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**To the Editor in Chief**

**Professor Geoff Hughes**

Dear Dr Hughes,

We, the authors, wish to submit this Original Research manuscript entitled:

*Epidemiology and clinical features of emergency department patients with suspected COVID-19: Insights from Australia's 'second wave' (COVED-4).*

For consideration and publication.

As the incidence of COVID-19 surges across much of the northern hemisphere, and Australia welcomes back large numbers of returned travellers, the potential for further “waves” of the COVID-19 pandemic in Australia remains. It is important, therefore, to continue to support Australian ED clinicians, and ED clinicians globally, with updated clinical data and tools to inform the ongoing responses currently demanded of emergency care systems. The COVID-19 Emergency Department (COVED) Quality Improvement Project has completed its cumulative analysis for the period from 1 July to 31 August, in the midst of the second wave of the pandemic in Australia. This manuscript reports that detailed analysis from an increasing number of participating sites, and COVID-19 cases, across Australia.

We look forward to hearing of your decision.

Best wishes,

A/Prof Gerard O'Reilly

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**Title**

*Epidemiology and clinical features of emergency department patients with suspected COVID-19: Insights from Australia's 'second wave' (COVED-4).*

**Short Running Title**

*COVED-4: Results from 1 July to 31 August 2020*

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### **Conflict of Interest Statement**

Gerard O'Reilly, Biswadev Mitra, Jeremy Furyk, Viet Tran and Peter Cameron are Section Editors for EMA. There are no other potential conflicts of interest to declare.

### **Ethics**

Ethics approval was obtained from the Alfred Human Research Ethics Committee (Project No: 188/20) on 26 March 2020 and approved as a multi-site project (63444) on 9 April 2020. The requirement for patient consent was waived.

### **Data Availability Statement**

Data that support the findings of this study may be available upon reasonable request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

### **Author Contribution Statement**

All authors listed have contributed to the concept and design of this Original Research, including its analysis plan, and have critically reviewed the Original Research for content.

## Funding Statement

GO'R is currently a NHMRC Research Fellow at the National Trauma Research Institute, Alfred Hospital, Melbourne, Australia, leading the project titled: "Maximising the usefulness and timeliness of trauma and emergency registry data for improving patient outcomes" (APP1142691). PC is funded by a PC is funded by a MRFF practitioner fellowship (MRF1139686). AW is supported by a NHMRC Research Fellowship ID 1159907. NC is funded by a research grant from Study, Education and Research Trust Account of Townsville Hospital and Health Service.

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GO'R is currently a NHMRC Research Fellow at the National Trauma Research Institute, Alfred Hospital, Melbourne, Australia, leading the project titled: "Maximising the usefulness and timeliness of trauma and emergency registry data for improving patient outcomes"

## **Abstract**

*Objective:* The aim of this study was to describe the epidemiology and clinical features of patients presenting to the emergency department (ED) with suspected and confirmed COVID-19 during Australia's 'second wave'.

*Methods:* The COVID-19 Emergency Department (COVED) Project is an ongoing prospective cohort study in Australian EDs. This analysis presents data from twelve sites across four Australian states for the period from 1 July to 31 August 2020. All adult patients who met criteria for 'suspected COVID-19' and underwent testing for SARS-CoV-2 in the ED were eligible for inclusion. Study outcomes included a positive SARS-CoV-2 test result, mechanical ventilation and in-hospital mortality.

*Results:* There were 106,136 presentations to the participating EDs and 12,055 (11.4%; 95% CI: 11.2-11.6) underwent testing for SARS-CoV-2. Of these, 255 (2%) patients returned a positive result. Among positive cases, 13 (5%) received mechanical ventilation during their hospital admission compared to 122 (2%) of the SARS-CoV-2 negative patients (OR 2.7; 95% CI: 1.5-4.9,  $p=0.001$ ). Nineteen (7%) SARS-CoV-2 positive patients died in hospital compared to 212 (3%) of the SARS-CoV-2 negative patients (OR 2.3; 95% CI: 1.4-3.7,  $p=0.001$ ). Strong clinical predictors of the SARS-CoV-2 test result included self-reported fever, sore throat, bilateral infiltrates on CXR, and absence of a leucocytosis on first ED blood tests ( $p<0.05$ ).

*Conclusions:* In this prospective multi-site study during Australia's 'second wave', a substantial proportion of ED presentations required SARS-CoV-2 testing and isolation. Presence of SARS-CoV-2 on nasopharyngeal swab was associated with an increase in the odds of death and mechanical ventilation in hospital.

### **Key words**

Emergency, registry, COVID-19, isolation, quality improvement

## Manuscript

### Introduction

Health systems across the world continue to be impacted by the COVID-19 pandemic. While Australia has been relatively successful at containing the virus, a ‘second wave’ of infections in mid-2020 has demonstrated the need for vigilance. As of 22 November 2020, 27,892 cases and 907 deaths have been reported nationally, with an overall admission rate of approximately 13%.<sup>1</sup>

Despite the significant decline in community transmission,<sup>1</sup> a substantial proportion of Australian emergency department (ED) patients continue to meet criteria for ‘suspected COVID-19’ and therefore require isolation and testing.<sup>2</sup> This has led to a number of issues for EDs, particularly in terms of maintaining ‘business as usual’ in parallel with rigorous infection prevention and control (IPC) for suspected and confirmed cases.<sup>3</sup> As ED presentations and hospital occupancy return to baseline (following substantial reductions during the ‘first wave’),<sup>4,5</sup> meeting these challenges has become increasingly complex.<sup>6,7</sup>

In this context, it is important that clinicians have access to contemporary data and evidence-based tools to guide clinical decisions and systems reform. In particular, there is a need for robust models that support timely risk-assessment and diagnosis.<sup>2,8</sup> Although the characteristics of hospitalised patients with confirmed COVID-19 are well described, relatively little has been published about the epidemiology, clinical features and outcomes of ED patients who undergo testing for SARS-CoV-2.<sup>2,9-14</sup> Additionally, no diagnostic and prognostic tools have been specifically developed, or validated, for the Australian ED context.<sup>15</sup>

The COVID-19 ED (COVED) Quality Improvement Project was initiated in response to these challenges.<sup>16</sup> COVED-1 and COVED-2, which coincided with Australia’s ‘first wave’, demonstrated a low positive test rate, with no SARS-CoV-2 positive patients receiving mechanical ventilation or dying in ED of the single participating site. These studies also identified a high number of patients meeting case definition criteria and requiring isolation.<sup>17,18</sup> COVED-3 reported data across eight EDs during July 2020, and revealed no difference in the rates of mechanical ventilation and in-hospital death between SARS-CoV-2 positive and negative patients. The main clinical predictors of a COVID-19 diagnosis were subjective fever, bilateral infiltrates on chest x-ray (CXR), non-smoking status and absence of leucocytosis.<sup>2</sup>

This study (COVED-4) builds on the findings of COVED-3 with a broader sample of patients.<sup>2</sup> It reports data from twelve EDs, distributed across four states in eastern Australia, for July and August 2020. The study aimed to further explore the association between the SARS-CoV-2 test result in the ED and mechanical ventilation and in-hospital mortality, and to identify the clinical and epidemiological variables predictive of a COVID-19 diagnosis.

### Methods

COVED is an ongoing prospective cohort study that commenced on 1 April 2020. The study protocol has been published previously.<sup>16</sup> The study includes adult patients that had a SARS-CoV-2 polymerase chain reaction (PCR) test requested in the ED and were managed with IPC precautions for ‘suspected COVID-19’. Testing criteria are guided by the various health jurisdictions and have evolved throughout the Project.<sup>19-22</sup> The criteria that were applicable during this study period are listed in **Box 1**. Patients

who underwent testing for surveillance purposes (i.e. patients who were tested for SARS-CoV-2 in the ED but were not subjected to IPC precautions) were excluded.

This analysis (COVED-4) describes study findings for eligible patients that presented to the twelve participating EDs (The Alfred Hospital, St Vincent's Hospital Melbourne, Austin Hospital, Box Hill Hospital, Royal Melbourne Hospital, University Hospital Geelong, Royal Hobart Hospital, Launceston General Hospital, North-West Regional Hospital, Mersey Community Hospital, Sutherland Hospital Sydney and Townsville University Hospital) over the period 1 July to 31 August 2020. These sites represent a mixture of urban and regional EDs across Victoria, Tasmania, New South Wales and Queensland (**Table 1**). In all of these locations, alternative non-ED testing sites (e.g. screening clinics) were in operation for those with minor symptoms who did not require ED care. These patients were not included in this study.

COVED outcome measures include SARS-CoV-2 PCR test result, mechanical ventilation and hospital discharge destination. The complete list of variables has previously been published in the study protocol.<sup>2,16</sup> These include history (age, sex, symptoms, epidemiological features, co-morbidities), findings on clinical examination, radiological and blood investigations, care provided in the ED and hospital (including ED disposition destination) and patient outcomes (including survival to hospital discharge).<sup>2</sup> COVED variables and definitions have been harmonised with international COVID-19 research tools developed by the World Health Organization and International Severe Acute Respiratory and Emerging Infection Consortium (ISARIC).<sup>23</sup>

The data for study participants are collected from hospital electronic medical record (EMR) systems. Some variables are automatically extracted from data warehouses; other variables require manual record review.<sup>2</sup> Data are entered into the COVED registry utilising Research Electronic Data Capture (REDCap) tools, hosted and managed by Helix (Monash University).<sup>24,25</sup> The data dictionary and case report form are available on The Alfred Hospital's academic programs website at <https://emergencyeducation.org.au/research/coved/>.<sup>2</sup>

Summary descriptive statistics have been determined for each pre-specified variable; these data have been stratified by the test result for the SARS-CoV-2 PCR swab taken in the ED. As for COVED-3,<sup>2</sup> there were sufficient SARS-CoV-2 positive cases to undertake inferential analyses (comparing predictors and outcomes by SARS-CoV-2 test result, with summary measures of association and 95% confidence intervals). Symmetrical numerical data have been summarised using the mean and standard deviation; skewed and ordinal data have been summarised using the median and inter-quartile range; and categorical data have been summarised using the frequency and percentage.

The final prediction model was derived to avoid overfitting, whereby the maximum number of clinical predictor variables included in the final (parsimonious) model was limited by the 'rule of thumb' whereby at least ten observations of each outcome (SARS-CoV-2 positive *and* negative) are required per predictor variable.<sup>2</sup> Data were analysed using Stata statistical software (version 15.1 StataCorp, Texas, USA). A p-value of <0.05 was defined to be statistically significant. Ethics approval was obtained from the Alfred Human Research Ethics Committee (Project No: 188/20).

## Results

There were 106,136 ED presentations during the study period, and 12,055 (11.4%; 95% CI: 11.2-11.6) met inclusion criteria. Of these, 255 (2%) patients returned a positive SARS-CoV-2 test result and 11,800 (98%) were negative (see **Table 1**).

**Table 2** summarises the baseline demographic and ED arrival characteristics of included patients. There were no differences in age or sex distribution. Patients who tested positive for SARS-CoV-2 were more likely to have arrived by ambulance ( $p < 0.001$ ), but there were no differences in assigned triage category.

Patient outcomes are summarised in **Table 3**. Of the SARS-CoV-2 positive patients, 19 (7%) died in hospital compared to 212 (3%) of the SARS-CoV-2 negative patients (OR 2.3; 95% CI: 1.4-3.7,  $p = 0.001$ ). Thirteen (5%) of the SARS-CoV-2 positive patients received invasive mechanical ventilation during their hospital admission, compared to 122 (2%) of the SARS-CoV-2 negative patients (OR 2.7; 95% CI: 1.5-4.9,  $p = 0.001$ ). SARS-CoV-2 positive patients were more likely to be admitted to the intensive care unit (ICU) (OR 5.0; 95% CI: 2.7-9.1,  $p < 0.001$ ) or the general ward (OR 2.8; 95% CI: 2.0-3.9,  $p < 0.001$ ) than SARS-CoV-2 negative patients respectively.

**Table 4** describes the clinical and epidemiological features of the sample (based on the available data from contributing sites, as summarised in **Table 1**). Cough (61%), fatigue (58%) and subjective fever (55%) were the most common presenting complaints among SARS-CoV-2 positive patients. Eighty (54%) SARS-CoV-2 positive patients reported prior contact with a positive case and 55 (40%) had bilateral infiltrates on CXR. Compared to SARS-CoV-2 negative patients, SARS-CoV-2 positive patients were more likely to identify cough, anosmia or dysgeusia, sore throat, fever, fatigue, myalgia or diarrhoea among their presenting symptoms. They were also more likely to reside in a residential aged care facility, identify as a health care worker, have a diagnosis of diabetes or be a non-smoker. In terms of examination findings, SARS-CoV-2 positive patients were more likely to have a fever (temperature  $\geq 38^{\circ}\text{C}$ ) or hypoxia (oxygen saturation  $< 92\%$ ). On investigation, SARS-CoV-2 positive patients were less likely to have a leucocytosis, more likely to have a thrombocytopenia and more likely to have bilateral infiltrates on first CXR than SARS-CoV-2 negative patients.

For those variables which demonstrated a univariable association with the SARS-CoV-2 test result, **Table 4** also provides the corresponding positive and negative likelihood ratios and summarises the parameters of a parsimonious clinical prediction model. Variables with a positive likelihood ratio of relatively large magnitude included contact with a confirmed SARS-CoV-2 positive case; a positive SARS-CoV-2 PCR swab in the previous 14 days; and anosmia or dysgeusia as a presenting complaint. The final set of four clinical variables (applying the “rule of thumb” outlined in the methods section) in the clinical prediction model for having a positive SARS-CoV-2 test results included self-reported fever, sore throat, bilateral infiltrates on CXR and absence of leucocytosis.

## Discussion

This study, undertaken during Australia’s ‘second wave’, is the largest analysis to date of patients with suspected and confirmed COVID-19 in Australian EDs. Although there was substantial variation in testing rates between sites, the overall burden of ‘suspected COVID-19’ was considerable. Only a small proportion returned a positive result.

A primary finding of this study is a difference in the rates of mechanical ventilation and death between SARS-CoV-2 positive and SARS-CoV-2 negative patients. Specifically, SARS-CoV-2 positive patients were more likely to receive mechanical ventilation and more likely to die, both in the ED and during their hospital admission. Although the rates of mechanical ventilation and death were relatively low in both groups, especially when compared to data from overseas settings,<sup>26,27</sup> this study demonstrates that ED patients diagnosed with COVID-19 have worse outcomes than comparable patients who return a negative SARS-CoV-2 test result.

COVID-4 is a cumulative analysis, incorporating data from the smaller set of sites and shorter time period reported in COVID-3.<sup>2</sup> With a five-fold increase in the number of COVID-19 patients subjected to analysis, across a broader selection of Australian EDs, the conservative conclusions of COVID-3, supporting a null effect of SARS-CoV-2 status on the outcomes of mechanical ventilation and in-hospital death, have been superseded. The difference may also reflect changes in testing criteria and

admission thresholds over the two month period, in addition to, amongst those testing positive for SARS-CoV-2 in the ED, an increasing age and an increasing representation of residential aged care facilities as the source of the ED referral.

The epidemiological and clinical predictors of a positive SARS-CoV-2 test identified in this study are generally consistent with the findings of COVED-3.<sup>2</sup> Not surprisingly, contact with a confirmed case and a recent positive SARS-CoV-2 test are very strong risk factors for a diagnosis of COVID-19. Presenting from a residential aged care facility, or being a health care worker, were also confirmed as predictive in this study. Anosmia remained a strong determinant of SARS-CoV-2 positivity, as did the independent presence of subjective fever, bilateral infiltrates on CXR or the absence of a leucocytosis.

These results are also broadly consistent with the findings of overseas analyses, particularly in relation to the frequency of fever and the predictive value of hyposmia and hypogeusia.<sup>9</sup> While few studies have been undertaken specifically in the emergency care context, a recent model derived from ED patients has identified a history of exposure, elevated temperature, reduced white cell count and positive CXR as the strongest predictors of a COVID-19 diagnosis.<sup>14</sup> However, this study also demonstrated that the absence of these variables did not exclude COVID-19 and should not be used as negative predictive tools.

Globally, several attempts have been made to use data of this nature to derive and validate severity prediction tools. These include the 4C mortality score, based on ISARIC data, and the QCOVID living risk prediction algorithm.<sup>13,28</sup> The relatively low number of COVID-19 cases in the COVED registry prohibits this type of analysis, but it may be possible to use the dataset to externally validate these approaches.

Consistent with previous observations, the burden of suspected COVID-19 cases was high and is likely to contribute to crowding and prolonged length of stay in the ED.<sup>2,6,29</sup> This has the potential to exacerbate access block and delay definitive care. Prolonged test turnaround times contribute to this burden because patients spend a longer period of time in isolation while awaiting test results. The potential for more widespread access to accurate rapid testing may mitigate this issue.

There are several limitations to this study. First, data on SARS-CoV-2 negative patients was not available for all sites (**Table 1**), limiting the generalisability of the inferential analyses to the EDs that provided complete data. Second, there was a significant amount of missing clinical data. As summarised in **Table 4**, some variables were missing up to 30% of observations. This reflects the challenges of systematic, prospective data collection in the dynamic environment of the ED. Third, the study used the results of PCR swab tests, ordered during the ED encounter, as the criterion for SARS-CoV-2 positivity. The sensitivity for this test, at least when conducted once, is estimated to be 70-80%.<sup>9,30</sup> A fourth limitation was that the study's inclusion criteria was defined, from the commencement of the COVED Project on 1 April 2020, as being tested for SARS-CoV-2 *in the ED*. As the second wave evolved, according to individual site-level policies, a proportion of patients with confirmed COVID-19 who were diagnosed in the community were not re-tested on arrival in the ED. The magnitude of this variation in practise has not been established. Finally, while more a caution than a limitation, it is important to emphasise that the data used in the COVED-3 analysis (eight EDs across July 2020) has been incorporated, as part of a planned series of reports, into this larger, cumulative analysis (twelve EDs across July and August 2020). These two reports are not independent of each other, but rather an intended progressive analysis on an expanding dataset, whereby the findings from the analysis of the larger dataset ought to be regarded as providing more precision and generalisability than the previous analysis of the then available data.

## Conclusion

Despite Australia's relative success in containing COVID-19, a substantial proportion of patients presenting to Australian EDs in July and August 2020 underwent SARS-CoV-2 testing and required

isolation. Only a small proportion were diagnosed with COVID-19, with self-reported fever, sore throat, bilateral infiltrates on CXR and absence of leucocytosis being strong predictors. In this sample, the presence of SARS-CoV-2 on nasopharyngeal testing was associated with mechanical ventilation and death in hospital.

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**Victoria**<sup>19</sup>

Any patient meeting the following criteria:

Fever OR chills in the absence of an alternative diagnosis that explains the clinical presentation  
OR

Acute respiratory infection (e.g. cough, sore throat, shortness of breath, runny nose, loss or change in sense of smell or taste).

OR

Onset of other clinical symptoms associated with COVID-19) (e.g. headache, myalgia, stuffy nose, nausea, vomiting, diarrhoea) AND any of the following epidemiological criteria:

- Close contacts of a confirmed case of coronavirus (COVID-19)
- Returned overseas travel in the past 14 days
- Health care or aged care workers

OR

Unable to complete adequate patient history to exclude all listed criteria (e.g. altered conscious state)

OR

Presenting from Residential Aged Care Facility (August 2020)

Additionally, testing should be considered in older people, who may present with other atypical symptoms including functional decline, delirium, exacerbation of underlying chronic condition, falls, loss of appetite, malaise, nausea, diarrhoea and myalgia (August 2020).

*Notes:*

These criteria underwent minor changes throughout the study period. Further information is available on the Department of Health and Human Services website.<sup>19</sup>

Patients meeting the testing criteria in St Vincent's Hospital ED during July 2020 were included in this analysis if they were triaged to the designated primary suspected COVID-19 area in ED.

**New South Wales**<sup>21</sup>

Any patient with respiratory symptoms (cough, sore throat, shortness of breath, runny nose), loss of sense of smell or taste, or unexplained fever.

**Queensland**<sup>22</sup>

Any patient meeting essential (clinical and epidemiological) OR enhanced (only clinical) testing criteria.

*Clinical criteria:* Fever ( $\geq 37.5^{\circ}\text{C}$ ) OR history of fever OR acute respiratory illness (rhinorrhoea/cough/sore throat/shortness of breath) OR acute fatigue/myalgia/arthralgia OR loss of smell/taste

*Epidemiological criteria:* Close contact of a confirmed case of COVID-19 OR international, interstate or cruise travel in the past 14 days OR Health, aged or residential care worker with patient contact OR Travelled through hotspot(s) OR admitted hospital patients with no other cause for their infection evident.

**Tasmania**<sup>20</sup>

Any patient with the following symptoms at any point in the last 7 days: fever or history of fever (e.g. night sweats, chills), rhinorrhoea, cough, sore throat, shortness of breath or loss of smell or taste.

**Box 1: Summary of SARS-CoV-2 testing criteria during July and August 2020**

Site	Total number of ED presentations <sup>a</sup>	Total adult cases tested for SARS-CoV-2 (n (%)) <sup>b</sup>	SARS-CoV-2 positive (n (%))	SARS-CoV-2 negative (n (%))	Case data included in Tables 2 and 3	Case data included in Table 4
The Alfred Hospital	8,481	2,396 (28)	41 (2)	2,355 (98)	All	All
Austin Hospital	11,796	1,481 (13)	29 (2)	1,452 (98)	SARS-CoV-2 Positive	SARS-CoV-2 Positive
Box Hill Hospital	8,803	937 (11)	20 (2)	917 (98)	All	SARS-CoV-2 Positive
Launceston General Hospital	7,224	237 (3)	0 (0)	237 (100)	All	SARS-CoV-2 Positive <sup>c</sup>
Mersey Community Hospital	3,037	53 (2)	0 (0)	53 (100)	All	SARS-CoV-2 Positive <sup>c</sup>
North West Regional Hospital	4,601	66 (1)	0 (0)	66 (100)	All	SARS-CoV-2 Positive <sup>c</sup>
Royal Hobart Hospital	10,978	354 (3)	1 (0)	353 (100)	All	SARS-CoV-2 Positive
Royal Melbourne Hospital	10,590	3,436 (32)	93 (3)	3,343 (97)	SARS-CoV-2 Positive	Not included
St Vincent's Hospital Melbourne	6,255	961 (15) <sup>d</sup>	61 (6) <sup>d</sup>	900 (94) <sup>d</sup>	July: All <sup>d</sup> August: SARS-CoV-2 Positive	July: All <sup>d</sup> August: SARS-CoV-2 Positive
Sutherland Hospital	9,243	579 (6)	0 (0)	579 (100)	All	SARS-CoV-2 Positive <sup>c</sup>
Townsville University Hospital	14,643	1,111 (8)	0 (0)	1,111 (100)	All	SARS-CoV-2 Positive <sup>c</sup>
University Hospital Geelong	10,485	444 (4)	10 (2)	434 (98)	All	SARS-CoV-2 Positive
Total	106,136	12,055 (11)	255 (2)	11,800 (98)	6,519	2,676

**Table 1:** Submitted cases for analysis and report by site

<sup>a</sup>All ages

<sup>b</sup>Testing criteria as per Box 1

<sup>c</sup>No SARS-CoV-2 positive cases in study period

<sup>d</sup>Only including patients triaged to designated suspected COVID-19 area in ED (i.e. not whole ED) in July 2020

Variable	Subgroups	SARS-CoV-2 Positive (n (%)) (n=255)	SARS-CoV-2 Negative (n (%)) (n=6,264)	OR (95%CI)	p-value
Age in years (mean (SD))	NA	58 (22)	58 (22)	1.0 (1.0-1.0)	0.85
Sex (n (%))	Male	130 (51)	3054 (49)	1.1 (0.9-1.4)	0.49
Mode of transport (n (%))	Private transport / Other	60 (24)	1544 (41)	Reference group	
	Ambulance – road	189 (73)	3501 (56)	2.6 (1.7-3.0)	<0.001
	Ambulance – helicopter	0 (0)	37 (1)	-	-
	Public transport	8 (3)	174 (3)	1.9 (0.9-4.1)	0.08
Triage category (median (IQR))	NA	3 (2,3)	3 (2,3)	NA	0.40
Triage category (n (%))	1	6 (2)	139 (2)	Reference group	
	2	58 (23)	1464 (23)	0.9 (0.4-2.2)	0.85
	3	142 (56)	3216 (51)	1.0 (0.4-2.4)	0.96
	4	48 (19)	1276 (20)	0.9 (0.4-2.1)	0.76
	5	1 (0)	160 (3)	0.1 (0.0-1.2)	0.08

**Table 2:** Baseline demographic and ED arrival details by SARS-CoV-2 result from ED PCR  
 CI, confidence interval; IQR, interquartile range; NA, not applicable; OR, odds ratio; SD, standard deviation;  
 -, category omitted from estimation because of perfect prediction (empty cell) or collinearity.

Variable	Subgroups	SARS-CoV-2 Test Positive (n=255)	SARS-CoV-2 Test Negative (n=6,264)	OR (95%CI)	p-value
Invasive mechanical ventilation in ED (n (%))	Yes	5 (2)	88 (1)	1.4 (0.6-3.5)	0.47
Disposition destination from ED (n (%))	Home	52 (20)	2,525 (40)	Reference group	
	Died in ED	3 (1)	8 (0)	18.2 (4.7-70.6)	<0.001
	ICU	15 (6)	146 (2)	5.0 (2.7-9.1)	<0.001
	OT	1 (0)	47 (1)	1.0 (0.1-7.6)	0.98
	Ward (not ICU)	142 (56)	2,453 (39)	2.8 (2.0-3.9)	<0.001
	ED Short Stay Unit	38 (15)	746 (12)	2.5 (1.6-3.8)	<0.001
	Transfer to other hospital	3 (1)	238 (4)	0.6 (0.2-2.0)	0.41
	DAMA	1 (0)	68 (1)	0.7 (1.0-5.2)	0.74
Other	0 (0)	33 (1)	-	-	
Invasive mechanical ventilation in hospital (n (%))	Yes	13 (5)	122 (2)	2.7 (1.5-4.9)	0.001
Discharge destination from hospital (n (%))	Home	185 (73)	5,082 (81)	Reference group	
	Died in hospital	19 (7)	212 (3)	2.5 (1.5-4.0)	<0.001
	Residential Care Facility	21 (8)	289 (5)	2.0 (1.3-3.2)	<0.001
	Transfer to other hospital	22 (9)	457 (7)	1.3 (0.8-2.1)	0.23
	Discharge against medical advice	1 (0)	141 (2)	0.2 (0.0-1.4)	0.10
	Hospital in the home	1 (0)	29 (0)	0.9 (0.1-7.0)	0.96
	Other (includes current inpatients)	5 (2)	52 (1)	2.6 (1.0-6.7)	0.04

**Table 3:** Outcomes by result of ED SARS-CoV-2 test

CI, confidence interval; ICU, intensive care unit; OR, odds ratio; OT, operating theatre;

–, category omitted from estimation because of perfect prediction (empty cell).

Variable	Missing >20% (Yes / No)	Subgroups	SARS-CoV-2 Test Positive <sup>a</sup> (n=162)	SARS-CoV-2 Test Negative (n=2,514)	OR (95%CI), p-value	Positive Likelihood Ratio	Negative Likelihood Ratio	Parsimonious model OR (95% CI), p-value <sup>b</sup>
<i>Presenting complaint (n (%))</i>								
Shortness of breath <sup>c</sup>	No	Yes	79 (51)	1,025 (48)	1.1 (0.8-1.6), 0.48	-	-	-
Cough <sup>c</sup>	No	Yes	92 (61)	705 (34)	3.0 (2.2-4.2), <0.001	1.8	0.6	-
Anosmia or dysgeusia <sup>c</sup>	Yes	Yes	20 (19)	43 (3)	8.9 (5.0-15.8), <0.001	7.4	0.8	-
Sore throat <sup>c</sup>	Yes	Yes	37 (30)	419 (21)	1.6 (1.1-2.4), 0.03	1.4	0.9	2.7 (1.3-5.6), 0.005
Runny nose <sup>c</sup>	Yes	Yes	30 (25)	444 (23)	1.1 (0.7-1.7), 0.58	-	-	-
Fever <sup>c</sup>	No	Yes	83 (55)	645 (31)	2.8 (2.0-3.9), <0.001	1.8	0.6	2.6 (1.4-4.9), 0.002
Fatigue	Yes	Yes	71 (58)	479 (27)	3.7 (2.5-5.3), <0.001	2.1	0.6	-
Myalgia <sup>c</sup>	Yes	Yes	42 (35)	245 (14)	3.4 (2.3-5.0), <0.001	2.5	0.8	-
Diarrhoea <sup>c</sup>	Yes	Yes	22 (18)	183 (10)	2.0 (1.2-3.2), <0.001	-	-	-
Number of days since first symptom (median (IQR))	Yes	NA	3 (1,7)	2 (1,5)	<0.001	-	-	-
<i>Other relevant history (n (%))</i>								
Overseas <sup>c</sup> in previous 28 days	Yes	Yes	0 (0)	1 (0)	-	-	-	-
Contact with a confirmed case <sup>c</sup>	Yes	Yes	80 (54)	56 (3)	36.6 (24.0-55.6), <0.001	17.3	0.5	-
Residential Aged Care Facility <sup>c</sup>	No	Yes	43 (27)	258 (13)	2.5 (1.8-3.7), <0.001	2.1	0.8	-
Health Care Worker <sup>c</sup>	Yes	Yes	12 (8)	80 (4)	1.9 (1.0-3.6), 0.04	1.9	1.0	-
Previous SARS-CoV-2 Swab (within 14 days prior to ED presentation)	No	SARS-CoV-2 negative	12 (8)	231 (9)	Reference	-	-	-
		SARS-CoV-2 positive	39 (38)	15 (1)	50.1 (21.8-114.9), <0.001	62.7	0.6	-
		Swab result unknown	3 (3)	47 (2)	1.2 (0.3-4.5), 0.76	-	-	-
		No prior swab	50 (48)	2,213 (88)	0.4 (0.2-0.8), 0.11	-	-	-
<i>Comorbidities (n (%))</i>								
Chronic respiratory	Yes	Yes	39 (25)	565 (29)	0.8 (0.6-1.2), 0.37	-	-	-
Obesity	Yes	Yes	18 (13)	293 (17)	0.7 (0.4-1.2), 0.17	-	-	-
Smoker	Yes	Yes	26 (20)	736 (40)	0.4 (0.2-0.6), <0.001	0.5	1.3	-
Chronic cardiac	No	Yes	35 (23)	540 (27)	0.8 (0.5-1.2), 0.23	-	-	-
Hypertension	No	Yes	53 (34)	710 (36)	0.9 (0.7-1.3), 0.69	-	-	-
Diabetes mellitus	Yes	Yes	43 (28)	326 (17)	1.9 (1.3-2.8), <0.001	1.7	0.9	-
Malignant neoplasm	Yes	Yes	7 (5)	182 (9)	0.5 (0.2-1.0), 0.05	-	-	-
Immunosuppressive pharmacotherapy	Yes	Yes	10 (7)	203 (11)	0.6 (0.3-1.1), 0.12	-	-	-
<i>Examination – first vital signs in ED</i>								
Temperature <sup>c</sup> (deg C) (mean (SD))	No	NA	37.0 (0.9)	36.6 (0.8)	2.5 (2.0-3.0), <0.001	-	-	-
Fever recorded <sup>c</sup> (Temperature >=38 deg C) (n (%))		Yes	26 (16)	82 (3)	5.5 (3.4-8.9), <0.001	4.8	0.9	-
SaO2 (%) (mean (SD))	No	NA	96 (4)	97 (3)	0.9 (0.9-0.9), <0.001	-	-	-
Hypoxia (SaO2 <92%) (n (%))		Yes	16 (11)	88 (4)	3.2 (1.8-5.6), <0.001	1.5	0.8	-
Systolic blood pressure (mmHg) (mean (SD))	No	NA	132 (25)	138 (27)	1.0 (1.0-1.0), 0.005	-	-	-
Hypotension (SBP<100mmHg) (n (%))		Yes	10 (6)	108 (4)	1.5 (0.7-2.8), 0.27	-	-	-
<i>Examination – other</i>								
Abnormality on chest auscultation <sup>d</sup> (n (%))	Yes	Yes	54 (41)	77 (59)	1.9 (1.3-2.8), <0.001	-	-	-
<i>Investigations – imaging<sup>d</sup></i>								

CXR Report (n (%))	Yes	No	48 (35)	1022 (63)	Reference	-	-	-
		Yes – bilateral infiltrates	55 (40)	76 (5)	15.4 (9.8-24.2), <0.001	8.6	0.6	15.3 (7.4-31.5), <0.001
		Yes – other abnormality	33 (24)	513 (32)	1.4 (0.9-2.2), 0.18	-	-	-
<i>Investigations – blood tests<sup>d</sup></i>								
White cell count (x10 <sup>9</sup> /L) (mean (SD))	No	NA	6 (3)	10 (7)	0.8 (0.7-0.8), <0.001	-	-	-
Leucocytosis (WCC > 11.0 (x10 <sup>9</sup> /L)) (n (%))		Yes	11 (7)	661 (29)	0.2 (0.1-0.4), <0.001	0.3	1.3	0.3 (0.1-0.7), 0.005
Platelet count (x10 <sup>9</sup> /L) (mean (SD))	No	NA	227 (103)	243 (92)	1.0 (1.0-1.0), 0.03	-	-	-
Thrombocytopenia (Platelet count <150x10 <sup>9</sup> /L) (n (%))		Yes	29 (19)	272 (12)	1.8 (1.1-2.7), 0.01	1.6	0.9	-
							AIC	347
							AUROC	0.80 (0.74-0.85)

**Table 4:** Results of analysis to determine univariable association and predictive performance of variables with being SARS-CoV-2 positive among patients tested for SARS-CoV-2 in the ED.

<sup>a</sup>SARS-CoV-2 positive cases are defined in this COVED report as having a SARS-CoV-2 test during their ED presentation for which the result is positive for SARS-CoV-2.

<sup>b</sup>Clinical variables with a statistically significant univariable association with a SARS-CoV-2 positive test in ED (i.e. excluding patients with a positive SARS-CoV-2 test in the previous 14 days or contact with a person confirmed as SARS-CoV-2 positive).

<sup>c</sup>One of the criteria for testing (i.e. inclusion in the present study).

<sup>d</sup>May not have been performed.

AIC, Akaike information criteria; AUROC, area under the receiver operating characteristic curve; CI, confidence interval; IQR, interquartile range; NA, not applicable; OR, odds ratio; SBP, systolic blood pressure; WCC, white blood cell count; –, not meeting criteria for calculation of likelihood ratios (no statistically significant association with SARS-CoV-2 test result) and/or not included in final parsimonious prediction model

**To the Editor in Chief**

**Professor Geoff Hughes**

Dear Dr Hughes,

We, the authors, wish to submit this Original Research manuscript entitled:

*Epidemiology and clinical features of emergency department patients with suspected COVID-19: Insights from Australia's 'second wave' (COVED-4).*

For consideration and publication.

As the incidence of COVID-19 surges across much of the northern hemisphere, and Australia welcomes back large numbers of returned travellers, the potential for further “waves” of the COVID-19 pandemic in Australia remains. It is important, therefore, to continue to support Australian ED clinicians, and ED clinicians globally, with updated clinical data and tools to inform the ongoing responses currently demanded of emergency care systems. The COVID-19 Emergency Department (COVED) Quality Improvement Project has completed its cumulative analysis for the period from 1 July to 31 August, in the midst of the second wave of the pandemic in Australia. This manuscript reports that detailed analysis from an increasing number of participating sites, and COVID-19 cases, across Australia.

We look forward to hearing of your decision.

Best wishes,

A/Prof Gerard O'Reilly

**Title**

*Epidemiology and clinical features of emergency department patients with suspected COVID-19: Insights from Australia's 'second wave' (COVED-4).*

**Short Running Title**

*COVED-4: Results from 1 July to 31 August 2020*

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### **Conflict of Interest Statement**

Gerard O'Reilly, Biswadev Mitra, Jeremy Furyk, Viet Tran and Peter Cameron are Section Editors for EMA. There are no other potential conflicts of interest to declare.

### **Ethics**

Ethics approval was obtained from the Alfred Human Research Ethics Committee (Project No: 188/20) on 26 March 2020 and approved as a multi-site project (63444) on 9 April 2020. The requirement for patient consent was waived.

### **Data Availability Statement**

Data that support the findings of this study may be available upon reasonable request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

### **Author Contribution Statement**

All authors listed have contributed to the concept and design of this Original Research, including its analysis plan, and have critically reviewed the Original Research for content.

### **Funding Statement**

GO'R is currently a NHMRC Research Fellow at the National Trauma Research Institute, Alfred Hospital, Melbourne, Australia, leading the project titled: "Maximising the usefulness and timeliness of trauma and emergency registry data for improving patient outcomes" (APP1142691). PC is funded

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### *The COVED Project Team*

*Project coordinating centre team:* Gerard O'Reilly, Rob Mitchell, Biswadev Mitra, Mike Noonan, Ryan Hiller, Andy Paton, De Villiers Smit, Carl Luckhoff, Lisa Brichko, Mark Santamaria, John Liman. *Project participating site teams - Alfred Health:* Joshua Ahn, Tim Amos, Holly Bannon-Murphy, Emily Bingle, Emily Blake, Helen Brennecke, Quillan Chan, Erica Chatterton, Jane Ford, Bismi Jomon, Sophie Parker, Emma Perkins, Pratheeba Selvam, Carlyne Sevier, Cristina Jessica Tonog, Maushmi Udaya Kumar, Andrew Wang, Binari Wijesundara; *Austin Health:* Anselm Wong, Muhuntha Sri-Ganeshan, Anthony Tran; *Barwon Health:* Jeremy Furyk, Nicole Lowry, Emma Beavon; *Box Hill Hospital:* Paul Buntine, Dylan Freeman, Steven Colwell, *Tomas McBride,* Maheswari Ramasubbu; *Royal Melbourne Hospital:* Jonathan Knott; *St Vincent's Hospital Melbourne:* Hamed Akhlaghi, Samuel Baker, Han Goh, Maria Walsh, Jessica Robinson; *Sutherland Hospital:* Max Raos, Sherman Siu; *Tasmanian Health Services:* Viet Tran, Ashley Loughman; *Townsville University Hospital:* Vinay Gangathimmaiah, Nicole Chapman, Colin Banks.

GO'R is currently a NHMRC Research Fellow at the National Trauma Research Institute, Alfred Hospital, Melbourne, Australia, leading the project titled: "Maximising the usefulness and timeliness of trauma and emergency registry data for improving patient outcomes"

## **Abstract**

*Objective:* The aim of this study was to describe the epidemiology and clinical features of patients presenting to the emergency department (ED) with suspected and confirmed COVID-19 during Australia's 'second wave'.

*Methods:* The COVID-19 Emergency Department (COVED) Project is an ongoing prospective cohort study in Australian EDs. This analysis presents data from twelve sites across four Australian states for the period from 1 July to 31 August 2020. All adult patients who met criteria for 'suspected COVID-19' and underwent testing for SARS-CoV-2 in the ED were eligible for inclusion. Study outcomes included a positive SARS-CoV-2 test result, mechanical ventilation and in-hospital mortality.

*Results:* There were 106,136 presentations to the participating EDs and 12,055 (11.4%; 95% CI: 11.2-11.6) underwent testing for SARS-CoV-2. Of these, 255 (2%) patients returned a positive result. Among positive cases, 13 (5%) received mechanical ventilation during their hospital admission compared to 122 (2%) of the SARS-CoV-2 negative patients (OR 2.7; 95% CI: 1.5-4.9,  $p=0.001$ ). Nineteen (7%) SARS-CoV-2 positive patients died in hospital compared to 212 (3%) of the SARS-CoV-2 negative patients (OR 2.3; 95% CI: 1.4-3.7,  $p=0.001$ ). Strong clinical predictors of the SARS-CoV-2 test result included self-reported fever, sore throat, bilateral infiltrates on CXR, and absence of a leucocytosis on first ED blood tests ( $p<0.05$ ).

*Conclusions:* In this prospective multi-site study during Australia's 'second wave', a substantial proportion of ED presentations required SARS-CoV-2 testing and isolation. Presence of SARS-CoV-2 on nasopharyngeal swab was associated with an increase in the odds of death and mechanical ventilation in hospital.

### **Key words**

Emergency, registry, COVID-19, isolation, quality improvement

## Manuscript

### Introduction

Health systems across the world continue to be impacted by the COVID-19 pandemic. While Australia has been relatively successful at containing the virus, a ‘second wave’ of infections in mid-2020 has demonstrated the need for vigilance. As of 22 November 2020, 27,892 cases and 907 deaths have been reported nationally, with an overall admission rate of approximately 13%.<sup>1</sup>

Despite the significant decline in community transmission,<sup>1</sup> a substantial proportion of Australian emergency department (ED) patients continue to meet criteria for ‘suspected COVID-19’ and therefore require isolation and testing.<sup>2</sup> This has led to a number of issues for EDs, particularly in terms of maintaining ‘business as usual’ in parallel with rigorous infection prevention and control (IPC) for suspected and confirmed cases.<sup>3</sup> As ED presentations and hospital occupancy return to baseline (following substantial reductions during the ‘first wave’),<sup>4,5</sup> meeting these challenges has become increasingly complex.<sup>6,7</sup>

In this context, it is important that clinicians have access to contemporary data and evidence-based tools to guide clinical decisions and systems reform. In particular, there is a need for robust models that support timely risk-assessment and diagnosis.<sup>2,8</sup> Although the characteristics of hospitalised patients with confirmed COVID-19 are well described, relatively little has been published about the epidemiology, clinical features and outcomes of ED patients who undergo testing for SARS-CoV-2.<sup>2,9-14</sup> Additionally, no diagnostic and prognostic tools have been specifically developed, or validated, for the Australian ED context.<sup>15</sup>

The COVID-19 ED (COVED) Quality Improvement Project was initiated in response to these challenges.<sup>16</sup> COVED-1 and COVED-2, which coincided with Australia’s ‘first wave’, demonstrated a low positive test rate, with no SARS-CoV-2 positive patients receiving mechanical ventilation or dying in ED of the single participating site. These studies also identified a high number of patients meeting case definition criteria and requiring isolation.<sup>17,18</sup> COVED-3 reported data across eight EDs during July 2020, and revealed no difference in the rates of mechanical ventilation and in-hospital death between SARS-CoV-2 positive and negative patients. The main clinical predictors of a COVID-19 diagnosis were subjective fever, bilateral infiltrates on chest x-ray (CXR), non-smoking status and absence of leucocytosis.<sup>2</sup>

This study (COVED-4) builds on the findings of COVED-3 with a broader sample of patients.<sup>2</sup> It reports data from twelve EDs, distributed across four states in eastern Australia, for July and August 2020. The study aimed to further explore the association between the SARS-CoV-2 test result in the ED and mechanical ventilation and in-hospital mortality, and to identify the clinical and epidemiological variables predictive of a COVID-19 diagnosis.

### Methods

COVED is an ongoing prospective cohort study that commenced on 1 April 2020. The study protocol has been published previously.<sup>16</sup> The study includes adult patients that had a SARS-CoV-2 polymerase chain reaction (PCR) test requested in the ED and were managed with IPC precautions for ‘suspected COVID-19’. Testing criteria are guided by the various health jurisdictions and have evolved throughout the Project.<sup>19-22</sup> The criteria that were applicable during this study period are listed in **Box 1**. Patients

who underwent testing for surveillance purposes (i.e. patients who were tested for SARS-CoV-2 in the ED but were not subjected to IPC precautions) were excluded.

This analysis (COVED-4) describes study findings for eligible patients that presented to the twelve participating EDs (The Alfred Hospital, St Vincent's Hospital Melbourne, Austin Hospital, Box Hill Hospital, Royal Melbourne Hospital, University Hospital Geelong, Royal Hobart Hospital, Launceston General Hospital, North-West Regional Hospital, Mersey Community Hospital, Sutherland Hospital Sydney and Townsville University Hospital) over the period 1 July to 31 August 2020. These sites represent a mixture of urban and regional EDs across Victoria, Tasmania, New South Wales and Queensland (**Table 1**). In all of these locations, alternative non-ED testing sites (e.g. screening clinics) were in operation for those with minor symptoms who did not require ED care. These patients were not included in this study.

COVED outcome measures include SARS-CoV-2 PCR test result, mechanical ventilation and hospital discharge destination. The complete list of variables has previously been published in the study protocol.<sup>2,16</sup> These include history (age, sex, symptoms, epidemiological features, co-morbidities), findings on clinical examination, radiological and blood investigations, care provided in the ED and hospital (including ED disposition destination) and patient outcomes (including survival to hospital discharge).<sup>2</sup> COVED variables and definitions have been harmonised with international COVID-19 research tools developed by the World Health Organization and International Severe Acute Respiratory and Emerging Infection Consortium (ISARIC).<sup>23</sup>

The data for study participants are collected from hospital electronic medical record (EMR) systems. Some variables are automatically extracted from data warehouses; other variables require manual record review.<sup>2</sup> Data are entered into the COVED registry utilising Research Electronic Data Capture (REDCap) tools, hosted and managed by Helix (Monash University).<sup>24,25</sup> The data dictionary and case report form are available on The Alfred Hospital's academic programs website at <https://emergencyeducation.org.au/research/coved/>.<sup>2</sup>

Summary descriptive statistics have been determined for each pre-specified variable; these data have been stratified by the test result for the SARS-CoV-2 PCR swab taken in the ED. As for COVED-3,<sup>2</sup> there were sufficient SARS-CoV-2 positive cases to undertake inferential analyses (comparing predictors and outcomes by SARS-CoV-2 test result, with summary measures of association and 95% confidence intervals). Symmetrical numerical data have been summarised using the mean and standard deviation; skewed and ordinal data have been summarised using the median and inter-quartile range; and categorical data have been summarised using the frequency and percentage.

The final prediction model was derived to avoid overfitting, whereby the maximum number of clinical predictor variables included in the final (parsimonious) model was limited by the 'rule of thumb' whereby at least ten observations of each outcome (SARS-CoV-2 positive *and* negative) are required per predictor variable.<sup>2</sup> Data were analysed using Stata statistical software (version 15.1 StataCorp, Texas, USA). A p-value of <0.05 was defined to be statistically significant. Ethics approval was obtained from the Alfred Human Research Ethics Committee (Project No: 188/20).

## Results

There were 106,136 ED presentations during the study period, and 12,055 (11.4%; 95% CI: 11.2-11.6) met inclusion criteria. Of these, 255 (2%) patients returned a positive SARS-CoV-2 test result and 11,800 (98%) were negative (see **Table 1**).

**Table 2** summarises the baseline demographic and ED arrival characteristics of included patients. There were no differences in age or sex distribution. Patients who tested positive for SARS-CoV-2 were more likely to have arrived by ambulance ( $p < 0.001$ ), but there were no differences in assigned triage category.

Patient outcomes are summarised in **Table 3**. Of the SARS-CoV-2 positive patients, 19 (7%) died in hospital compared to 212 (3%) of the SARS-CoV-2 negative patients (OR 2.3; 95% CI: 1.4-3.7,  $p = 0.001$ ). Thirteen (5%) of the SARS-CoV-2 positive patients received invasive mechanical ventilation during their hospital admission, compared to 122 (2%) of the SARS-CoV-2 negative patients (OR 2.7; 95% CI: 1.5-4.9,  $p = 0.001$ ). SARS-CoV-2 positive patients were more likely to be admitted to the intensive care unit (ICU) (OR 5.0; 95% CI: 2.7-9.1,  $p < 0.001$ ) or the general ward (OR 2.8; 95% CI: 2.0-3.9,  $p < 0.001$ ) than SARS-CoV-2 negative patients respectively.

**Table 4** describes the clinical and epidemiological features of the sample (based on the available data from contributing sites, as summarised in **Table 1**). Cough (61%), fatigue (58%) and subjective fever (55%) were the most common presenting complaints among SARS-CoV-2 positive patients. Eighty (54%) SARS-CoV-2 positive patients reported prior contact with a positive case and 55 (40%) had bilateral infiltrates on CXR. Compared to SARS-CoV-2 negative patients, SARS-CoV-2 positive patients were more likely to identify cough, anosmia or dysgeusia, sore throat, fever, fatigue, myalgia or diarrhoea among their presenting symptoms. They were also more likely to reside in a residential aged care facility, identify as a health care worker, have a diagnosis of diabetes or be a non-smoker. In terms of examination findings, SARS-CoV-2 positive patients were more likely to have a fever (temperature  $\geq 38^{\circ}\text{C}$ ) or hypoxia (oxygen saturation  $< 92\%$ ). On investigation, SARS-CoV-2 positive patients were less likely to have a leucocytosis, more likely to have a thrombocytopenia and more likely to have bilateral infiltrates on first CXR than SARS-CoV-2 negative patients.

For those variables which demonstrated a univariable association with the SARS-CoV-2 test result, **Table 4** also provides the corresponding positive and negative likelihood ratios and summarises the parameters of a parsimonious clinical prediction model. Variables with a positive likelihood ratio of relatively large magnitude included contact with a confirmed SARS-CoV-2 positive case; a positive SARS-CoV-2 PCR swab in the previous 14 days; and anosmia or dysgeusia as a presenting complaint. The final set of four clinical variables (applying the “rule of thumb” outlined in the methods section) in the clinical prediction model for having a positive SARS-CoV-2 test results included self-reported fever, sore throat, bilateral infiltrates on CXR and absence of leucocytosis.

## Discussion

This study, undertaken during Australia’s ‘second wave’, is the largest analysis to date of patients with suspected and confirmed COVID-19 in Australian EDs. Although there was substantial variation in testing rates between sites, the overall burden of ‘suspected COVID-19’ was considerable. Only a small proportion returned a positive result.

A primary finding of this study is a difference in the rates of mechanical ventilation and death between SARS-CoV-2 positive and SARS-CoV-2 negative patients. Specifically, SARS-CoV-2 positive patients were more likely to receive mechanical ventilation and more likely to die, both in the ED and during their hospital admission. Although the rates of mechanical ventilation and death were relatively low in both groups, especially when compared to data from overseas settings,<sup>26,27</sup> this study demonstrates that ED patients diagnosed with COVID-19 have worse outcomes than comparable patients who return a negative SARS-CoV-2 test result.

COVID-4 is a cumulative analysis, incorporating data from the smaller set of sites and shorter time period reported in COVID-3.<sup>2</sup> With a five-fold increase in the number of COVID-19 patients subjected to analysis, across a broader selection of Australian EDs, the conservative conclusions of COVID-3, supporting a null effect of SARS-CoV-2 status on the outcomes of mechanical ventilation and in-hospital death, have been superseded. The difference may also reflect changes in testing criteria and

admission thresholds over the two month period, in addition to, amongst those testing positive for SARS-CoV-2 in the ED, an increasing age and an increasing representation of residential aged care facilities as the source of the ED referral.

The epidemiological and clinical predictors of a positive SARS-CoV-2 test identified in this study are generally consistent with the findings of COVED-3.<sup>2</sup> Not surprisingly, contact with a confirmed case and a recent positive SARS-CoV-2 test are very strong risk factors for a diagnosis of COVID-19. Presenting from a residential aged care facility, or being a health care worker, were also confirmed as predictive in this study. Anosmia remained a strong determinant of SARS-CoV-2 positivity, as did the independent presence of subjective fever, bilateral infiltrates on CXR or the absence of a leucocytosis.

These results are also broadly consistent with the findings of overseas analyses, particularly in relation to the frequency of fever and the predictive value of hyposmia and hypogeusia.<sup>9</sup> While few studies have been undertaken specifically in the emergency care context, a recent model derived from ED patients has identified a history of exposure, elevated temperature, reduced white cell count and positive CXR as the strongest predictors of a COVID-19 diagnosis.<sup>14</sup> However, this study also demonstrated that the absence of these variables did not exclude COVID-19 and should not be used as negative predictive tools.

Globally, several attempts have been made to use data of this nature to derive and validate severity prediction tools. These include the 4C mortality score, based on ISARIC data, and the QCOVID living risk prediction algorithm.<sup>13,28</sup> The relatively low number of COVID-19 cases in the COVED registry prohibits this type of analysis, but it may be possible to use the dataset to externally validate these approaches.

Consistent with previous observations, the burden of suspected COVID-19 cases was high and is likely to contribute to crowding and prolonged length of stay in the ED.<sup>2,6,29</sup> This has the potential to exacerbate access block and delay definitive care. Prolonged test turnaround times contribute to this burden because patients spend a longer period of time in isolation while awaiting test results. The potential for more widespread access to accurate rapid testing may mitigate this issue.

There are several limitations to this study. First, data on SARS-CoV-2 negative patients was not available for all sites (**Table 1**), limiting the generalisability of the inferential analyses to the EDs that provided complete data. Second, there was a significant amount of missing clinical data. As summarised in **Table 4**, some variables were missing up to 30% of observations. This reflects the challenges of systematic, prospective data collection in the dynamic environment of the ED. Third, the study used the results of PCR swab tests, ordered during the ED encounter, as the criterion for SARS-CoV-2 positivity. The sensitivity for this test, at least when conducted once, is estimated to be 70-80%.<sup>9,30</sup> A fourth limitation was that the study's inclusion criteria was defined, from the commencement of the COVED Project on 1 April 2020, as being tested for SARS-CoV-2 *in the ED*. As the second wave evolved, according to individual site-level policies, a proportion of patients with confirmed COVID-19 who were diagnosed in the community were not re-tested on arrival in the ED. The magnitude of this variation in practise has not been established. Finally, while more a caution than a limitation, it is important to emphasise that the data used in the COVED-3 analysis (eight EDs across July 2020) has been incorporated, as part of a planned series of reports, into this larger, cumulative analysis (twelve EDs across July and August 2020). These two reports are not independent of each other, but rather an intended progressive analysis on an expanding dataset, whereby the findings from the analysis of the larger dataset ought to be regarded as providing more precision and generalisability than the previous analysis of the then available data.

## Conclusion

Despite Australia's relative success in containing COVID-19, a substantial proportion of patients presenting to Australian EDs in July and August 2020 underwent SARS-CoV-2 testing and required

isolation. Only a small proportion were diagnosed with COVID-19, with self-reported fever, sore throat, bilateral infiltrates on CXR and absence of leucocytosis being strong predictors. In this sample, the presence of SARS-CoV-2 on nasopharyngeal testing was associated with mechanical ventilation and death in hospital.

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**Victoria<sup>19</sup>**

Any patient meeting the following criteria:

Fever OR chills in the absence of an alternative diagnosis that explains the clinical presentation  
OR

Acute respiratory infection (e.g. cough, sore throat, shortness of breath, runny nose, loss or change in sense of smell or taste).

OR

Onset of other clinical symptoms associated with COVID-19) (e.g. headache, myalgia, stuffy nose, nausea, vomiting, diarrhoea) AND any of the following epidemiological criteria:

- Close contacts of a confirmed case of coronavirus (COVID-19)
- Returned overseas travel in the past 14 days
- Health care or aged care workers

OR

Unable to complete adequate patient history to exclude all listed criteria (e.g. altered conscious state)

OR

Presenting from Residential Aged Care Facility (August 2020)

Additionally, testing should be considered in older people, who may present with other atypical symptoms including functional decline, delirium, exacerbation of underlying chronic condition, falls, loss of appetite, malaise, nausea, diarrhoea and myalgia (August 2020).

*Notes:*

These criteria underwent minor changes throughout the study period. Further information is available on the Department of Health and Human Services website.<sup>19</sup>

Patients meeting the testing criteria in St Vincent's Hospital ED during July 2020 were included in this analysis if they were triaged to the designated primary suspected COVID-19 area in ED.

**New South Wales<sup>21</sup>**

Any patient with respiratory symptoms (cough, sore throat, shortness of breath, runny nose), loss of sense of smell or taste, or unexplained fever.

**Queensland<sup>22</sup>**

Any patient meeting essential (clinical and epidemiological) OR enhanced (only clinical) testing criteria.

*Clinical criteria:* Fever ( $\geq 37.5^{\circ}\text{C}$ ) OR history of fever OR acute respiratory illness (rhinorrhoea/cough/sore throat/shortness of breath) OR acute fatigue/myalgia/arthritis OR loss of smell/taste

*Epidemiological criteria:* Close contact of a confirmed case of COVID-19 OR international, interstate or cruise travel in the past 14 days OR Health, aged or residential care worker with patient contact OR Travelled through hotspot(s) OR admitted hospital patients with no other cause for their infection evident.

**Tasmania<sup>20</sup>**

Any patient with the following symptoms at any point in the last 7 days: fever or history of fever (e.g. night sweats, chills), rhinorrhoea, cough, sore throat, shortness of breath or loss of smell or taste.

**Box 1: Summary of SARS-CoV-2 testing criteria during July and August 2020**

Site	Total number of ED presentations <sup>a</sup>	Total adult cases tested for SARS-CoV-2 (n (%)) <sup>b</sup>	SARS-CoV-2 positive (n (%))	SARS-CoV-2 negative (n (%))	Case data included in Tables 2 and 3	Case data included in Table 4
The Alfred Hospital	8,481	2,396 (28)	41 (2)	2,355 (98)	All	All
Austin Hospital	11,796	1,481 (13)	29 (2)	1,452 (98)	SARS-CoV-2 Positive	SARS-CoV-2 Positive
Box Hill Hospital	8,803	937 (11)	20 (2)	917 (98)	All	SARS-CoV-2 Positive
Launceston General Hospital	7,224	237 (3)	0 (0)	237 (100)	All	SARS-CoV-2 Positive <sup>c</sup>
Mersey Community Hospital	3,037	53 (2)	0 (0)	53 (100)	All	SARS-CoV-2 Positive <sup>c</sup>
North West Regional Hospital	4,601	66 (1)	0 (0)	66 (100)	All	SARS-CoV-2 Positive <sup>c</sup>
Royal Hobart Hospital	10,978	354 (3)	1 (0)	353 (100)	All	SARS-CoV-2 Positive
Royal Melbourne Hospital	10,590	3,436 (32)	93 (3)	3,343 (97)	SARS-CoV-2 Positive	Not included
St Vincent's Hospital Melbourne	6,255	961 (15) <sup>d</sup>	61 (6) <sup>d</sup>	900 (94) <sup>d</sup>	July: All <sup>d</sup> August: SARS-CoV-2 Positive	July: All <sup>d</sup> August: SARS-CoV-2 Positive
Sutherland Hospital	9,243	579 (6)	0 (0)	579 (100)	All	SARS-CoV-2 Positive <sup>c</sup>
Townsville University Hospital	14,643	1,111 (8)	0 (0)	1,111 (100)	All	SARS-CoV-2 Positive <sup>c</sup>
University Hospital Geelong	10,485	444 (4)	10 (2)	434 (98)	All	SARS-CoV-2 Positive
<b>Total</b>	<b>106,136</b>	<b>12,055 (11)</b>	<b>255 (2)</b>	<b>11,800 (98)</b>	<b>6,519</b>	<b>2,676</b>

**Table 1:** Submitted cases for analysis and report by site

<sup>a</sup>All ages

<sup>b</sup>Testing criteria as per Box 1

<sup>c</sup>No SARS-CoV-2 positive cases in study period

<sup>d</sup>Only including patients triaged to designated suspected COVID-19 area in ED (i.e. not whole ED) in July 2020

Variable	Subgroups	SARS-CoV-2 Positive (n (%)) (n=255)	SARS-CoV-2 Negative (n (%)) (n=6,264)	OR (95%CI)	p-value
Age in years (mean (SD))	NA	58 (22)	58 (22)	1.0 (1.0-1.0)	0.85
Sex (n (%))	Male	130 (51)	3054 (49)	1.1 (0.9-1.4)	0.49
Mode of transport (n (%))	Private transport / Other	60 (24)	1544 (41)	Reference group	
	Ambulance – road	189 (73)	3501 (56)	2.6 (1.7-3.0)	<0.001
	Ambulance – helicopter	0 (0)	37 (1)	-	-
	Public transport	8 (3)	174 (3)	1.9 (0.9-4.1)	0.08
Triage category (median (IQR))	NA	3 (2,3)	3 (2,3)	NA	0.40
Triage category (n (%))	1	6 (2)	139 (2)	Reference group	
	2	58 (23)	1464 (23)	0.9 (0.4-2.2)	0.85
	3	142 (56)	3216 (51)	1.0 (0.4-2.4)	0.96
	4	48 (19)	1276 (20)	0.9 (0.4-2.1)	0.76
	5	1 (0)	160 (3)	0.1 (0.0-1.2)	0.08

**Table 2:** Baseline demographic and ED arrival details by SARS-CoV-2 result from ED PCR  
 CI, confidence interval; IQR, interquartile range; NA, not applicable; OR, odds ratio; SD, standard deviation;  
 -, category omitted from estimation because of perfect prediction (empty cell) or collinearity.

Variable	Subgroups	SARS-CoV-2 Test Positive (n=255)	SARS-CoV-2 Test Negative (n=6,264)	OR (95%CI)	p-value
Invasive mechanical ventilation in ED (n (%))	Yes	5 (2)	88 (1)	1.4 (0.6-3.5)	0.47
Disposition destination from ED (n (%))	Home	52 (20)	2,525 (40)	Reference group	
	Died in ED	3 (1)	8 (0)	18.2 (4.7-70.6)	<0.001
	ICU	15 (6)	146 (2)	5.0 (2.7-9.1)	<0.001
	OT	1 (0)	47 (1)	1.0 (0.1-7.6)	0.98
	Ward (not ICU)	142 (56)	2,453 (39)	2.8 (2.0-3.9)	<0.001
	ED Short Stay Unit	38 (15)	746 (12)	2.5 (1.6-3.8)	<0.001
	Transfer to other hospital	3 (1)	238 (4)	0.6 (0.2-2.0)	0.41
	DAMA	1 (0)	68 (1)	0.7 (1.0-5.2)	0.74
Other	0 (0)	33 (1)	-	-	
Invasive mechanical ventilation in hospital (n (%))	Yes	13 (5)	122 (2)	2.7 (1.5-4.9)	0.001
Discharge destination from hospital (n (%))	Home	185 (73)	5,082 (81)	Reference group	
	Died in hospital	19 (7)	212 (3)	2.5 (1.5-4.0)	<0.001
	Residential Care Facility	21 (8)	289 (5)	2.0 (1.3-3.2)	<0.001
	Transfer to other hospital	22 (9)	457 (7)	1.3 (0.8-2.1)	0.23
	Discharge against medical advice	1 (0)	141 (2)	0.2 (0.0-1.4)	0.10
	Hospital in the home	1 (0)	29 (0)	0.9 (0.1-7.0)	0.96
	Other (includes current inpatients)	5 (2)	52 (1)	2.6 (1.0-6.7)	0.04

**Table 3:** Outcomes by result of ED SARS-CoV-2 test

CI, confidence interval; ICU, intensive care unit; OR, odds ratio; OT, operating theatre;

–, category omitted from estimation because of perfect prediction (empty cell).

Variable	Missing >20% (Yes / No)	Subgroups	SARS-CoV-2 Test Positive <sup>a</sup> (n=162)	SARS-CoV-2 Test Negative (n=2,514)	OR (95%CI), p-value	Positive Likelihood Ratio	Negative Likelihood Ratio	Parsimonious model OR (95% CI), p-value <sup>b</sup>
<i>Presenting complaint (n (%))</i>								
Shortness of breath <sup>c</sup>	No	Yes	79 (51)	1,025 (48)	1.1 (0.8-1.6), 0.48	-	-	-
Cough <sup>c</sup>	No	Yes	92 (61)	705 (34)	3.0 (2.2-4.2), <0.001	1.8	0.6	-
Anosmia or dysgeusia <sup>c</sup>	Yes	Yes	20 (19)	43 (3)	8.9 (5.0-15.8), <0.001	7.4	0.8	-
Sore throat <sup>c</sup>	Yes	Yes	37 (30)	419 (21)	1.6 (1.1-2.4), 0.03	1.4	0.9	2.7 (1.3-5.6), 0.005
Runny nose <sup>c</sup>	Yes	Yes	30 (25)	444 (23)	1.1 (0.7-1.7), 0.58	-	-	-
Fever <sup>c</sup>	No	Yes	83 (55)	645 (31)	2.8 (2.0-3.9), <0.001	1.8	0.6	2.6 (1.4-4.9), 0.002
Fatigue	Yes	Yes	71 (58)	479 (27)	3.7 (2.5-5.3), <0.001	2.1	0.6	-
Myalgia <sup>c</sup>	Yes	Yes	42 (35)	245 (14)	3.4 (2.3-5.0), <0.001	2.5	0.8	-
Diarrhoea <sup>c</sup>	Yes	Yes	22 (18)	183 (10)	2.0 (1.2-3.2), <0.001	-	-	-
Number of days since first symptom (median (IQR))	Yes	NA	3 (1,7)	2 (1,5)	<0.001	-	-	-
<i>Other relevant history (n (%))</i>								
Overseas <sup>c</sup> in previous 28 days	Yes	Yes	0 (0)	1 (0)	-	-	-	-
Contact with a confirmed case <sup>c</sup>	Yes	Yes	80 (54)	56 (3)	36.6 (24.0-55.6), <0.001	17.3	0.5	-
Residential Aged Care Facility <sup>c</sup>	No	Yes	43 (27)	258 (13)	2.5 (1.8-3.7), <0.001	2.1	0.8	-
Health Care Worker <sup>c</sup>	Yes	Yes	12 (8)	80 (4)	1.9 (1.0-3.6), 0.04	1.9	1.0	-
Previous SARS-CoV-2 Swab (within 14 days prior to ED presentation)	No	SARS-CoV-2 negative	12 (8)	231 (9)	Reference	-	-	-
		SARS-CoV-2 positive	39 (38)	15 (1)	50.1 (21.8-114.9), <0.001	62.7	0.6	-
		Swab result unknown	3 (3)	47 (2)	1.2 (0.3-4.5), 0.76	-	-	-
		No prior swab	50 (48)	2,213 (88)	0.4 (0.2-0.8), 0.11	-	-	-
<i>Comorbidities (n (%))</i>								
Chronic respiratory	Yes	Yes	39 (25)	565 (29)	0.8 (0.6-1.2), 0.37	-	-	-
Obesity	Yes	Yes	18 (13)	293 (17)	0.7 (0.4-1.2), 0.17	-	-	-
Smoker	Yes	Yes	26 (20)	736 (40)	0.4 (0.2-0.6), <0.001	0.5	1.3	-
Chronic cardiac	No	Yes	35 (23)	540 (27)	0.8 (0.5-1.2), 0.23	-	-	-
Hypertension	No	Yes	53 (34)	710 (36)	0.9 (0.7-1.3), 0.69	-	-	-
Diabetes mellitus	Yes	Yes	43 (28)	326 (17)	1.9 (1.3-2.8), <0.001	1.7	0.9	-
Malignant neoplasm	Yes	Yes	7 (5)	182 (9)	0.5 (0.2-1.0), 0.05	-	-	-
Immunosuppressive pharmacotherapy	Yes	Yes	10 (7)	203 (11)	0.6 (0.3-1.1), 0.12	-	-	-
<i>Examination – first vital signs in ED</i>								
Temperature <sup>c</sup> (deg C) (mean (SD))	No	NA	37.0 (0.9)	36.6 (0.8)	2.5 (2.0-3.0), <0.001	-	-	-
Fever recorded <sup>c</sup> (Temperature >=38 deg C) (n (%))		Yes	26 (16)	82 (3)	5.5 (3.4-8.9), <0.001	4.8	0.9	-
SaO2 (%) (mean (SD))	No	NA	96 (4)	97 (3)	0.9 (0.9-0.9), <0.001	-	-	-
Hypoxia (SaO2 <92%) (n (%))		Yes	16 (11)	88 (4)	3.2 (1.8-5.6), <0.001	1.5	0.8	-
Systolic blood pressure (mmHg) (mean (SD))	No	NA	132 (25)	138 (27)	1.0 (1.0-1.0), 0.005	-	-	-
Hypotension (SBP<100mmHg) (n (%))		Yes	10 (6)	108 (4)	1.5 (0.7-2.8), 0.27	-	-	-
<i>Examination – other</i>								
Abnormality on chest auscultation <sup>d</sup> (n (%))	Yes	Yes	54 (41)	77 (59)	1.9 (1.3-2.8), <0.001	-	-	-
<i>Investigations – imaging<sup>d</sup></i>								

CXR Report (n (%))	Yes	No	48 (35)	1022 (63)	Reference	-	-	-
		Yes – bilateral infiltrates	55 (40)	76 (5)	15.4 (9.8-24.2), <0.001	8.6	0.6	15.3 (7.4-31.5), <0.001
		Yes – other abnormality	33 (24)	513 (32)	1.4 (0.9-2.2), 0.18	-	-	-
<i>Investigations – blood tests<sup>d</sup></i>								
White cell count (x10 <sup>9</sup> /L) (mean (SD))	No	NA	6 (3)	10 (7)	0.8 (0.7-0.8), <0.001	-	-	-
Leucocytosis (WCC > 11.0 (x10 <sup>9</sup> /L)) (n (%))		Yes	11 (7)	661 (29)	0.2 (0.1-0.4), <0.001	0.3	1.3	0.3 (0.1-0.7), 0.005
Platelet count (x10 <sup>9</sup> /L) (mean (SD))	No	NA	227 (103)	243 (92)	1.0 (1.0-1.0), 0.03	-	-	-
Thrombocytopenia (Platelet count <150x10 <sup>9</sup> /L) (n (%))		Yes	29 (19)	272 (12)	1.8 (1.1-2.7), 0.01	1.6	0.9	-
							AIC	347
							AUROC	0.80 (0.74-0.85)

**Table 4:** Results of analysis to determine univariable association and predictive performance of variables with being SARS-CoV-2 positive among patients tested for SARS-CoV-2 in the ED.

<sup>a</sup>SARS-CoV-2 positive cases are defined in this COVED report as having a SARS-CoV-2 test during their ED presentation for which the result is positive for SARS-CoV-2.

<sup>b</sup>Clinical variables with a statistically significant univariable association with a SARS-CoV-2 positive test in ED (i.e. excluding patients with a positive SARS-CoV-2 test in the previous 14 days or contact with a person confirmed as SARS-CoV-2 positive).

<sup>c</sup>One of the criteria for testing (i.e. inclusion in the present study).

<sup>d</sup>May not have been performed.

AIC, Akaike information criteria; AUROC, area under the receiver operating characteristic curve; CI, confidence interval; IQR, interquartile range; NA, not applicable; OR, odds ratio; SBP, systolic blood pressure; WCC, white blood cell count; –, not meeting criteria for calculation of likelihood ratios (no statistically significant association with SARS-CoV-2 test result) and/or not included in final parsimonious prediction model