A descriptive study of the surge response and outcomes of ICU patients with COVID-19 during first wave in Nordic countries

Chew, Michelle S.

2022-01

Chew , M S , Kattainen , S , Haase , N , Buanes , E A , Kristinsdottir , L B , Hofso , K , Laake , J H , Kvåle , R , Hästbacka , J , Reinikainen , M , Bendel , S , Varpula , T , Walther , S , Perner , A , Flaatten , H K & Sigurdsson , M I 2022 , ' A descriptive study of the surge response and outcomes of ICU patients with COVID-19 during first wave in Nordic countries ' , Acta Anaesthesiologica Scandinavica , vol. 66 , no. 1 , pp. 56-64 . https://doi.org/10.1111/aas.13983

http://hdl.handle.net/10138/348403
https://doi.org/10.1111/aas.13983

acceptedVersion

DR EIRIK ALNES BUANES (Orcid ID : 0000-0002-1295-6734)
DR JON HENRIK LAAKE (Orcid ID : 0000-0001-6157-5359)
DR JOHANNA HÄSTBACKA (Orcid ID : 0000-0002-3613-7231)
DR MATTI REINIKAINEN (Orcid ID : 0000-0001-6878-3740)
PROFESSOR STEN WALTHER (Orcid ID : 0000-0002-3862-2556)
PROFESSOR HANS KRISTIAN FLAATTEN (Orcid ID : 0000-0001-9186-3482)
DR MARTIN INGI SIGURDSSON (Orcid ID : 0000-0001-7054-0844)

Article type : Research Article

A descriptive study of the surge response and outcomes of ICU patients with COVID-19 during first wave in Nordic countries

Michelle S. Chew[1], Salla Kattainen[2,3], Nicolai Haase[4], Eirik A. Buanes[5], Linda B. Kristinsdottir[6], Kristin Hofso[7,8], Jon Henrik Laake[9], Reidar Kvåle[10,11], Johanna Hästbacka[2,3], Matti Reinikainen[12,13], Stepani Bendel[12,13], Tero Varpula[2,3], Sten Walther[14,15], Anders Perner[4], Hans K Flaatten[10,11], Martin I. Sigurdsson[6,16]

[1]Departments of Anaesthesia and Intensive Care, Biomedical and Clinical Sciences, Linköping University, Linköping, Sweden; [2] Department of Anaesthesiology, Intensive Care and Pain Medicine, Helsinki University Hospital, Helsinki, Finland; [3]Faculty of Medicine, University of Helsinki, Helsinki, Finland; [4]Department of Intensive Care, Rigshospitalet, University of Copenhagen, Copenhagen; [5]Norwegian Intensive Care and Pandemic Registry, Helse Bergen Health Trust, Norway; [6]Department of Anaesthesiology and Critical Care, Perioperative services, Landspitali – The National University Hospital of Iceland, Reykjavik, Iceland; [7]Department of Research and Development, Division of Emergencies and Critical Care, Oslo University Hospital, Oslo, Norway; [8]Lovisenberg Diaconal University College, Oslo, Norway; [9]Department of Anaesthesiology and Department of Research and Development, Division of Critical Care and

Emergencies, Oslo University Hospital, Oslo, Norway; [10]; [12]Institute of Clinical Medicine, University of Eastern Finland, Kuopio, Finland; [13]Department of Anaesthesiology and Intensive Care, Kuopio University Hospital, Kuopio Finland; [14]Swedish Intensive Care Registry, Värmland County Council, Karlstad, Sweden,[15]Departments of Cardiothoracic and Vascular Surgery and Health, Medicine and Caring Sciences, Linköping University Hospital, Linköping, Sweden;[16]Faculty of Medicine, University of Iceland, Reykjavik, Iceland

Corresponding author:

Martin I. Sigurdsson, MD, PhD.

Department of Anaesthesiology and Critical Care, Perioperative Services, Landspitali – The National University Hospital of Iceland, Reykjavik, Iceland and Faculty of Medicine, University of Iceland, Reykjavik, Iceland

e-mail: martin@landspitali.is, Phone +354 8248282

Prior Presentations: None

Access to data and data analysis: Representatives from each country listed in author list had full access to the data for their individual countries and are responsible for the integrity of the data and the accuracy of the data analysis for their individual countries.

Number of words: 2721 (main text)

Number of figures: 1; Number of tables: 4; Number of supplemental files: 1

Running Headline: Nordic ICU response to COVID-19

Funding: NordForsk (Nordic COVID-19 Activities), Finnish Society of Intensive Care

Conflict of Interest: None

Abstract

Background

We sought to provide a description of surge response strategies and characteristics, clinical management and outcomes of patients with severe COVID-19 in the intensive care unit (ICU) during the first wave of the pandemic in Denmark, Finland, Iceland, Norway and Sweden.

Methods

Representatives from the national ICU registries for each of the five countries provided clinical data and a description of the strategies to allocate ICU resources and increase the ICU capacity during the pandemic. All adult patients admitted to the ICU for COVID-19 disease during the first wave of COVID-19 were included. The clinical characteristics, ICU management and outcomes of individual countries were described with descriptive statistics.

Results

Most countries more than doubled their ICU capacity during the pandemic. For patients positive for SARS-CoV-2, the ratio of requiring ICU admission for COVID-19 varied substantially (1.6-6.7%). Apart from age (proportion of patients aged 65 years or over between 29-62%), baseline characteristics, chronic comorbidity burden and acute presentations of COVID-19 disease were similar among the five countries. While utilization of invasive mechanical ventilation was high (59-85%) in all countries, the proportion of patients receiving renal replacement therapy (7-26%) and various experimental therapies for COVID-19 disease varied substantially (e.g. use of hydroxychloroquine 0-85%). Crude ICU mortality ranged from 11% to 33%.

Conclusion

There was substantial variability in the critical care response in Nordic ICUs to the first wave of COVID-19 pandemic, including usage of experimental medications. While ICU mortality was low in all countries, the observed variability warrants further attention.

Editorial Comment

In this report, Nordic country ICU responses to the surge in patient with the COVID-19 pandemic is described, including strategies to adapt ICU capacities as need changed. Contrasts are presented between the different Nordic country results.

Keywords

COVID19, SARS-COv2, Mortality, Nordic

Introduction

With the onset of the COVID-19 pandemic, there were understandable concerns about the number of patients requiring intensive care and whether the capacity of individual health care systems would be surpassed.[1] With an increasing number of COVID-19 cases in most countries, extensive modifications of infrastructure were required in many hospitals to accommodate patients with severe COVID-19 infection that required critical care, including delays of elective procedures.[2]

Adding to these concerns was the lack of specific therapeutic options available to shorten the course of the disease or improve the outcomes for severely ill patients.[3] Lack of personal protective equipment and vaccines, and uncertainties regarding the use of high-flow nasal oxygen therapy and non-invasive ventilation to reduce the need for invasive mechanical ventilation fuelled concerns about the risk of spreading the infection and personal safety of the intensive care unit (ICU) personnel.[4] As clinicians grappled with an unknown disease, various experimental treatment modalities such as antiretroviral medications[5-7] and immunomodulatory therapy[8] were introduced in some hospitals, bypassing general principles of good clinical practice and evidence-based medicine. In addition, more traditional methods to manage severe ARDS such as prone positioning,[9] usage of diuretics[10,11] and ECMO[12] were utilized in the management of the most critically ill patients.

At the same time, initial reports from Northern Italy and China reported a high burden of ICU care as well as poor outcomes for those patients that required critical care, with over 5% of all confirmed cases requiring ICU management[13] and short-term mortality rates between 39-62%.[14-16] It is possible that these early outcomes were related to the number of patients exceeding surge capacity.

In the Nordic countries, epidemiology of COVID-19 as well as public health policies have differed substantially. The public health response in each country ranged from lockdown-policies including border closures and widespread testing, to ostensibly more permissive approaches.[17] Given the demographic similarities of the populations in the Nordic countries and the differences in the overall structure and response to COVID –19 in each country, understanding the variability

in ICU surge response as well as the epidemiology and outcomes of patients admitted to ICUs is of interest.

To investigate this, a working group of researchers working on national ICU registries in the Nordic countries was formed, with the overall goal of creating a Nordic network for epidemiological research of ICU patients with COVID-19. In this first publication, we sought to describe the national response, surge response and ICU outcomes of patients admitted to Nordic ICUs in the first wave of COVID-19, to shed light on similarities and differences between the countries. Our hope is that this will aid in understanding this pandemic and improve the preparation for future pandemics.

Materials and methods

Data collection

Given that data collection was either through pre-existing registries in some countries, or was already largely collected, it was decided that each country would provide pre-approved summary statistics of their cohort, and a description of national surge response. A consensus on variables describing surge response and clinical data was reached via email communication between all researchers prior to any data entry and converted into tables 1-5. An individual from each country was responsible for answering a questionnaire regarding surge response and filling in clinical data for patients admitted to the ICU. The outcomes of interest were the incidence of ICU admission, use of various ICU treatment modalities (medications, mode of respiratory and other organ support) and ICU mortality. It was decided that each country would at minimum describe all adult patients with COVID-19 admitted within two months following ICU admission of the first patient with COVID-19. Thus, this study presents descriptive summary statistics using prospectively and retrospectively collected data, and individual databases were not merged for data protection reasons. The details of individual datasets are described below.

Denmark

Details of the data collection and outcomes in Denmark have been published previously.[18] Ethics approval for the study was not required, but access to data was granted by the Danish Patient Safety Authority (ref. no. 31-1521-293). Data were collected retrospectively from electronic patient records by study authors. The data included all patients positive for SARS-CoV-2 infection who were admitted to any of the 29 ICUs in Denmark treating patients with COVID-19 during the pandemic.

Finland

The data from Finland have not been previously published. Ethics approval was not required due to the registry-based design. Approval for obtaining and using registry data in summary form for purposes of this study was obtained from the Finnish Institute of Health and Welfare (THL/6074/14.02.00/2020) and from the Helsinki University Hospital (HUS/419/2021). The data were collected retrospectively from the Finnish Intensive Care Consortium's (FICC) database

(TietoEvry, Finland). All patients who tested positive for SARS-CoV-2 infection and were admitted to any of the ICUs in Finland caring for patients with COVID-19 were included.

Iceland

Details of the data collection and outcomes from Iceland have been published previously.[19] Institutional Review Board (IRB) approval with a waiver for informed consent was granted by the National Bioethics Committee (VSN-20-071). The data was prospectively registered in a customized database by two clinicians. The data included information on all patients with a SARS-CoV-2 infection confirmed with real-time polymerase chain reaction (qPCR) and admitted for hypoxic respiratory failure to the ICUs at Landspitali University Hospital and Akureyri Regional Hospital, the only two hospitals providing intensive care in Iceland.

Norway

Details of the data collection and outcomes from Norway have been published previously.[20] IRB approval with a waiver for informed consent was granted by the South-East Norway Regional Committee for Medical and Health Research Ethics (reference no. 135310). The data were collected from a preexisting registry, the Norwegian Intensive Care and Pandemic Registry (NIPaR), that was modified during the pandemic to include additional comorbidities as well as type and duration of respiratory support. The data included patients admitted to ICUs in Norway with a laboratory confirmed COVID-19 diagnosis during the study period.

Sweden

Details of the data collection and outcomes from Sweden have been published previously.[21] IRB approval with a waiver for informed consent was granted by the Swedish Ethical Review Authority (no. 2020-01884 and 2020-02498). The data were collected from a preexisting registry, the Swedish Intensive Care Registry that routinely and prospectively collects data from all ICUs in Sweden. The data included all patients admitted to ICU with a positive test for SARS-CoV-2 and the ICD10 diagnosis code U07.1.

Statistical analysis

The frequencies of cases per day per country were obtained from Our World in Data.[22] Because data collection differed among participating countries, this work provides a description of a minimal set of data from each country that did not require merging of data sets. Where

appropriate, data are presented normalized to the population (per million people), and exact 95% confidence intervals (Clopper-Pearson exact method). All statistics and image processing were performed in R, Version 3.4.3 (R Foundation for Statistical Computing, Vienna, Austria), using RStudio, Version 1.1.423 (RStudio, Boston, MA).

Results

General overview of the first wave of COVID-19

All participating countries reported data from the beginning of March 2020 until the beginning of May (Table 1). Figure 1 shows a comparison of new cases and number of new ICU admissions per one million people. During this period both the highest incidence of cases, highest number of new cases and total number of cases per capita was in Iceland, and the lowest number of new cases and total number of cases per capita was in Finland (Figure 1, Table 1). There was a high variability in case fatality rate (CFR, deaths per individual positive for SARS-CoV-2 infection by qPCR); the highest CFR was in Sweden (14.4%) and the lowest CFR was in Iceland (0.6%) (Table 1). Three countries had available estimates of the total number of infections based on antibody screening following the first wave, and this revealed that number of infections was 2-5 times higher than cases diagnosed via qPCR (Table 1).

National disaster and ICU surge response

A summary of public health measures to control the pandemic are shown in Table 2. All countries imposed widespread restrictions on visits to hospitals and nursing homes as well as the overall mobility and social contact, including limitations off the number of people allowed to convene (Table 2). All countries except Sweden additionally closed primary and secondary schools and restricted non-essential services substantially.

An overview of the ICU capacity prior to and during the first wave is shown in Table 3. Prior to the onset of the pandemic the lowest and highest number of beds available were, respectively, in Iceland (4.3 beds per hundred thousand people) and in Denmark (5.7 beds per hundred thousand people). Prior to the pandemic, all countries except Iceland had high-dependency beds (with enhanced monitoring and management capabilities compared to regular ward beds). During the pandemic, Nordic countries increased their maximum ICU bed availability by 30-128% (Table 3). In general, there were centralized registries to track available ICU beds as well as the availability of ICU staff, equipment and medications as well as a system on a regional level to share these resources between ICUs (Table 3).

Characteristics of patients admitted to the ICU during the first wave of COVID-19

Table 4 shows the characteristics of COVID-19-patients admitted to ICUs. The proportion of SARS-CoV-2 positive patients by qPCR who were admitted to ICUs ranged from 1.6% (Iceland) to 6.7% (Sweden), but the number of ICU admissions per capita ranged from 3.4 (Finland) to 15.1 (Sweden) per hundred thousand individuals. The largest proportion of patients 50 years or younger was in Finland and the largest proportion of patients 70 years or older was in Denmark. Males were more commonly admitted to the ICU than females in all countries. The incidence of comorbidities was comparable amongst the countries (Table 4). Individuals admitted to the ICU in all countries suffered from moderate or severe respiratory failure graded by their PaO_2/FiO_2 ratio, and modest to severe acuity of illness at presentation as per APACHEII / SAPSII / SAPSIII classes (Table 4). Patients were most commonly admitted at day 9 after symptom onset and 1-2 days after admission to the hospital, with no major differences noted between countries.

ICU management and mortality

The median duration of days spent in the ICU ranged from 10 (Iceland) to 14 (Norway) (Table 5). Invasive mechanical ventilation was utilized in 59% (Iceland) to 85% (Norway) of patients admitted to the ICU with COVID-19, most commonly for 10-13 days. Prone positioning was used in more than a third of all cases in the countries with available data but use of extracorporeal membrane oxygenation (ECMO) was uncommon (Table 5). Acute kidney injury was common (19-47%), but the number of patients that received renal replacement therapy varied substantially between countries (7-33%).

Overall ICU mortality ranged from 11% (Iceland) to 33% (Denmark) and did not rise substantially following discharge from the ICU (Table 5).

Discussion

Here we describe substantial variability in the ICU surge response, characteristics and outcomes of patients admitted to Nordic ICUs during the first wave of the COVID-19 pandemic.

Public health responses varied somewhat between countries. In general, all countries experienced substantial restriction on social activities, although there were fewer mandatory restrictions in Sweden compared to the other countries.[17] There was also likely a difference between the countries in the availability of qPCR- testing during the first wave of COVID-19. This is important to consider when interpreting the descriptive data in this report. For example, both the case fatality rate as well as the ratio of patients admitted to ICUs from those positive for SARS-CoV-2 were highest in Sweden and lowest in Iceland. Both figures reflect the availability and strategy of qPCR-testing for the disease. A limit on the capacity for testing makes it more likely that the more severely ill are tested, raising both the case fatality rate and the ratio of patients admitted to the ICU. However, since all Nordic ICU patients had confirmed SARS-CoV-2 infection, it is unlikely that outcomes within this population are affected by national population testing strategies.

Prior to the pandemic, there was a substantial variability in the number of available ICU beds between the countries. The Nordic ICU population was characterized by moderate burden of acute disease reflecting that most patients had only a single organ failure on ICU admission. Consistent with prior studies most of the ICU patients were male and had comorbid diseases such as obesity, diabetes and cardiovascular disease.[23-25] There was a higher proportion of elderly patients in Denmark compared with the other Nordic countries, that might explain a slightly higher mortality observed there. Invasive mechanical ventilation was used in 59-85% of patients requiring ICU care, compared with 38-82% in other countries.[20,26] Local guidelines for the use of non-invasive ventilation and high-flow nasal oxygen and concerns about risk of contamination by aerosols, as well as the availability of intermediate care units for provision of non-invasive respiratory support may explain these differences. With limited data available on risks and benefits of various pharmacological interventions, a substantial use of medications with unknown effectiveness (antiviral therapy, IL-6 antagonists)[6,8,27] and medications later found to be harmful (azithromycin, hydroxychloroquine)[28] is of concern. Early guidance recommended against the use of corticosteroids, and this explains low usage at this stage of the pandemic.[29]

Short-term mortality during the first wave of COVID-19 in this study was 11-33%, somewhat lower than reported in other countries at this stage of the pandemic. A meta-analysis of 24 mostly single-centre studies of ICU patients with outcomes, reported until May 31st, 2020, found that the average ICU mortality rate was 41.6% in patients who had completed their ICU stay. Whole-nation registries in the UK, Scotland, Germany and the Netherlands have similarly reported ICU mortality rates of 39%, 38%, 23% and 26%, respectively.[30] Overall, there has been a trend towards lower ICU mortality later in the pandemic,[30,31] but the current study cannot answer if this is also the case in the Nordic countries.

The variability in reported mortality is of interest and warrants further attention. This could certainly be due to difference in patient demographics (such as age), acuity of disease (such as coexisting organ failures), or other factors. A higher burden of COVID-19 either regionally or nationally may additionally influence patient treatment and outcomes, but whether this is the case in the well-funded Nordic health care systems cannot be assessed in our study of aggregated data covering only the initial part of the pandemic. We are furthermore unable to directly assess the impact of general public health measures on ICU admission rates using our data, and any assessment requires a thorough evaluation of confounders affecting the likelihood of ICU admission.

There are several common characteristics in the Nordic ICU response to COVID-19. The Nordic intensive care response demonstrated a coordinated effort to prepare for an excessive need for ICU services, generally employing existing centralized registries to track available ICU beds, equipment, staff and medications and distribute these on a regional level. The Nordic countries have traditionally had a culture of coordinated care, uniform within each country, emphasizing teamwork and adherence to best practice guidelines. In 2015 and 2016, the Scandinavian Society of Anaesthesia and Intensive Care (SSAI) issued evidence-based guidelines for the management of patients with ARDS.[11,32] Another advantage was the fact that Anaesthesiology and Intensive Care is a combined speciality in the Nordic countries, ensuring the availability of a pool of specialists with proper training that could be rapidly deployed to provide ICU care. This ensured that postponement of elective surgery increased the availability of a pool of specialists with proper training that could be rapidly deployed to provide ICU care. In all countries, ICUs are staffed by specialized nurses in a relatively high nurse:patient ratio (usually

between 1-2). During COVID highly qualified nurse anaesthetists who often have ICU experience could expand the pool of qualified ICU nurses. This means that a pool of clinicians could be mobilised from operating theatres with short course training to support ICU staffing.[33]

The primary strength of the study is the inclusion in all countries of all COVID-19 patients admitted to ICU, minimizing the risk of bias. Most Nordic countries used established databases that allowed prospective data collection, increasing accuracy of the registries. The major weaknesses are our inability to pool datasets to allow direct comparisons between individual patient groups, and inconsistent inclusion and definition of variables, limiting direct comparisons between the countries. This should encourage a joint effort between the Nordic countries towards unifying the design of their ICU registries. This would facilitate direct comparisons between the Nordic countries and enable a common platform for research and quality improvement projects to benchmark, audit and improve Nordic ICU care. Finally, vaccination and novel strains of SARS-CoV2 have substantially altered the dynamics of the pandemic and can impair the generalizability of the findings from this cohort onto recent and future outbreaks.

In conclusion, we report a robust but variable ICU response towards the first wave of COVID-19 in the Nordic countries. Additionally, while ICU mortality was overall low, the outcomes of ICU patients with COVID-19 in the Nordic countries varied substantially, likely reflecting differences in surge capacity and admission criteria. Future efforts should focus on unifying variable selection and definitions, to facilitate merging of existing ICU registries and allow direct comparison of the Nordic ICU population to optimize their care.

References

1. Grasselli G, Pesenti A, Cecconi M. Critical Care Utilization for the COVID-19 Outbreak in Lombardy, Italy: Early Experience and Forecast During an Emergency Response. Jama 2020; 323: 1545-46.
2. Aziz S, Arabi YM, Alhazzani W, Evans L, Citerio G, Fischkoff K, Salluh J, Meyfroidt G, Alshamsi F, Oczkowski S, Azoulay E, Price A, Burry L, Dzierba A, Benintende A, Morgan J, Grasselli G, Rhodes A, Moller MH, Chu L, Schwedhelm S, Lowe JJ, Bin D, Christian MD. Managing ICU surge during the COVID-19 crisis: rapid guidelines. Intensive Care Med 2020; 46: 1303-25.
3. Li L, Li R, Wu Z, Yang X, Zhao M, Liu J, Chen D. Therapeutic strategies for critically ill patients with COVID-19. Ann Intensive Care 2020; 10: 45.
4. Wei H, Jiang B, Behringer EC, Hofmeyr R, Myatra SN, Wong DT, Sullivan EPO, Hagberg CA, McGuire B, Baker PA, Li J, Pylypenko M, Ma W, Zuo M, Senturk NM, Klein U. Controversies in airway management of COVID-19 patients: updated information and international expert consensus recommendations. Br J Anaesth 2021; 126: 361-66.
5. Beigel JH, Tomashek KM, Dodd LE, Mehta AK, Zingman BS, Kalil AC, Hohmann E, Chu HY, Luetkemeyer A, Kline S, Lopez de Castilla D, Finberg RW, Dierberg K, Tapson V, Hsieh L, Patterson TF, Paredes R, Sweeney DA, Short WR, Touloumi G, Lye DC, Ohmagari N, Oh MD, Ruiz-Palacios GM, Benfield T, Fatkenheuer G, Kortepeter MG, Atmar RL, Creech CB, Lundgren J, Babiker AG, Pett S, Neaton JD, Burgess TH, Bonnett T, Green M, Makowski M, Osinusi A, Nayak S, Lane HC, Members A-SG. Remdesivir for the Treatment of Covid-19 - Final Report. N Engl J Med 2020; 383: 1813-26.
6. Joshi S, Parkar J, Ansari A, Vora A, Talwar D, Tiwaskar M, Patil S, Barkate H. Role of favipiravir in the treatment of COVID-19. Int J Infect Dis 2021; 102: 501-08.
7. Sanders JM, Monogue ML, Jodlowski TZ, Cutrell JB. Pharmacologic Treatments for Coronavirus Disease 2019 (COVID-19): A Review. Jama 2020; 323: 1824-36.
8. Salama C, Han J, Yau L, Reiss WG, Kramer B, Neidhart JD, Criner GJ, Kaplan-Lewis E, Baden R, Pandit L, Cameron ML, Garcia-Diaz J, Chavez V, Mekebeb-Reuter M, Lima de Menezes F, Shah R, Gonzalez-Lara MF, Assman B, Freedman J, Mohan SV. Tocilizumab in Patients Hospitalized with Covid-19 Pneumonia. N Engl J Med 2021; 384: 20-30.

9. Langer T, Brioni M, Guzzardella A, Carlesso E, Cabrini L, Castelli G, Dalla Corte F, De Robertis E, Favarato M, Forastieri A, Forlini C, Girardis M, Grieco DL, Mirabella L, Noseda V, Previtali P, Protti A, Rona R, Tardini F, Tonetti T, Zannoni F, Antonelli M, Foti G, Ranieri M, Pesenti A, Fumagalli R, Grasselli G, Group P-C. Prone position in intubated, mechanically ventilated patients with COVID-19: a multi-centric study of more than 1000 patients. Crit Care 2021; 25: 128.

10. Seitz KP, Caldwell ES, Hough CL. Fluid management in ARDS: an evaluation of current practice and the association between early diuretic use and hospital mortality. J Intensive Care 2020; 8: 78.

11. Claesson J, Freundlich M, Gunnarsson I, Laake JH, Moller MH, Vandvik PO, Varpula T, Aasmundstad TA. Scandinavian clinical practice guideline on fluid and drug therapy in adults with acute respiratory distress syndrome. Acta Anaesthesiol Scand 2016; 60: 697-709.

12. Barbaro RP, MacLaren G, Boonstra PS, Iwashyna TJ, Slutsky AS, Fan E, Bartlett RH, Tonna JE, Hyslop R, Fanning JJ, Rycus PT, Hyer SJ, Anders MM, Agerstrand CL, Hryniewicz K, Diaz R, Lorusso R, Combes A, Brodie D, Extracorporeal Life Support O. Extracorporeal membrane oxygenation support in COVID-19: an international cohort study of the Extracorporeal Life Support Organization registry. Lancet 2020; 396: 1071-78.

13. Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72314 Cases From the Chinese Center for Disease Control and Prevention. Jama 2020.

14. Grasselli G, Zangrillo A, Zanella A, Antonelli M, Cabrini L, Castelli A, Cereda D, Coluccello A, Foti G, Fumagalli R, Iotti G, Latronico N, Lorini L, Merler S, Natalini G, Piatti A, Ranieri MV, Scandroglio AM, Storti E, Cecconi M, Pesenti A, Network C-LI. Baseline Characteristics and Outcomes of 1591 Patients Infected With SARS-CoV-2 Admitted to ICUs of the Lombardy Region, Italy. Jama 2020; 323: 1574-81.

15. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, Xiang J, Wang Y, Song B, Gu X, Guan L, Wei Y, Li H, Wu X, Xu J, Tu S, Zhang Y, Chen H, Cao B. 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.

16. Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, Wu Y, Zhang L, Yu Z, Fang M, Yu T, Wang Y, Pan S, Zou X, Yuan S, Shang Y. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. Lancet Respir Med 2020.

17. Islam N, Sharp SJ, Chowell G, Shabnam S, Kawachi I, Lacey B, Massaro JM, D'Agostino RB, Sr., White M. Physical distancing interventions and incidence of coronavirus disease 2019: natural experiment in 149 countries. BMJ (Clinical research ed) 2020; 370: m2743.

18. Haase N, Plovsing R, Christensen S, Poulsen LM, Brochner AC, Rasmussen BS, Helleberg M, Jensen JUS, Andersen LPK, Siegel H, Ibsen M, Jorgensen V, Winding R, Iversen S, Pedersen HP, Madsen J, Solling C, Garcia RS, Michelsen J, Mohr T, Mannering A, Espelund US, Bundgaard H, Kirkegaard L, Smitt M, Buck DL, Ribergaard NE, Pedersen HS, Christensen BV, Perner A. Characteristics, interventions, and longer term outcomes of COVID-19 ICU patients in Denmark-A nationwide, observational study. Acta Anaesthesiol Scand 2021; 65: 68-75.

19. Kristinsson B, Kristinsdottir LB, Blondal AT, Thormar KM, Kristjansson M, Karason S, Sigvaldason K, Sigurdsson MI. Nationwide Incidence and Outcomes of Patients With Coronavirus Disease 2019 Requiring Intensive Care in Iceland. Crit Care Med 2020; 48: e1102-e05.

20. Laake JH, Buanes EA, Smastuen MC, Kvale R, Olsen BF, Rustoen T, Strand K, Sorensen V, Hofso K. Characteristics, management and survival of ICU patients with coronavirus disease-19 in Norway, March-June 2020. A prospective observational study. Acta Anaesthesiol Scand 2021; 65: 618-28.

21. Chew MS, Blixt PJ, Ahman R, Engerstrom L, Andersson H, Berggren RK, Tegnell A, McIntyre S. National outcomes and characteristics of patients admitted to Swedish intensive care units for COVID-19: A registry-based cohort study. European journal of anaesthesiology 2021; 38: 335-43.

22. Hasell J, Mathieu E, Beltekian D, Macdonald B, Giattino C, Ortiz-Ospina E, Roser M, Ritchie H. A cross-country database of COVID-19 testing. Sci Data 2020; 7: 345.

23. Iaccarino G, Grassi G, Borghi C, Carugo S, Fallo F, Ferri C, Giannattasio C, Grassi D, Letizia C, Mancusi C, Minuz P, Perlini S, Pucci G, Rizzoni D, Salvetti M, Sarzani R, Sechi L, Veglio F, Volpe M, Muiesan ML, Investigators S-R. Gender differences in predictors of intensive care units

admission among COVID-19 patients: The results of the SARS-RAS study of the Italian Society of Hypertension. PLoS One 2020; 15: e0237297.

24. Bennett KE, Mullooly M, O'Loughlin M, Fitzgerald M, O'Donnell J, O'Connor L, Oza A, Cuddihy J. Underlying conditions and risk of hospitalisation, ICU admission and mortality among those with COVID-19 in Ireland: A national surveillance study. Lancet Reg Health Eur 2021; 5: 100097.

25. Guan WJ, Liang WH, Zhao Y, Liang HR, Chen ZS, Li YM, Liu XQ, Chen RC, Tang CL, Wang T, Ou CQ, Li L, Chen PY, Sang L, Wang W, Li JF, Li CC, Ou LM, Cheng B, Xiong S, Ni ZY, Xiang J, Hu Y, Liu L, Shan H, Lei CL, Peng YX, Wei L, Liu Y, Hu YH, Peng P, Wang JM, Liu JY, Chen Z, Li G, Zheng ZJ, Qiu SQ, Luo J, Ye CJ, Zhu SY, Cheng LL, Ye F, Li SY, Zheng JP, Zhang NF, Zhong NS, He JX, China Medical Treatment Expert Group for C. Comorbidity and its impact on 1590 patients with COVID-19 in China: a nationwide analysis. Eur Respir J 2020; 55.

26. Quah P, Li A, Phua J. Mortality rates of patients with COVID-19 in the intensive care unit: a systematic review of the emerging literature. Crit Care 2020; 24: 285.

27. Butler E, Munch MW, Venkatesh B. Time for tocilizumab in COVID-19? Intensive Care Med 2021; 47: 692-94.

28. Axfors C, Schmitt AM, Janiaud P, Van't Hooft J, Abd-Elsalam S, Abdo EF, Abella BS, Akram J, Amaravadi RK, Angus DC, Arabi YM, Azhar S, Baden LR, Baker AW, Belkhir L, Benfield T, Berrevoets MAH, Chen CP, Chen TC, Cheng SH, Cheng CY, Chung WS, Cohen YZ, Cowan LN, Dalgard O, de Almeida EVFF, de Lacerda MVG, de Melo GC, Derde L, Dubee V, Elfakir A, Gordon AC, Hernandez-Cardenas CM, Hills T, Hoepelman AIM, Huang YW, Igau B, Jin R, Jurado-Camacho F, Khan KS, Kremsner PG, Kreuels B, Kuo CY, Le T, Lin YC, Lin WP, Lin TH, Lyngbakken MN, McArthur C, McVerry BJ, Meza-Meneses P, Monteiro WM, Morpeth SC, Mourad A, Mulligan MJ, Murthy S, Naggie S, Narayanasamy S, Nichol A, Novack LA, O'Brien SM, Okeke NL, Perez L, Perez-Padilla R, Perrin L, Remigio-Luna A, Rivera-Martinez NE, Rockhold FW, Rodriguez-Llamazares S, Rolfe R, Rosa R, Rosjo H, Sampaio VS, Seto TB, Shahzad M, Soliman S, Stout JE, Thirion-Romero I, Troxel AB, Tseng TY, Turner NA, Ulrich RJ, Walsh SR, Webb SA, Weehuizen JM, Velinova M, Wong HL, Wrenn R, Zampieri FG, Zhong W, Moher D, Goodman SN, Ioannidis JPA, Hemkens LG. Mortality outcomes with hydroxychloroquine and chloroquine in COVID-19 from an international collaborative meta-analysis of randomized trials. Nat Commun 2021; 12: 2349.

29. Group RC, Horby P, Lim WS, Emberson JR, Mafham M, Bell JL, Linsell L, Staplin N, Brightling C, Ustianowski A, Elmahi E, Prudon B, Green C, Felton T, Chadwick D, Rege K, Fegan C, Chappell LC, Faust SN, Jaki T, Jeffery K, Montgomery A, Rowan K, Juszczak E, Baillie JK, Haynes R, Landray MJ. Dexamethasone in Hospitalized Patients with Covid-19. N Engl J Med 2021; 384: 693-704.

30. Armstrong RA, Kane AD, Kursumovic E, Oglesby FC, Cook TM. Mortality in patients admitted to intensive care with COVID-19: an updated systematic review and meta-analysis of observational studies. Anaesthesia 2021; 76: 537-48.

31. Armstrong RA, Kane AD, Cook TM. Decreasing mortality rates in ICU during the COVID-19 pandemic. Anaesthesia 2021; 76 Suppl 3: 10.

32. Claesson J, Freundlich M, Gunnarsson I, Laake JH, Vandvik PO, Varpula T, Aasmundstad TA, Scandinavian Society of A, Intensive Care M. Scandinavian clinical practice guideline on mechanical ventilation in adults with the acute respiratory distress syndrome. Acta Anaesthesiol Scand 2015; 59: 286-97.

33. Engberg M, Bonde J, Sigurdsson ST, Moller K, Nayahangan LJ, Berntsen M, Eschen CT, Haase N, Bache S, Konge L, Russell L. Training non-intensivist doctors to work with COVID-19 patients in intensive care units. Acta Anaesthesiol Scand 2021; 65: 664-73.

Table 1 Population characteristics and overall outcomes in Nordic countries during the first wave of COVID-19.

	Denmark	**Finland**	**Iceland**	**Norway**	**Sweden**
Population January 1st 2020	5,820,000	5,525,292	364,134	5,367,580	10,327,589
Dates for data capture of ICU population	March 10th – May 19th 2020	March 16th – May 17th 2020	March 14th – May 14th 2020	March 10th – June 30th 2020	March 6th – May 6th 2020
Number of qPCR-positive **SARS-CoV**-2 **positive cases** during **data capture period**	11,044	6,244	1,660	8,389	23,177
Cases per million people (95% CI)	1898 (1862-1933)	1130 (1102-1158)	4559 (4343-4783)	1563 (1530-1597)	2244 (2215-2273)
Estimated total number of SARS-CoV2 positive cases during data capture period by antibody screening	61,000	NA	3,277	24,100	NA
Total number of deaths due to COVID-19 during data	551	323	10	250	3,332

capture period					
Case fatality rate (%) (95% CI)	5.0 (4.6-5.4) %	5.2 (4.6-5.8) %	0.6 (0.3-1.1)%	3.0 (2.6-3.4)%	14.4 (13.9-14.8)%
Infection fatality rate	0.9 (0.8-1.0) %	NA	0.3 (0.1-0.6) %	1.0 (0.9-1.1) %	NA

Table 2. List of government-imposed public health measures to control the pandemic during first-wave of COVID-19

	Denmark	Finland	Iceland	Norway	Sweden
Lockdown	Yes	Yes	No	No	No
Closure of primary schools	Yes	Yes	Partially	Partially	No
Closure of secondary schools	Yes	Yes	Yes	Partially	No
Closure of tertiary institutions	Yes	Yes	Yes	Yes	Yes
Restrictions for grocery shopping	No	No	Yes	No	No
Restrictions for public transport	Yes	Actively discouraged	Yes	Yes	Actively discouraged
Closure of public transport	No	No	No	No	No
Restricted visiting on aged care and nursing homes	Yes	Yes	Yes	Yes	Yes
Restricted visiting to hospitals and	Yes	Yes	Yes	Yes	Yes

primary care institutions					
Closure of sporting venues	Yes	Yes	Yes	Yes	Yes
Closure of non-essential services	Yes	Yes	Yes	Partially	No
Closure of non-essential workplaces	Partially	Yes	Yes	Partially	No
Furloughs	Yes	No	Yes	Yes	Yes

Table 3 Overview of ICU capacity prior to and during the first wave of COVID-19 pandemic and overview of national responses.

	Denmark	Finland	Iceland	Norway	Sweden
Number of ICU beds prior to COVID19	330	311	16	254	497
Number of ICU beds prior to COVID-19 per hundred thousand people	5.7	5.6	4.3	4.7	4.8
High-dependency / Step-down beds available prior to COVID-19	Yes	Yes	No	Yes	Yes
Number of ICU beds during COVID –19 (maximum)	430	480	39	NA	1131
Number of ICU beds during COVID-19 per hundred thousand people	7.4	8.7	10.7	NA	11.0
Inventory on ICU beds	Regional	Regional	National	Regional	National
Inventory on ICU staff	Regional	Regional	Regional	Regional	Regional
Inventory on ICU equipment	Regional	National	Regional	Regional	Regional
Inventory on essential medications	National	National	Regional	National	Regional
Distribution of ICU staff	Regional	Regional	Regional	Regional	Regional
Distribution of ICU equipment	Regional	Regional	Regional	Regional	Regional
Distribution on personal protective equipment	Regional	National	National	Regional	Regional
Distribution of essential medications	National	Regional	Regional	National	Regional

Table 4 Characteristics of patients admitted to Nordic ICUs for COVID-19 during the first wave.

	Denmark	**Finland**	**Iceland**	**Norway**	**Sweden**
Number of patients admitted to the ICU	323	192	27	224	1563
Number of patients admitted to the ICU per 30 day period per hundred thousand people	2.3	1.6	3.6	1.1	7.4
Ratio of patients admitted to the ICU per diagnosed case	2.9 (2.6-3.3)%	3.1 (2.7-3.5)%	1.6 (1.1-2.4)%	2.7 (2.3-3.0)%	6.7 (6.4-7.1)%
Age groups					
Under 50	38 (12%)	42 (22%)	3 (11%)	39 (17%)	313 (20%)
50-59	52 (16%)	63 (33%)	5 (19%)	52 (23%)	416 (27%)
60-69	82 (25%)	48 (25%)	13 (48%)	66 (30%)	479 (31%)
70-79	115 (36%)	35 (18%)	5 (19%)	52 (23%)	302 (19%)
80 and over	36 (11%)	4 (2%)	1 (4%)	15 (7%)	53 (3%)
65 and over	199 (62%)	56 (29%)	13 (48%)	98 (44%)	590 (38%)
Female gender	84 (26%)	65 (34%)	9 (33%)	56 (25%)	395 (25%)
Comorbidities					
Hypertension	160 (50%)	91 (47.4%)	12 (44%)	a)	609 (39%)
Chronic heart disease	47 (15%)	16 (8.3%)	1(4%)	89 (40%)	185 (12%)
Chronic lung disease	63 (20%)	45 (23%)	8 (29%)	17 (8%)	228 (15%)
Diabetes mellitus	68 (21%)	70 (37%)	5 (19%)	45 (20%)	385 (25%)
Chronic renal disease	39 (12%)	2 (1%)	1 (4%)	18 (8%)	64 (4%)
Chronic hepatic disease	3 (1%)	2 (1%)	0 (0%)	NA	14 (1%)
Immunosuppression	34 (11%)	8 (4%)	1 (4%)	16 (7%)	809 (6%)
Obesity (BMI>30)	91 (31%)	95 (50%)	18 (67%)	35 (16%)	NA

Days from symptom onset to ICU admission median[IQR]	9 [7-13]	9 [7-11]	9 [8-12.5]	NA	10 [7-13]
Days in hospital prior to ICU admission median[IQR]	2 [1-4]	1 [0-2]	1 [0-2]	2[2-4]	2 [1-4]
Grading of respiratory failure					
Mild (PaO_2/FiO_2 ratio>26.7 kPa)	NA	12 (8%)	2 (7%)	16 (9%) [b]	87 (7%)
Moderate (PaO2/FiO2 ratio 13.3-26.7 kPa)	NA	86 (53%)	9 (33%)	108(62%) [b]	535 (43%)
Severe (PaO2/FiO2 ratio:< 13.3 kPa)	NA	64 (40%)	16 (59%)	49 (28%) [b]	623 (50%)
Grading of disease severity on admission					
SAPS II / SAPS III Median [IQR]	NA	30 (22-38) (SAPSII)	25 [21.5-31.5] (SAPS III)	35[27.2-43] (SAPS II)	53 [46-59] (SAPS III)
APACHE II Median [IQR]	NA	17 [14-21]	14 [12-17]	NA	NA

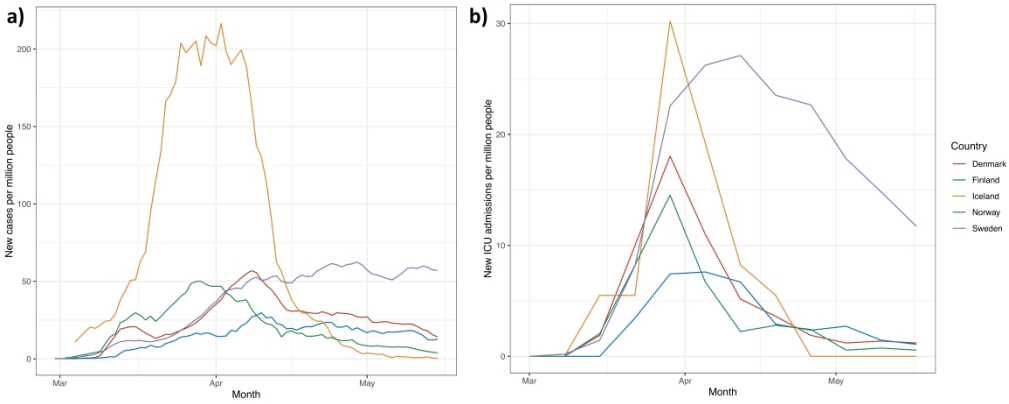
[a] Included in chronic heart disease. [b] only amongst ventilated patients. For individual variables in individual countries, percentages do not reflect all treated individuals since the individuals with missing data were omitted. NA – not available, IQR-interquartile range.

Table 5. Overview of the ICU management and outcomes of patients admitted to Nordic ICUs for COVID-19 during the first wave.

	Denmark	**Finland**	**Iceland**	**Norway**	**Sweden**
Invasive mechanical ventilation, N (%)	265 (82%)	127 (66%)	16 (59%)	190 (85%)	1222 (81%)
Days on mechanical ventilation, median [IQR]	13 [7-21]	8 [1.75-15]	10 [4-13]	12 [8-21]	12 [7-20]
Prone positioning, N (%)	NA	73 (38%)	13 (48%)	85 (38%)	603 (40%)
ECMO,N (%)	25 (8%)	2 (1%)	0 (0%)	2(0.9%)	<20 (<1%)
Potential antiviral therapy (oseltamivir, remdesivir, favipiravir), N (%)	NA	49 (25.5%)	0 (0%)	51(23%)	348 (22.3%)
Hydroxychloroquine/Chloroquine, N (%)	NA	0 (0%)	23 (85%)	NA	310 (20%)
IL-6 antagonists, N (%)	NA	0 (0%)	14 (52%)	NA	28 (2%)
Steroids, N (%)	NA	27 (14%)	2 (7%)	NA	27 (2%)
Acute kidney injury (KDIGO AKI stage1)	NA	NA	5 (19%)	72 (32%)[a]	116 (47%)
CRRT	84 (26%)	19 (10%)	2 (7%)	30 (13%)	271 (18%)
Number of days in ICU median [IQR]	13 [6-22]	12 [5-19]	10 [3-14.5]	14 [7-23]	12 [5-21]
Number of days in hospital median [IQR]	20 (11-32)	18 [13-27]	18 [11-35]	22 [15-35]	NA
Mortality					
ICU	108 (33%)	25 (13%)	3 (11%)	40(18%)	361 (23%)
Hospital	118 (37%)	31 (16%)	5 (19%)	46(21%)	NA
28-day	93 (29%)	NA	5 (19%)	NA	NA
30-day	98 (30%)	NA	5 (19%)	40(18%)	417 (27%)
90-day	118 (37%)	NA	5 (19%)	47(21%)	NA

[a)] Based on acute kidney injury by SAPSII definition. For individual variables in individual countries, percentages do not reflect all treated individuals since the individuals with missing data were omitted. NA – not available, IQR- interquartile range. ECMO – extracorporeal membrane oxygenation, KDIGO – Kidney Disease Improving Global Outcomes, AKI – acute Kidney Injury. CRRT – continuous renal replacement therapy

Figure 1 – Number of new individuals (a) diagnosed and b) admitted to the ICU per million people diagnosed with COVID-19 between March 1st – May 16th 2021 in the five Nordic countries. Note that both figures are very dependent on the testing strategy in the early phase of the pandemic.



aas_13983_f1.jpg