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ORIGINAL ARTICLE

Clinical characteristics and outcomes of COVID-19 in a low-prevalence, well resourced setting, Sydney, Australia

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Abstract

Background: The Northern Sydney Local Health District was one of the first health regions to be affected by COVID-19 in Australia.
Aims: To describe the clinical characteristics, risk factors and outcomes in our low-prevalence Australian population.
Methods: This is a retrospective analysis of 517 laboratory-confirmed COVID-19 cases between January and June 2020. Patient information was collected as part of routine care within the COVID-19 Virtual Hospital system. Outcomes examined were death, recovery at 30 days and intensive care unit (ICU) admission.
Results: The case fatality rate was 1.8%. Multivariate analysis showed factors independently associated with death, composite outcome of death/ICU admission or incomplete recovery at 30 days were age >80 years and presence of two or more comorbidities. Most cases acquired COVID-19 through international (50.9%) or cruise ship travel (9.1%). Healthcare workers comprised 12.8% of the cohort and represented a disproportionately high percentage of the 'unknown' source group (27.6%). The median incubation period was 5 days (interquartile range 3–8); one patient had an incubation period of 15 days. Hospitalisation was required in 11.8%, ICU admission in 2.1% and ventilation in 1.4%. A Radiographic Assessment of Lung Oedema score on chest X-ray of >10 was independently associated with death.
Conclusions: In this low prevalence, well resourced Australian setting, we report an overall low mortality. Factors associated with adverse patient outcomes on multivariate analysis were age greater than 80 and the presence of two or more comorbidities. These data can assist in early risk stratification of COVID-19 patients, and in surge capacity planning for hospitals.

Introduction

Since the coronavirus disease 2019 (COVID-19) pandemic, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was officially declared on 11 March 2020, there have been 174 million confirmed infections and over 3.75 million deaths worldwide.[1] Australia's first COVID-19 case was identified on 25 January 2020, and there have since been over 30 000 confirmed cases and 910 deaths nationwide.[2]

The Northern Sydney Local Health District (NSLHD), a health region in New South Wales (NSW), provides health services to a population of approximately 950 000 people. It experienced one of the earliest surges of COVID-19 cases in Australia, and most patients were managed through the NSLHD COVID-19 Virtual Hospital as outpatients.

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Conflict of interest: None.

Several studies globally report on clinical characteristics of COVID-19, with the most common symptoms of fever, cough, fatigue or myalgia.[3–8] We are also seeing more varied symptoms, including gastrointestinal symptoms,[8] anosmia and dysgeusia[9] in high numbers of COVID-19 patients. Comorbidities such as obesity, hypertension, diabetes, cardiovascular disease and older age are associated with more severe disease.[3,6,8,10]

We seek to characterise an Australian laboratory-confirmed COVID-19 population in a low-prevalence setting, with particular focus on patient symptoms, comorbidities and outcomes. This information will help to identify high-risk COVID-19 patients, thereby assisting with appropriate triage and management of patients, and informing surge capacity planning.

Methods

Study approval was granted by the NSLHD Human Research and Ethics Committee and registered with the NSLHD Quality Unit and the Clinical Governance Unit, as a quality assurance project.

Routine diagnosis and management of COVID-19 cases in the NSLHD

The Communicable Diseases Network Australia (CDNA) National Guidelines for Public Health Units (PHU)[11] and emerging local epidemiological patterns were used to establish NSLHD COVID-19 clinics. Nasopharyngeal swabs were collected on symptomatic patients or those with epidemiological risk factors. Diagnosis of COVID-19 was made through detection of SARs-CoV-2 on polymerase chain reaction (PCR) of respiratory tract specimens, using the AusDiagnostics (Mascot, Australia) SARS-CoV-2 multiplex-tandem PCR assay in the NSLHD public laboratory. Swabs processed in private laboratories were tested using a variety of other commercially available or in-house methods.

Positive COVID-19 cases were either admitted through the emergency department (ED) or referred to the Infectious Diseases and Microbiology team at Royal North Shore Hospital, either directly by the laboratory or through the PHU. Patients who did not require admission were monitored by the Virtual Hospital. Contact identification and classification were performed according to the CDNA guidelines.[11] The NSLHD COVID-19 Virtual Hospital team, made up of doctors and nurses, contacted each patient within 24 h of positive COVID-19 diagnosis. Initial assessment and risk stratification were based on World Health Organization (WHO) and CDNA guidelines and known risk factors for severe diseases, including age, sex, comorbidities and symptoms.[3,6,8,10–12] Patients had regular follow-up phone consultations and were referred to hospital if there were clinical concerns based on underlying risk factors, age and clinical progress. The ED assessment then determined whether the patient required admission on clinical grounds. Patients who were unable to quarantine in their home were admitted to specialised quarantine hotels. When hospital was required, patients were managed across the four hospitals within the health district. The Virtual Hospital operated 7 days a week, from 0800–2200 hours. After hours, patients were advised to contact their local ED.

Radiology and laboratory investigations were conducted according to each patient's clinical need.

Inclusion and exclusion criteria

All laboratory-confirmed COVID-19 patients within the NSLHD from January to June 2020 were retrospectively included in the study if they had 30-day follow up available. Patients were excluded if there were insufficient data available for analysis or if they were quarantined outside our district.

Data collection

The electronic medical record for each patient, including ED assessments, COVID-19 clinic notes, inpatient admission and follow-up notes from the NSLHD COVID-19 Virtual Hospital team were reviewed retrospectively. Using a standardised form, data were collected on patient demographics, epidemiological risk, comorbidities, clinical symptoms or signs, laboratory and radiological findings, need for hospitalisation or intensive care and patient outcome (Appendix I). Body mass index (BMI) was assessed using standard classification.[13] Severity classification of COVID-19 was assessed using the WHO COVID-19 severity definition.[12]

The incubation period was defined as the interval between the earliest date of contact from a proven COVID-19 contact and the date of symptom onset.[11] This was only included if the date of exposure and source was clear. Most likely acquisition source was determined by the investigators through identification of patients' epidemiological risk factors. Close and casual contacts were defined as per CDNA guidelines.[11] Transmission was classified as 'unknown' if a specific source could not be identified. Fever was defined as an axillary or forehead scan temperature of 37.5°C or higher.[11] Comorbidities including immunodeficiency were defined according to the CDNA guidelines.[11]

Study investigators contacted the patient at or after day 30 to determine recovery and to clarify information if required. Outcomes of the study were death, recovery

at 30 days and the composite outcome of death or ICU admission. Patients were admitted to ICU based on clinical need. In addition, some patients with poor pre-morbid status were not deemed appropriate for ICU. Recovery was defined as the resolution of all symptoms and self-reported patient estimate of returning to 90% or above their pre-morbid function, when asked as binary questions.

Retrospective analysis of chest imaging was performed by two thoracic radiologists independently, involving a third radiologist when consensus was not achieved. Radiologists were blinded to the patients' outcome and to the original report. The Radiographic Assessment of Lung Oedema (RALE) score was used to determine the extent of COVID-19 pulmonary involvement.[14]

Statistics

Data were analysed using SPSS for Windows, version 26.0 (IBM Corp., Armonk, NY, USA). For categorical variables, Pearson Chi-squared or Fisher exact test was used. For continuous variables, Student *t*-test or one-way analysis of variance with Bonferroni correction was used. Two-tailed tests of significance and *P*-values <0.05 were considered. Univariate analysis for death, incomplete recovery at 30 days and composite end-point (death or ICU) identified significant factors that were then selected for inclusion in a logistic regression model, using a backward stepwise selection algorithm with entry and removal criteria of $P \leq 0.05$ and $P \leq 0.1$ respectively.

Results

Demographics, COVID-19 acquisition and clinical characteristics

There were 520 patients in our original cohort, three were excluded due to insufficient data, leaving 517 patients for analysis. A total of 49.9% of our cohort was female, with a median age of 48 years (range 3 months to 95 years) (Table 1).

A total of 265 (51.3%) patients acquired COVID-19 through international travel, while an additional 47 (9.1%) patients were infected following recent travel on a cruise ship. There were 108 (20.9%) cases of community-acquired infection, of which, 83 (16.1%) were identified as close contacts, 22 (4.3%) as casual contacts and 3 (0.6%) that had no identified confirmed COVID-19 contact.

A total of 66 (12.8%) patients were healthcare workers (HCW). The main acquisition source for HCW was international or cruise ship travel (23 patients, 34.8%). Sixteen (24.2%) HCW patients had an unknown source, 12 (18.2%) acquired COVID-19 from hospital, 11 (16.7%) from community source and 4 (6.0%) from aged care facilities. Almost one-third (27.6%) of 58 patients with unknown source in our cohort were HCW. The median age of our HCW subset was 45 years (range 17–81 years), and three (4.5%) HCW required hospitalisation. There were no deaths in our HCW subgroup.

Both date of exposure and symptom onset could be accurately identified in 100 cases. The median incubation period was 5 days (interquartile range 3–8), with one case having an incubation period of 15 days.

The main comorbidities in the cohort were hypertension (81 patients, 15.7%), asthma or other chronic lung condition (57 patients, 13.9%), obesity (38 patients, 12.9%) and diabetes (33 patients, 6.4%) (Table 2). Twenty-one (4.1%) patients were current smokers. The predominant symptoms of COVID-19 were cough (313 patients, 60.5%), fatigue (307 patients, 59.4%), subjective fever (254 patients, 49.1%), myalgia or arthralgia (191 patients, 49.1%), sore throat (213 patients, 41.2%) and anosmia (188 patients, 36.4%) or ageusia (177 patients, 34.2%).

Table 1 Epidemiology

Characteristic	Patient cohort ($n = 517$)
Age (years)	
Median (interquartile range)	47.8 (31–62)
Distribution, no./total no. (%)	
0–14	11/517 (2.2)
15–29	109/517 (21.1)
30–44	98/517 (19)
45–59	140/517 (27.1)
60–74	110/517 (21.3)
≥75	49/517 (9.5)
Female sex, no./total no. (%)	258/517 (49.9)
Current smoker, no./total no. (%)	21/517 (4.1)
Transmission source, no./total no. (%)	
International travel	265/517 (51.3)
Cruise ship	47/517 (9.1)
Community	108/517 (20.9)
Close contact	83/517 (16.1)
Casual contact	22/517 (4.3)
Contact type not defined	3/517 (0.6)
Nursing home acquired	
Resident	10/517 (1.9)
Healthcare worker	4/517 (0.8)
Nosocomial	
Patient	5/517 (1)
Healthcare worker	12/517 (2.3)
Family	8/517 (1.5)
Unknown	58/517 (11.2)
Median incubation period (days)	5
Healthcare worker, no./total no. (%)	66/517 (12.8)

Table 2 Patient clinical features

Characteristic	Patient cohort ($n = 517$)
Comorbidities, no./total no. (%)	
Hypertension	81/517 (15.7)
Ischaemic heart disease	24/517 (4.7)
Cerebrovascular disease	9/517 (1.7)
Chronic obstructive pulmonary disease	10/517 (1.9)
Asthma	47/517 (9.1)
Other chronic lung disease	15/517 (2.9)
Chronic renal disease	7/517 (1.4)
Diabetes	33/517 (6.4)
Immunodeficiency	13/517 (2.5)
Malignancy	16/517 (3.1)
Symptoms, no./total no. (%)	
Nasal congestion	166/517 (32.1)
Anosmia	188/517 (36.4)
Loss of taste	177/517 (34.2)
Headache	220/517 (42.6)
Cough	313/517 (60.5)
Dry	243/313 (77.6)
Wet	70/313 (22.4)
Sputum production	63/313 (20.1)
Fatigue	307/517 (59.4)
Sore throat	213/517 (41.2)
Shortness of breath	159/517 (30.8)
Pleuritic chest pain	56/517 (10.8)
Anorexia	123/517 (23.8)
Nausea/vomiting	74/517(14.3)
Diarrhoea	103/517 (19.9)
Abdominal pain	38/517 (7.4)
Myalgia or arthralgia	191/517 (36.9)
Subjective fever	254/517 (49.1)
Experienced worsening of symptoms in week 2 of symptoms	74/517 (14.3)
Recorded temperature	
Temperature checked	158/517 (30.6)
≥37.5°C	79/158 (50)
<37.5°C	79/158 (50)
No temperature recorded	359/517 (69.4)
Weight, no./total no. (%)	
Underweight (BMI <18.5 kg/m^2)	5/295 (1.7)
Healthy (BMI 18.5–24.9 kg/m^2)	151/295 (51.2)
Overweight (BMI 25–29.9 kg/m^2)	101/295 (34.2)
Obese (BMI ≥30 kg/m^2)	38/295 (12.9)
Weight not known	222/517 (42.9)

BMI, body mass index.

Radiological and laboratory findings

The majority of our cohort did not require laboratory or radiological investigations. Blood tests were performed in 81 (15.6%) patients, while 82 (15.9%) patients had imaging, with either chest X-ray (CXR) or chest computed tomography (CT).

A significant correlation between clinical and radiological severity was observed in the subset of 78 patients who had a CXR performed. The median RALE score for patients who were determined to have clinically severe COVID-19 was 16.4, compared with a median RALE score of 3.0 for those who were determined to be non-severe. Multivariate analysis of this subset demonstrated that age over 80 years and having a RALE score of over 10 were independently associated with death ($P = 0.011$ for both age and RALE score) and with incomplete recovery at 30 days ($P = 0.047$ for age and $P = 0.008$ for RALE score).

The most common blood test abnormalities were elevated D-dimer, C-reactive protein and procalcitonin (Appendix II).

Table 3 Adverse outcomes

Event	Patient cohort, no./total no. (%)
Severity at diagnosis	
Asymptomatic	11/517 (2.1)
Mild	453/517 (87.6)
Moderate	43/517 (8.3)
Severe	10/517 (1.9)
Incomplete recovery at 30 days	28/517 (5.5)
Death	9/517 (1.8)
Persistent symptoms	19/517 (3.7)
Complication	
Pulmonary embolism	1/517 (0.2)
Transverse myelitis	1/517 (0.2)
Brachial neuritis	1/517 (0.2)
Renal dialysis	1/517 (0.2)
Hospitalisation	61/517 (11.8)
Intensive care admission	11/517 (2.1)
Invasive ventilation	7/517 (1.4)

Clinical outcomes

At the time of diagnosis, 11 (2.1%) patients were asymptomatic, 453 (87.6%) had mild disease, 43 (8.3%) had moderate disease and 10 (1.9%) had severe disease (Table 3). During the course of their COVID-19 illness, 61 (11.8%) patients required hospitalisation, 11 (2.1%) patients required intensive care admission and seven (1.4%) patients required ventilation. The median hospital length of stay was 10 days. There were nine deaths (case fatality rate 1.8%) with a median age of 86 years in this subset. Among the ICU patients, three (27.3%) died, all of whom required invasive ventilation, giving a mortality rate among those on ventilation 42.8% (3/7 patients).

Incomplete recovery was reported in 28 (5.5%) patients at 30 days. Persistent symptoms included pleuritic chest pain, cough, fatigue, headache, anosmia, upper respiratory tract symptoms and diarrhoea. A single case was recorded of each of the following complications:

Table 4 Risk factors for adverse patient outcomes

Outcome	Death	Composite outcome death or ICU admission	Incomplete recovery at 30 days
Univariate analysis (*P*-value)			
Age >80 years	<0.001	<0.001	<0.001
≥2 comorbidities	<0.001	<0.001	<0.001
Overweight or obese	0.022	0.01	0.012
Hypertension	0.001	<0.001	0.001
Ischaemic heart disease	0.006	0.039	0.006
Cerebrovascular disease	<0.001	0.002	<0.001
COPD	NS	0.039	NS
Other chronic lung disease	0.025	NS	NS
Chronic renal disease	NS	0.019	NS
Diabetes	NS	0.018	NS
Malignancy	0.002	<0.001	0.045
Multivariate analysis (*P*-value, RR (95% CI))			
Age >80 years	<0.001, 24.4 (4.1–144.8)	NS	0.002, 5.6 (1.9–16.7)
≥2 comorbidities	0.004, 27.6 (2.9–258.9)	<0.001, 20.3 (5.2–79.8)	0.002, 4.3 (1.7–11.1)

Patient characteristics that were not significant on univariate analysis on any outcome were: asthma, current smoker and immunodeficiency.
CI, confidence interval; COPD, chronic obstructive pulmonary disease; ICU, intensive care unit; NS, not significant; RR, relative risk.

pulmonary embolism, transverse myelitis, brachial neuritis and earlier need for permanent renal dialysis.

Age greater than 80 years ($P < 0.001$), having two or more comorbidities ($P < 0.001$) or being overweight or obese ($P \leq 0.022$) were associated with death, composite outcome of death or ICU admission and incomplete recovery at 30 days on univariate analysis (Table 4). Other characteristics and risk factors associated with the study end-points on univariate analysis are also shown in Table 4. Age greater than 80 years (relative risk (RR) 24.4, 95% confidence interval (CI) 4.1–144.8) and having two or more comorbidities (RR 27.6, 95% CI 2.9–258.9) remained independently associated with death on multivariate analysis. Having two or more comorbidities (RR 20.3, 95% CI 5.2–79.8) was also independently associated with composite outcome of death or ICU admission. Age greater than 80 years (RR 5.6, 95% CI 1.9–16.7) and having two or more comorbidities (RR 4.3, 95% CI 1.7–11.1) were independently associated with incomplete recovery at 30 days. A total of 402 (97.1%) patients of our cohort did not receive any COVID-19-specific treatment (Appendix III).

Discussion

This is the largest Australian cohort study of COVID-19 outcomes and characteristics to date. The majority of cases in our cohort were acquired overseas, with most managed as outpatients through the NSLHD Virtual Hospital. This Virtual Hospital was established to manage COVID-19 in our local health district and will now be utilised for non-COVID-19 diagnoses. We report a cohort with relatively mild disease and low case fatality rate, in a well resourced setting. Hospital-in-the-home services have been found to provide safe and resource-efficient care to patients in other Australian settings.[15–17]

The median incubation period of 5 days seen in this cohort is consistent with international studies and guidelines.[5,18] However, one patient did have an incubation period of 15 days, falling outside of the widely recommended 14-day quarantine period. There have been other cases published with incubation periods beyond 14 days.[19] The incubation period could only be calculated in less than one fifth of our cohort, predominantly due to the main acquisitions being international, where source could not be identified.

COVID-19 remains a challenging clinical diagnosis. The most commonly reported manifestations in our cohort were non-specific symptoms of cough, fatigue and fever, consistent with Australian and international studies.[3–8,17,20] Most patients were afebrile on admission and characterised as mild severity or asymptomatic. The variability of initial symptoms can result in difficulty identifying those at risk of deterioration. Our study identified the following risks for adverse outcome: age over 80 years, presence of two or more comorbidities and being overweight or obese. These findings are similar to large international studies and recent Australian studies where age, male sex and comorbidities, including obesity, were associated with worse overall outcomes.[3,8,10,21]

We note a relatively high percentage of HCW in our study. Although there may be a testing bias, this shows that HCW are a key vulnerable group where early identification is critical and public health measures including vaccination should be targeted. The majority of HCW in

our cohort acquired COVID-19 in the community, rather than a nosocomial setting. This predominance of community acquisition among HCW is a consistent finding in different healthcare settings.[22,23]

The significant difference found in our cohort between the RALE score in those with severe versus non-severe disease is in line with previous reports[14] and, together with abnormal pathology investigations, can be utilised to identify a subset of patients with severe disease who require closer follow up.

Hospitalisation was required in 11.8% of our cases, with ICU requirement appropriate and necessary in 2.1%. These figures can assist health systems to prepare for future COVID-19 surges. Very few patients in our cohort received COVID-19 specific treatment, reflecting the limited available evidence during the early stages of the pandemic. This cohort predated any established effective therapy for COVID-19 including the results of the Randomised Evaluation of COVID-19 Therapy (RECOVERY) trial showing efficacy of dexamethasone.[24] Treatment used in several patients in our cohort, including hydroxychloroquine alone or in combination with azithromycin, has been later shown to have no effect and can even increase COVID-19 associated mortality.[25] Despite small numbers, our ICU mortality figures are higher than reported in other Australian ICU studies.[20,26]

Our case fatality rate of 1.8% compares favourably to the Australian wide rate of 3.0%.[2] We hypothesise that the comparatively lower mortality rate seen in this study is reflective of several factors. First, the rates of testing in this health district were relatively high, thus enabling the early detection of asymptomatic cases that increases the denominator in our overall calculations. Furthermore, the relatively low prevalence in the NSLHD allowed a swift and sustained health response from the PHU, microbiology laboratories, hospital systems and ICU, thus facilitating containment, rapid diagnosis and effective medical management. The general population's compliance with public health measures such as physical distancing, enforced periods of lockdown, along with tight border control, have contributed to the low prevalence and sustained response. Finally, the relatively low rates of comorbidities and good premorbid function[27] seen in the cohort are likely to have had an impact on lowering the case fatality rate.

However, it is noted that the case fatality rate in this study is slightly higher than the NSW overall rate of 1.0%.[2] We suggest that this may be reflective of a subset of patients from a single aged care facility in which a COVID-19 outbreak was experienced during the study period. Five of the nine patients who died from COVID-19 were from this aged care facility. Our analysis of the subgroup of aged care was underpowered; however, we know that aged care facilities account for a large proportion of COVID-19 deaths globally and in Australia.[28] This association is likely to be largely driven by the association between age and COVID-19 mortality, as we noted in our study.

On a global scale, our case fatality rate compares favourably to countries such as the United Kingdom, China and Italy, with case fatality rates of 2.9%, 4.7% and 3.0% respectively; and similarly to the United States with a case fatality rate of 1.8%.[29]

Limitations of our study include the retrospective collection of patient self-reported recovery, which makes it liable to recall bias. Additionally, we do not have the complete data detailing dates of patient follow up comparative to their diagnosis, making it difficult to determine the extent of the recall bias. Ascertainment bias may have been introduced where residents of NSLHD were managed by alternative health districts while in hotel quarantine. The data sets for patient BMI and recorded fever were incomplete, limiting the power of multivariate analysis. Analysis of laboratory and radiological investigations were limited, with less than 16% requiring further investigations. This reflects the overall mild disease in our cohort. Our study was conducted in an area of high socioeconomic status with lower rates of obesity and smoking than the average Australian community, therefore limiting generalisability to the Australian population. Similarly, these data are from last year, limiting generalisability in such a fast-moving field, with unprecedented rate of new data emerging.

Conclusions

We report an Australian cohort analysis of 517 laboratory-confirmed COVID-19 patients with predominantly mild disease and a low mortality in a low prevalence, well resourced setting. Factors associated with poor patient outcomes on multivariate analysis were age over 80 years and the presence of two or more comorbidities. Our data can inform risk stratification in the COVID-19 Virtual Hospital to determine resource allocation and early hospital admission. Rates of hospitalisation, ICU admission and ventilation requirement in this cohort, have assisted NSLHD in surge capacity planning for subsequent COVID-19 waves.

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References

1 World Health Organization (WHO). WHO Coronavirus (COVID-19) Dashboard. Geneva, Switzerland: WHO; 2020 [cited 2021 Jun 11]. Available from URL: https://covid19.who.int/

2 Australian Government Department of Health. Coronavirus (COVID-19) Current Situation and Case Numbers. 2021 [cited 2021 Jun 11]. Available from URL: https://www.health.gov.au/news/health-alerts/novel-coronavirus-2019-ncov-health-alert/coronavirus-covid-19-current-situation-and-case-numbers

3 Zhu J, Ji P, Pang J, Zhong Z, Li H, He C *et al*. Clinical characteristics of 3,062 COVID-19 patients: a meta-analysis. *J Med Virol* 2020; **92**: 1902–14.

4 Jiang F, Deng L, Zhang L, Cai Y, Cheung CW, Xia Z. Review of the clinical characteristics of coronavirus disease 2019 (COVID-19). *J Gen Intern Med* 2020; **35**: 1545–9.

5 Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX *et al*. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med* 2020; **382**: 1708–20.

6 Goyal P, Choi JJ, Pinheiro LC, Schenck EJ, Chen R, Jabri A *et al*. Clinical characteristics of Covid-19 in New York City. *N Engl J Med* 2020; **382**: 2372–4.

7 Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW *et al*. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area. *JAMA* 2020; **323**: 2052–9.

8 Docherty A, Harrison E, Green C, Hardwick H, Pius R, Norman L *et al*. Features of 16,749 hospitalised UK patients with COVID-19 using the ISARIC WHO Clinical Characterisation Protocol. *BMJ* 2020; **369**: m1985.

9 Klopfenstein T, Kadiane-Oussou NJ, Toko L, Royer PY, Lepiller Q, Gendrin V *et al*. Features of anosmia in COVID-19. *Med Mal Infect* 2020; **50**: 436–9.

10 Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z *et al*. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet* 2020; **395**: 1054–62.

11 Communicable Diseases Network Australia Coronavirus Disease 2019 (COVID-19): CDNA National Guidelines for Public Health Units. 2020 [cited 2021 May 6]. Available from URL: https://www1.health.gov.au/internet/main/publishing.nsf/Content/cdna-song-novel-coronavirus.htm

12 World Health Organization (WHO). *Clinical Management of COVID-19: Interim Guidance*. Geneva, Switzerland: WHO; 2020.

13 Centers for Disease Control and Prevention Defining Adult Overweight and Obesity. 2020 [cited 2021 Feb 7]. Available from URL: https://www.cdc.gov/obesity/adult/defining.html#:~:text=Adult%20Body%20Mass%20Index%20(BMI)&text=If%20your%20BMI%20is%20less,falls%20within%20the%20obese%20range

14 Cozzi D, Albanesi M, Cavigli E, Moroni C, Bindi A, Luvarà S *et al*. Chest X-ray in new coronavirus disease 2019 (COVID-19) infection: findings and correlation with clinical outcome. *Radiol Med* 2020; **125**: 730–7.

15 Hutchings O, Dearing C, Jagers D, Shaw M, Raffan F, Jones A *et al*. Virtual health care for community management of patients with COVID-19. *J Med Internet Res* 2020; **9**: e21064.

16 Lwin N, Burgess J, Johnston C, Johnson N, Chung S. Hospital-in-the-home experience of first 23 COVID-19 patients at a regional NSW hospital. *Intern Med J* 2020; **50**: 1271–3.

17 Louie T, Kwan B, Susanto C, Ng A. Respiratory failure, clinical course and community management of COVID-19 patients in a large Australian cohort. *Intern Med J* 2021; **51**: 334–40.

18 McAloon C, Collins Á, Hunt K, Barber A, Byrne AW, Butler F *et al*. Incubation period of COVID-19: a rapid systematic review and meta-analysis of observational research. *BMJ Open* 2020; **10**: e039652.

19 Jiang X, Niu Y, Li X, Li L, Cai W, Chen Y *et al*. Is a 14-day quarantine period optimal for effectively controlling coronavirus disease 2019 (COVID-19)? *medRxiv* 2020. doi:10.1101/2020.03.15.20036533

20 Burrell AJ, Pellegrini B, Salimi F, Begum H, Broadley T, Campbell LT *et al*. Outcomes for patients with COVID-19 admitted to Australian intensive care units during the first four months of the pandemic. *Med J Aust* 2021; **214**: 23–30.

21 Toh DJW, Rowe E, Nelson R, O'Connell A, Lim K, Fielke L *et al*. Outcomes for the first wave of hospitalised patients with COVID-19 in the South Australian context: a retrospective audit. *Intern Med J* 2021; **51**: 189–98.

22 Al Maskari Z, Al Blushi A, Khamis F, Al Tai A, Al Salmi I, Al Harthi H *et al*. Characteristics of healthcare workers infected with COVID-19: a cross-sectional observational study. *Int J Infect Dis* 2021; **102**: 32–6.

23 Hogan RJ, McEvoy S. Acquisition of COVID-19 by health care workers: the importance of non-patient workplace sources. *Med J Aust* 2021; **214**: 332–e1.

24 Group RC, Horby P, Lim WS, Emberson JR, Mafham M, Bell JL *et al*. Dexamethasone in hospitalized patients with Covid-19. *N Engl J Med* 2021; **384**: 693–704.

25 Fiolet T, Guihur A, Rebeaud ME, Mulot M, Peiffer-Smadja N, Mahamat-Saleh Y. Effect of hydroxychloroquine with or without azithromycin on the mortality of coronavirus disease 2019 (COVID-19) patients: a systematic review and meta-analysis. *Clin Microbiol Infect* 2021; **27**: 19–27.

26 Nadkarni A, Alderson S, Collett L, Maiden M, Reddi B, Sundararajan K. Impact of COVID-19 on an Australian intensive care unit: lessons learned from South Australia. *Intern Med J* 2020; **50**: 1146–50.

27 Australian Bureau of Statistics Data by Region. 2020 [cited 2021 Feb 9]. Available from URL: https://itt.abs.gov.au/itt/r.jsp?databyregion#/

28 Comas-Herrera A, Zalakaín J, Lemmon E, Henderson D, Litwin C, Hsu AT *et al*. Mortality Associated with COVID-19 in Care Homes: International Evidence. International Long-Term Care Policy Network, CPEC-LSE. 2020 [updated 2021 Feb 1; cited 2021 May 13]. Available from URL: http://ltccovid.org/

29 Johns Hopkins University & Medicine: Coronavirus Resource Centre Mortality Analyses. 2021 [cited 2021 May 16]. Available from URL: https://coronavirus.jhu.edu/data/mortality

Appendix I

Table A1 Standardised data collection form

Patient number:															
Investigator:															
Demographics															
Hospital/Location of testing		MRN	Suburb		DOB		Age at diagnosis	Sex		Acquisition		HCW (Yes/No)		Date of first contact with known source	
Comorbiditiess (Yes/No)															
Hypertension	IHD	Cerebrovascular disease		COPD	Asthma		Other CLD	Current smoker		CKD	Diabetes		Immunodeficiency	Malignancy	
Symptoms (Yes/No)															
Symptom onset:															
Incubation period:															
Nasal congestion	Anosmia	Ageusia	Headache	Cough (dry/ wet/none)	Sputum production	Fatigue	Shortness of breath	Pleuritic chest pain	Anorexia	Nausea and vomiting	Diarrhoea	Abdominal pain	Myalgia or arthralgia	Subjective fever	Week 2 deterioration SOB/cough
Observations															
Presenting temperature				Highest temperature in first 24 h				Underweight (<18.5 kg/m^2), healthy (18.5–24.9 kg/m^2), overweight (25–29.9 kg/m^2), obesity (≥30 kg/m^2)				Patient BMI (either reported or measured)			
Testing															
Date of test (–/–/–)					Difference between date of test and symptom onset					Any preceding that was negative (Yes/No)					
Radiology (Yes/No/Not done)															
CXR ground glass opacity		CXR local patchy shadowing		CXR bilateral patchy shadowing		CXR interstitial abnormalities		CT ground glass opacity		CT local patchy shadowing		CT bilateral patchy shadowing		CT interstitial abnormalities	
Laboratory investigations															
Lymphocyte count	Platelet count	CRP		LDH	AST	ALT		Bilirubin	Cr	CK		Troponin	PCT	D-dimer	
Patient outcomes															
Severity at diagnosis (mild/moderate/severe)		Hospital Admission required (Yes/No)	Days in hospital		Oxygen therapy (Yes/No)		COVID-19 specific treatment (specify)	Adverse drug reaction? (Yes/No)		Details of ADR or reason for cessation		IV antibiotics (Yes/No, which antibiotic)		Glucocorticoids (Yes/No)	
Patient outcomes															
ICU requirement (Yes/No)		ICU days	Invasive ventilation (Yes/No)		ECMO (Yes/No)		Renal replacement therapy (Yes/No)	Secondary bacterial pneumonia (Yes/No)		Recovery at 30 days (Yes/No)		Death (Yes/No)		Days to death from symptom onset	
Further comments:															

ALT alanine transaminase; AST, aspartate aminotransferase; BMI, body mass index; CK, creatinine kinase; CKD, chronic kidney disease; CLD, chronic liver disease; COPD, chronic obstructive pulmonary disease; Cr, creatinine; CRP, C-reactive protein; CT, computed tomography; CXR, chest X-ray; ECMO, extracorporeal membrane oxygenation; HCW, healthcare worker; ICU, intensive care unit; IHD, ischaemic heart disease; IV, intravenous; PCT, procalcitonin; SOB, shortness of breath.

Appendix II

Table A2 Pathology findings

Investigation	Patient cohort	Disease severity	
		Mild/Moderate	Severe ($n = 10$)
Laboratory findings, no./total no. (%)			
Lymphocyte count $<1 \times 10^9$/L	33/81 (40.7)	27/71 (38)	6/10 (60)
Platelet count $<150 \times 10^9$/L	19/81 (23.5)	17/71 (23.9)	2/10 (20)
CRP ≥10 mg/L	55/80 (68.8)	45/70 (64.3)	10/10 (100)
LDH >250 U/L	6/10 (60)	4/8 (50)	2/2 (100)
AST >35 U/L	35/71 (49.3)	27/62 (43.5)	8/9 (88.9)
ALT >50 U/L	16/73 (21.9)	13/63 (20.6)	3/10 (30)
Bilirubin >20 μmol/L	3/73 (4.1)	2/63 (3.2)	1/10 (10)
Creatinine >110 μmol/L	11/80 (13.8)	9/71 (12.7)	2/10 (20)
Creatinine kinase >250 U/L	0/2 (0)	0/2 (0)	0/0
Troponin >26 ng/L	3/30 (10)	2/26 (7.7)	1/4 (25)
Procalcitonin >0.05 μg/L	8/13 (61.5)	6/9 (66.7)	2/4 (50)
D-dimer >0.50 mg/L	23/26 (88.5)	18/21 (85.7)	5/5 (100)

ALT, alanine transaminase; AST, aspartate aminotransferase; CRP, C-reactive protein; LDH, lactate dehydrogenase.

Appendix III

A total of 97.1% of our cohort (402 patients) did not receive any COVID-19-specific treatment. Of the 15 patients who did receive specific treatment, five received hydroxychloroquine alone, seven received hydroxychloroquine and azithromycin in combination, two received lopinavir/ritonavir and hydroxychloroquine in combination and one received lopinavir/ritonavir alone. Only eight of these 15 patients completed their treatment as planned, with prolonged QTc interval (42.9%) and gastrointestinal upset (28.6%) being the main side effects. One patient had their treatment stopped due to prescriber concern regarding potential drug interaction causing prolonged QTc, while another patient's treatment was stopped due to concern regarding the lack of evidence for the COVID-19 specific treatment.