindenauer PK, Wiener RS, Walkey AJ. Do-not-resuscitate status and observational comparative effectiveness research in patients with septic shock. Crit Care Med 2014; 42(9): 2042-7.
- 13. Powell E, Sauser K, Cheema N, Pirotte M, Quattromani E, Avula U, et al. Severe sepsis in donot-resuscitate patients: intervention and mortality rates. J Emerg Med 2013; 44(4): 742–9.
- 14. Huang CT, Chuang YC, Tsai YJ, Ko WJ, Yu CJ. High Mortality in Severe Sepsis and Septic Shock Patients with Do-Not-Resuscitate Orders in East Asia. PLoS One 2016; 11(7):e0159501.

- Goodacre S, Thomas B, Lee E, Sutton L, Loban A, Waterhouse S, et al. (2020) Characterisation of 22445 patients attending UK emergency departments with suspected COVID-19 infection: Observational cohort study. PLoS ONE 15(11): e0240206.
- Royal College of Physicians. (2017). National Early Warning Score (NEWS) 2: Standardising the assessment of acute-illness severity in the NHS. Updated report of a working party. London: RCP.
- 17. Goodacre S, Thomas B, Sutton L, Bursnall M, Lee E, Bradburn M, et al. Derivation and validation of a clinical severity score for acutely ill adults with suspected COVID-19: The PRIEST observational cohort study. medRxiv 2020.10.12.20209809; doi: https://doi.org/10.1101/2020.10.12.20209809
- 18. Perkins GD, Griffiths F, Slowther AM, George R, Fritz Z, Satherley P, Williams B, Waugh N, Cooke MW, Chambers S, Mockford C, Freeman K, Grove A, Field R, Owen S, Clarke B, Court R, Hawkes C. Do-not-attempt-cardiopulmonary-resuscitation decisions: an evidence synthesis. Southampton (UK): NIHR Journals Library; 2016 Apr.
- 19. Resuscitation Council UK. Resuscitation Council UK Statement on the role of the ReSPECT Process during COVID-19, 23 April 2020. <u>https://www.resus.org.uk/sites/default/files/2020-</u>06/COVID%20ReSPECT%20Guidance%2023042020_0.pdf (accessed 14/01/2021)
- 20. Bailey FA, Allen RS, Williams BR, Goode PS, Granstaff S, Redden DT, Burgio KL. Do-notresuscitate orders in the last days of life. J Palliat Med 2012; 15(7): 751-9.
- Burgio KL, Williams BR, Dionne-Odom JN, Redden DT, Noh H, Goode PS, Kvale E, Bakitas M, Bailey FA. Racial Differences in Processes of Care at End of Life in VA Medical Centers: Planned Secondary Analysis of Data from the BEACON Trial. J Palliat Med 2016; 19(2): 157-63.
- 22. Richardson DK, Zive DM, Newgard CD. End-of-life decision-making for patients admitted through the emergency department: hospital variability, patient demographics, and changes over time. Acad Emerg Med 2013; 20(4): 381-7.
- Mack JW, Paulk ME, Viswanath K, Prigerson HG. Racial disparities in the outcomes of communication on medical care received near death. Arch Intern Med 2010; 170(17): 1533-40.
- 24. LoPresti MA, Dement F, Gold HT. End-of-Life Care for People With Cancer From Ethnic Minority Groups: A Systematic Review. Am J Hosp Palliat Care 2016; 33(3): 291-305.
- 25. Fang ML, Sixsmith J, Sinclair S, Horst G. A knowledge synthesis of culturally- and spirituallysensitive end-of-life care: findings from a scoping review. BMC Geriatr 2016;16: 107.

- Alhatem A, Spruijt O, Heller DS, Chokshi RJ, Schwartz RA, Lambert WC. "Do-Not-Resuscitate (DNR)" Status Determines Mortality in Patients with COVID-19. Clin Dermatol 2020 Nov 28. doi: 10.1016/j.clindermatol.2020.11.013. Epub ahead of print.
- Coleman JJ, Botkai A, Marson EJ, et al. Bringing into focus treatment limitation and DNACPR decisions: How COVID-19 has changed practice. Resuscitation. 2020;155:172-179. doi:10.1016/j.resuscitation.2020.08.006

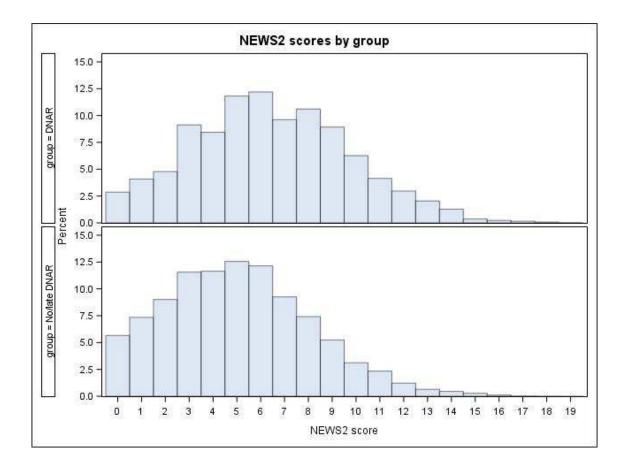


Figure 1. NEWS2 score distribution by DNAR status

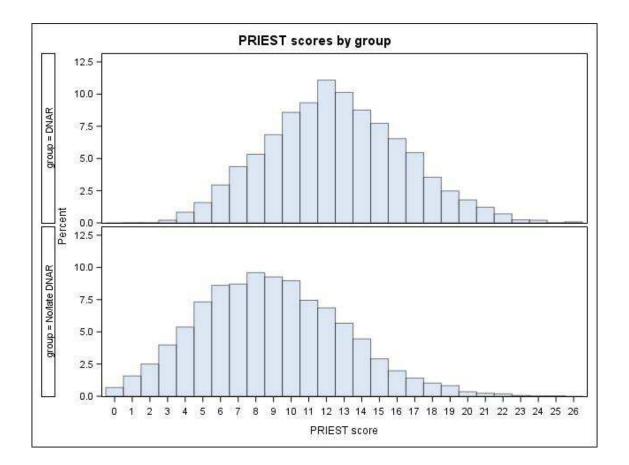


Figure 2. PRIEST score distribution by DNAR status