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Original article

Length of hospital stay and risk of intensive care admission and in-hospital death among COVID-19 patients in Norway: a register-based cohort study comparing patients fully vaccinated with an mRNA vaccine to unvaccinated patients

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ABSTRACT

Objectives: We estimated the length of stay (LoS) in hospital and the intensive care unit (ICU) and risk of admission to ICU and in-hospital death among COVID-19 patients ≥18 years in Norway who had been fully vaccinated with an mRNA vaccine (at least two doses or one dose and previous SARS-CoV-2 infection), compared to unvaccinated patients.

Methods: Using national registry data, we analyzed SARS-CoV-2–positive patients hospitalized in Norway between 1 February and 30 November 2021, with COVID-19 as the main cause of hospitalization. We ran Cox proportional hazards models adjusting for vaccination status, age, sex, county of residence, regional health authority, date of admission, country of birth, virus variant, and underlying risk factors.

Results: We included 716 fully vaccinated patients (crude overall median LoS: 5.2 days; admitted to ICU: 103 (14%); in-hospital death: 86 (13%)) and 2487 unvaccinated patients (crude overall median LoS: 5.0 days; admitted to ICU: 480 (19%); in-hospital death: 102 (4%)). In adjusted models, fully vaccinated patients had a shorter overall LoS in hospital (adjusted log hazard ratios (aHR) for discharge: 1.61, 95% CI: 1.24–2.08), shorter LoS without ICU (aHR: 1.27, 95% CI: 1.07–1.52), and lower risk of ICU admission (aHR: 0.50, 95% CI: 0.37–0.69) compared to unvaccinated patients. We observed no difference in the LoS in ICU or in risk of in-hospital death between fully vaccinated and unvaccinated patients.

Discussion: Fully vaccinated patients hospitalized with COVID-19 in Norway have a shorter LoS and lower risk of ICU admission than unvaccinated patients. These findings can support patient management and ongoing capacity planning in hospitals. **Robert Whittaker, Clin Microbiol Infect 2022;28:871**

Introduction

COVID-19 vaccination programmes have drastically reduced the burden of COVID-19–related hospitalizations and deaths [1–5]. However, the risk of breakthrough cases of severe COVID-19 after vaccination remains, particularly among groups at higher risk of severe disease [6,7].

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Norway (population 5.4 million) started COVID-19 vaccination in December 2020, initially focusing on individuals ≥65 years of age, health care workers, and individuals at increased risk of severe COVID-19 [8]. The mRNA vaccines Comirnaty (BioNTech-Pfizer, Mainz, Germany/New York, NY) and Spikevax (mRNA-1273, Moderna, Cambridge, MA) are the two predominant vaccines administered [9]. National second dose coverage among those ≥18 years of age reached 87% by 30 November 2021. Persons with specific immunosuppressive conditions were offered a third dose as part of the primary series from September 2021 [10]. Booster doses have been offered to persons ≥65 years of age and care home residents since October and health care workers since November 2021 [11].

With high national vaccination coverage, an increasing number and proportion of COVID-19–related hospitalizations are occurring among vaccinated patients, characterized by advanced age and underlying comorbidities that increase the risk of severe COVID-19 [8,12]. It is therefore essential to understand how vaccination may affect clinical endpoints among hospitalized COVID-19 patients to support patient management and capacity planning in hospitals. Published data on this are currently limited [13,14].

We linked individual-level data from national registries to estimate the length of stay (LoS) in hospital (with and without intensive care unit (ICU) stay) and ICU and the risk of ICU admission and in-hospital death among COVID-19 patients aged ≥18 years in Norway who had been fully vaccinated with an mRNA vaccine, compared to unvaccinated patients.

Methods

Patient cohort

We conducted a cohort study on patients aged ≥18 years hospitalized between 1 February and 30 November 2021 who had a national identity number registered. We included patients hospitalized ≤2 days before and ≤28 days after a positive SARS-CoV-2 test, where COVID-19 was the reported main cause of hospitalization. Patients hospitalized with other or unknown main cause were excluded. We did not restrict admissions by LoS. Initially, the Alpha variant was the predominant circulating variant, before being superseded by Delta in early July [15].

Data sources

We obtained data from the Norwegian national emergency preparedness registry for COVID-19 [16]. This registry contains individual-level data on all laboratory-confirmed COVID-19 cases, COVID-19 related hospitalizations and ICU admissions, and COVID-19 vaccinations among Norwegian residents. Further details are presented in supplementary materials A, part 1. We extracted data from the preparedness registry on 14 December 2021, ensuring a minimum 13 days follow-up since last date of hospitalization.

Definition of COVID-19 vaccination status

Vaccination status was defined on the date of positive SARS-CoV-2 test:

1. Unvaccinated: Not vaccinated with a COVID-19 vaccine.
2. Fully vaccinated: Positive test ≥7 days after second dose with at least the absolute minimum interval between doses depending on vaccine type [17], or ≥7 days after first dose if previously diagnosed with a SARS-CoV-2 infection ≥21 days before vaccination.

We excluded patients vaccinated with only one dose, those who had received a second dose <7 days before positive test, and patients vaccinated with a non-mRNA vaccine only. We also excluded unvaccinated patients with reported SARS-CoV-2 reinfections.

Outcome measures

Our outcomes were discharge from hospital (with and without ICU admission), admission to ICU, discharge from ICU, and in-hospital death. We calculated LoS as the time between first admission and last discharge. For patients with >1 registered hospital stay, we included the time between consecutive stays if < 24 hours. For LoS in ICU, we included the time between consecutive stays if < 12 hours. Separate stays were registered if a patient was discharged and readmitted, or transferred between wards or hospitals. Patients with unknown date of discharge from their last stay were considered to still be hospitalized. In-hospital death was registered at discharge.

Data analysis

Explanatory variables to analyze differences in our outcomes were vaccination status, age, sex, county of residence, regional health authority, date of admission, country of birth, virus variant, and underlying risk factors (Table 1).

Outcomes were explored univariably in a Cox proportional hazards model and by calculating Kaplan-Meier curves, with right censoring of patients still admitted to hospital. Crude log hazard ratios with medians and interquartile ranges (IQR) for LoS were obtained. Explanatory variables with $p < 0.2$ were further explored in multivariable models. Forward model selection was performed based on the Akaike information criterion. Only variables with a correlation of <0.5 were used in the same model. Vaccination status was maintained in all models regardless of significance. Continuous variables (date of admission and age) were tested as linear, spline, or categorical. The multivariable model was checked for the assumption of proportional hazards by checking Schoenfeld residuals, and some explanatory variables were stratified to satisfy the assumption. We also checked for interactions between variables included in multivariable models. Adjusted log hazard ratios (aHRs) obtained in the multivariable models were reported. For LoS outcomes, because hazard rates are not explicitly estimated in Cox regression, we also estimated a proxy for the expected difference in LoS as $1 - (1/\text{aHR})$ by assuming an exponential survival distribution [18]. The fit of LoS outcomes to an exponential distribution is presented in supplementary materials A, part 2.

We ran models on all patients and the following age subgroups: 18–64, 65–79, and ≥80 years. Patients vaccinated with three doses were not analysed separately due to small numbers. LoS in ICU was not analyzed by age subgroup due to the small number of vaccinated ICU patients in each subgroup (≤50).

We also conducted sensitivity analyses by changing the definition of our study population, study period, or outcome definitions (supplementary materials A, part 3). The statistical analysis was performed in R version 3.6.2.

Ethics

Ethical approval for this study was granted by Regional Committees for Medical Research Ethics, South East Norway, reference number 249509. The need for informed consent was waived.

Table 1
Characteristics of SARS-CoV-2–positive patients aged ≥18 years hospitalized with COVID-19 as the main cause of hospitalization, by vaccination status (Norway, 1 February–30 November 2021)

Characteristics	Vaccination status		p value
	Unvaccinated ($n = 2487$)	Fully vaccinated ($n = 716$)	
Sex, *n* (%)			
Male	1472 (59.2%)	414 (57.8%)	0.531
Female	1015 (40.8%)	302 (42.2%)	
Age group, *n* (%)			
18–29 y	157 (6.3%)	6 (0.8%)	<0.001
30–44 y	640 (25.7%)	32 (4.5%)	
45–54 y	645 (25.9%)	49 (6.8%)	
55–64 y	510 (20.5%)	93 (13.0%)	
65–79 y	453 (18.2%)	260 (36.3%)	
≥80 y	82 (3.3%)	276 (38.5%)	
Age (y), median (IQR)	51 (41–62)	76 (64–83)	<0.001
Born in Norway, *n* (%)			
Yes, with at least one parent born in Norway	1037 (41.7%)	546 (76.3%)	<0.001
Yes, two parents born outside of Norway	62 (2.5%)	4 (0.6%)	
No	1311 (52.7%)	113 (15.8%)	
Unknown	77 (3.1%)	53 (7.4%)	
Underlying risk factors, *n* (%)			
Asthma	272 (10.9%)	74 (10.3%)	<0.001
Cancer[a]	63 (2.5%)	93 (13.0%)	
Chronic lung disease, excluding asthma	134 (5.4%)	143 (20.0%)	
Chronic neurological or neuromuscular disease	88 (3.5%)	60 (8.4%)	
Diabetes (type 1 and 2)	352 (14.2%)	166 (23.2%)	
Heart disease, including hypertension	659 (26.5%)	433 (60.5%)	
Immunosuppression, including HIV and immunosuppressive treatment[b]	63 (2.5%)	96 (13.4%)	
Kidney disease, including kidney failure	73 (2.9%)	126 (17.6%)	
Liver disease, including liver failure	24 (1.0%)	13 (1.8%)	
BMI ≥30 kg/m^2 [c]	585 (23.5%)	104 (14.5%)	
Pregnant	66 (2.7%)	1 (0.1%)	
Current smoker	104 (4.2%)	25 (3.5%)	
Virus variant, *n* (%)			
Alpha	1038 (41.7%)	12 (1.7%)	<0.001
Beta	22 (0.9%)	1 (0.1%)	
Delta	375 (15.1%)	341 (47.6%)	
Non-VOC	70 (2.8%)	3 (0.4%)	
Uncategorized[d]	58 (2.3%)	2 (0.3%)	
Unknown	924 (37.2%)	357 (49.9%)	
Month of admission, *n* (%)			
February	197 (7.9%)	0 (0.0%)	<0.001
March	733 (29.5%)	6 (0.8%)	
April	560 (22.5%)	9 (1.3%)	
May	201 (8.1%)	3 (0.4%)	
June	97 (3.9%)	4 (0.6%)	
July	48 (1.9%)	11 (1.5%)	
August	113 (4.5%)	44 (6.1%)	
September	161 (6.5%)	105 (14.6%)	
October	121 (4.9%)	167 (23.3%)	
November	256 (10.3%)	367 (51.3%)	
Regional health authority, *n* (%)			
South-East	146 (5.9%)	86 (12.0%)	<0.001
West	142 (5.7%)	90 (12.6%)	
Mid	1919 (77.2%)	457 (63.8%)	
North	280 (11.3%)	83 (11.6%)	
Admission to ICU, *n* (%)			
No	2007 (80.7%)	613 (85.6%)	0.003

(*continued on next page*)

Table 1 (*continued*)

Characteristics	Vaccination status		p value
	Unvaccinated ($n = 2487$)	Fully vaccinated ($n = 716$)	
Yes	480 (19.3%)	103 (14.4%)	
Death, *n* (%)[e]			<0.001
Died in ICU	67 (2.7%)	30 (4.4%)	
Died in hospital, not in ICU	35 (1.4%)	56 (8.2%)	
Alive at discharge	2346 (95.8%)	594 (87.4%)	
In ICU	18 (0.7%)	15 (2.1%)	<0.001
Patients still in hospital at end of follow-up (13 December 2021), *n* (%)			
In hospital, not in ICU	21 (0.8%)	21 (2.9%)	
Discharged from hospital	2448 (98.4%)	680 (95.0%)	

P values compared to unvaccinated calculated using χ^2 tests or Wilcoxon rank sum tests as appropriate. P values for underlying risk factors based on proportion having any one of the listed risk factors. Equivalent descriptive data per age subgroup are available in supplementary materials B. BMI, body mass index; ICU, intensive care unit; IQR, interquartile range; VOC, variant of concern.

[a] Refers to patients with cancer undergoing treatment or with regular controls (>1 per year).

[b] Includes ongoing use of steroids in doses equivalent to at least 5 mg prednisolone daily.

[c] In our dataset, 1270 patients (40%) had unknown information on height and weight and thus unknown data on BMI. Of these 1270, 962 were unvaccinated (39% of all unvaccinated) and 308 fully vaccinated (43%). In our models, BMI was therefore included as a three-level categorical variable: yes, no, and unknown.

[d] Cases for which VOC and non-VOC could not clearly be distinguished based on the available information. This does not potentially include cases of the Omicron VOC, which was not detected in any patients in our study cohort.

[e] Excludes patients still in hospital at end of follow-up.

Results

Description of cohort

During the study period, 3541 reported cases of COVID-19 were hospitalized with COVID-19 as the main cause of hospitalization ≤2 days before and ≤28 days after a positive SARS-CoV-2 test. Of these, 3476 (98%) had a national identity number registered. We excluded 262 patients vaccinated with only one dose or a second dose <7 days before positive test, four patients vaccinated with non-mRNA vaccines, one patient with unknown vaccine type, and two unvaccinated patients who had a reported SARS-CoV-2 reinfection. We also dropped four patients with a reported stay in ICU outside of their hospital stay, assuming incomplete reporting on hospital stays. Our study cohort included the remaining 3203 patients.

The median time from positive test to hospitalization was 5 days (IQR 1–8), and 3157 (99%) patients were admitted within 14 days of a positive test. In total, 583 (18%) patients were admitted to the ICU. At the end of follow-up, 75 (2.3%) patients were still hospitalized. Of the 3128 discharged patients, 188 (6.0%) died in hospital. In total, 716 (22%) patients were fully vaccinated, of whom 666 (93%) had received two doses, 47 (6.6%) three doses, and three (0.4%) one dose with a previous SARS-CoV-2 infection. Most patients (658, 92%) received a homologous Comirnaty regimen. A breakdown of vaccine types and time between doses is presented in supplementary materials A, part 4. The median time from last dose to diagnosis was 174 days (IQR: 126–217). Age and the frequency of certain underlying risk factors such as cancer, chronic lung disease, heart disease, immunosuppression (due to illness or treatment), and kidney disease were higher among fully vaccinated patients. Detailed characteristics of the study cohort by vaccination status are presented in Table 1. Equivalent descriptive data per age subgroup are available in supplementary materials B.

Length of stay in hospital and intensive care and risk of admission to intensive care and in-hospital death by vaccination status

Descriptive data and crude and adjusted hazard ratios for each outcome by age subgroup and vaccination status are presented in Tables 2 and 3 and Fig. 1. Estimates from all univariable and multivariable models in the main analysis are presented in supplementary materials Band C.

Our multivariable models suggested that fully vaccinated patients ≥18 years had a shorter overall LoS in hospital (aHR for discharge: 1.61, 95% CI: 1.24–2.08) and shorter LoS without ICU admission (aHR: 1.28, 95% CI: 1.07–1.52) compared to unvaccinated patients. Assuming exponential distribution, an aHR of 1.61 translates into an expected 38% (95% CI: 19%–52%) shorter LoS. Fully vaccinated patients also had a 50% lower risk of ICU admission (aHR: 0.50, 95% CI: 0.37–0.69) compared to unvaccinated patients. We did not observe a difference in the LoS in ICU (aHR: 1.03, 95% CI: 0.80–1.31) or risk of in-hospital death (aHR: 1.00, 95% CI: 0.54–1.85) between vaccinated and unvaccinated patients (Fig. 1, Table 3).

By age subgroup, fully vaccinated patients aged 18–64 years had an expected 48% (95% CI: 27%–62%) shorter overall LoS (aHR: 1.91, 95% CI: 1.37–2.66), 32% (95% CI: 10%–48%) shorter LoS without ICU admission (aHR: 1.46, 95% CI: 1.11–1.91), and 47% lower risk of ICU admission (aHR: 0.53, 95% CI: 0.32–0.88), compared to unvaccinated individuals. Fully vaccinated patients aged 65–79 years had an expected 22% (95% CI: 9%–34%) shorter overall LoS (aHR: 1.29, 95% CI: 1.10–1.52) and 36% lower risk of ICU admission (aHR: 0.64, 95% CI: 0.46–0.89) compared to unvaccinated patients. There was no difference in the adjusted risk of in-hospital death between vaccinated and unvaccinated patients in any age subgroup. We did

Table 2
Number of patients, median number of days from admission to discharge from hospital or ICU, admissions to ICU and deaths in hospital, and SARS-CoV-2–positive patients aged ≥18 years hospitalized with COVID-19 as the main cause of hospitalization (by vaccination status and age group, Norway, 1 February–30 November 2021)

Age group	Patients, *n*	Time from admission to discharge from hospital (d), median (IQR)[a]	Time from admission to discharge for patients not admitted to ICU (d), median (IQR)[a]	Patients admitted to ICU, *n* (%)	Time from admission to discharge from ICU (d), median (IQR)[a,b]	Deaths in hospital, *n* (%)[c]
Unvaccinated						
18–64 y	1952	4.8 (2.5–8.7)	3.9 (2.0–6.5)	343 (18%)	—	38 (2.0%)
65–79 y	453	7.1 (3.8–14.2)	5.0 (3.0–8.7)	131 (29%)	—	47 (11%)
≥80 y	82	5.6 (2.9–8.0)	5.4 (2.9–7.1)	6 (7.3%)	—	17 (21%)
≥18 y	2487	5.0 (2.7–9.6)	4.0 (2.1–6.8)	480 (19%)	9.9 (5.3–18.0)	102 (4.2%)
Fully vaccinated						
18–64 y	180	4.1 (2.0–10.6)	3.4 (1.6–6.5)	35 (19%)	—	9 (5.4%)
65–79 y	260	7.0 (3.3–12.4)	5.9 (2.8–9.2)	50 (19%)	—	33 (14%)
≥80 y	276	4.7 (2.2–9.1)	4.1 (2.1–8.1)	18 (6.5%)	—	61 (16%)
≥18 y	716	5.2 (2.6–10.5)	4.2 (2.1–8.1)	103 (14%)	9.9 (4.1–17.7)	86 (13%)

ICU, intensive care unit; IQR, interquartile range.
[a] Estimates from univariable Cox regression; see supplementary materials B.
[b] Median number of days from admission to discharge from ICU not presented for age subgroups due to the small number of fully vaccinated patients admitted to ICU in each age subgroup (≤50).
[c] Proportions calculated excluding those still admitted at the end of the study period. For 18–64 years: 25 unvaccinated, 12 fully vaccinated; 65–79 years: 13 unvaccinated, 17 fully vaccinated; ≥80 years: 1 unvaccinated, 7 fully vaccinated.

Table 3
Crude and adjusted hazard ratios for discharge from hospital with and without stay in ICU, ICU admission, discharge from ICU, and in-hospital death from a Cox proportional hazards model (SARS-CoV-2–positive patients aged ≥18 years hospitalized with COVID-19 as the main cause of hospitalization, by age group, Norway, 1 February–30 November 2021)

	Discharge from hospital		Discharge from hospital, patients not admitted to ICU		ICU admission		Discharge from ICU		Death in hospital	
Age group	Crude hazard ratio compared to unvaccinated (95% CI)	Adjusted[a] hazard ratio compared to unvaccinated (95% CI)	Crude hazard ratio compared to unvaccinated (95% CI)	Adjusted[a] hazard ratio compared to unvaccinated (95% CI)	Crude hazard ratio compared to unvaccinated (95% CI)	Adjusted[a] hazard ratio compared to unvaccinated (95% CI)	Crude hazard ratio compared to unvaccinated (95% CI)[b]	Adjusted[a,b] hazard ratio compared to unvaccinated (95% CI)	Crude hazard ratio compared to unvaccinated (95% CI)	Adjusted[a] hazard ratio compared to unvaccinated (95% CI)
18–64 y	0.913 (0.779–1.069)	**1.909 (1.372–2.658)**[c]	0.962 (0.811–1.142)	**1.455 (1.106–1.914)**[c]	1.137 (0.803–1.610)	**0.530 (0.319–0.882)**[c]	-	—	**2.177 (1.050–4.516)**[c]	1.351 (0.636–2.871)
65–79 y	**1.173 (1.001–1.375)**[c]	**1.287 (1.092–1.517)**[c]	0.866 (0.725–1.034)	1.218 (0.939–1.580)	**0.627 (0.453–0.869)**[c]	**0.639 (0.461–0.886)**[c]	-	—	**1.687 (1.074–2.651)**[c]	1.427 (0.892–2.284)
≥80 y	1.117 (0.869–1.434)	1.080 (0.839–1.389)	1.043 (0.806–1.349)	0.996 (0.769–1.290)	0.953 (0.378–2.403)	0.910 (0.361–2.295)	—	—	0.829 (0.473–1.453)	0.765 (0.436–1.340)
≥18 y	0.981 (0.901–1.068)	**1.607 (1.243–2.077)**[c]	**0.785 (0.716–0.861)**[c]	**1.272 (1.068–1.516)**[c]	**0.689 (0.556–0.852)**[c]	**0.503 (0.368–0.689)**[c]	1.027 (0.817–1.292)	1.025 (0.803–1.308)	**3.229 (2.417–4.315)**[c]	0.995 (0.536–1.847)

ICU, intensive care unit.
[a] Adjusted for age, sex, county of residence, regional health authority, date of admission, country of birth, virus variant, and underlying risk factors (Table 1). The variables included in the final multivariable models were obtained by forward model selection based on the Akaike information criterion (see supplementary materials C).
[b] Not analyzed for age subgroups due to the small number of fully vaccinated patients admitted to ICU in each age subgroup (≤50).
[c] Statistically significant results.

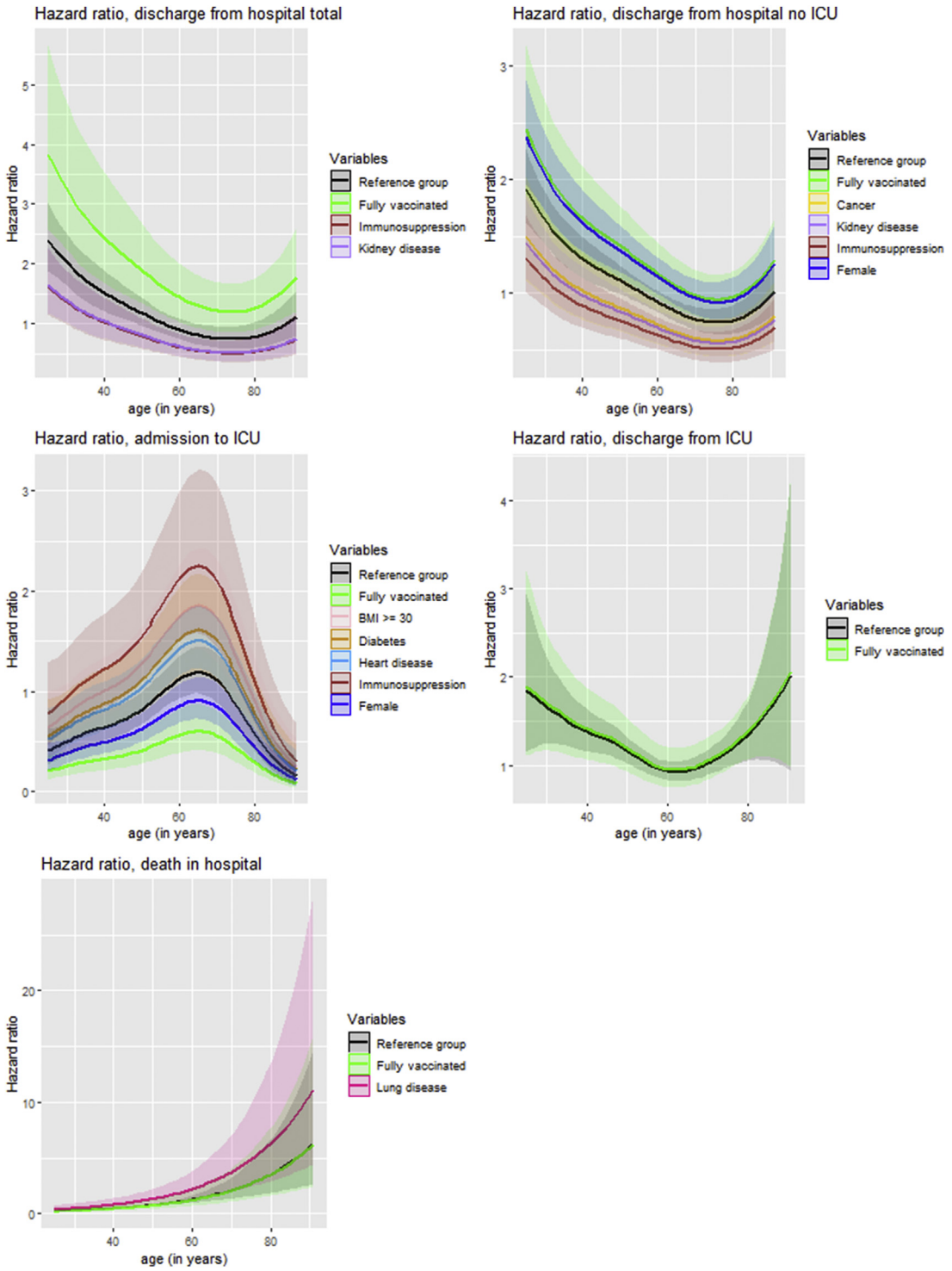

Fig. 1. Adjusted hazard ratios for discharge from hospital with and without stay in ICU, ICU admission, discharge from ICU, and in-hospital death from a Cox proportional hazards model for SARS-CoV-2 positive patients aged ≥18 years hospitalized with COVID-19 as the main cause of hospitalization, by age (Norway, 1 February–30 November 2021). The reference group with a hazard ratio = 1 is patients who are male, aged 56 years (median age in dataset), AND without underlying risk factors and unvaccinated. Hazard ratios were calculated using a Cox proportional hazards model. The variables shown in each panel are those significantly associated with each outcome in multivariable models, which were not stratified on (see supplementary materials C). The Akaike information criterion was used to determine whether age was included linearly or with a spline. ICU, intensive care unit.

not observe a difference between vaccinated and unvaccinated patients aged ≥80 years in adjusted estimates for any outcome.

Results were generally robust in our sensitivity analyses, including when analyzing a period after which all persons in different age subgroups had been offered two vaccine doses (supplementary materials A, part 3).

Discussion

In this study, we find that fully vaccinated patients with COVID-19 in Norway had a shorter LoS in hospital (both with and without ICU admission) and lower risk of ICU admission compared to unvaccinated patients. There was no difference in the LoS in ICU or

risk of in-hospital death. In line with other reports [7,13,14,19], vaccinated patients were generally older and had a higher prevalence of underlying risk factors than unvaccinated patients.

Our results suggest that, once hospitalized, the risk of death among fully vaccinated and unvaccinated patients in Norway is similar. However, for survivors the disease trajectory is milder in fully vaccinated patients, with reduced need for hospital care and organ support. For patients not admitted to ICU, the observed reduction in LoS may have been attenuated by vaccinated patients, who may have ended up in ICU if unvaccinated but now instead spend more time in regular wards.

In our subgroup analyses, patients aged 18–64 years appeared to have larger relative reductions in LoS and risk of ICU admission, although CIs overlapped with estimates for patients aged 65–79 years, and we did not observe an interaction between age and vaccination status in our model for patients aged ≥18 years. Analyses of larger cohorts may better discern if there are differences in the effect of vaccination status on these outcomes by age. For all outcomes, we observed no difference between vaccinated and unvaccinated patients aged ≥80 years. Vaccine effectiveness against hospitalization has been reported to be lower among older age groups in Norway [20]. This age group is also less frequently admitted to ICU, and treatment limitations could confound vaccine effects in the elderly. The small number of unvaccinated patients aged ≥80 years should also be considered. Our results also highlight that factors other than vaccination continue to influence patient outcomes. A longer LoS and/or increased risk of ICU admission or death were associated with advanced age, male sex, and certain risk factors such as immunosuppression, kidney disease, obesity and diabetes, as reported by others [21–24].

These findings build on previous evidence of high vaccine effectiveness against severe disease [1–5,20] and have important implications for patient management and ongoing capacity planning in hospitals. A study including 142 patients fully vaccinated with an mRNA vaccine from 21 sites across the United States also reported a shorter LoS, lower risk of death or invasive mechanical ventilation, and a lower level of clinical disease severity among vaccinated patients [13]. In contrast, a study from Michigan did not find a lower risk of ICU admission, mechanical ventilation, or death when comparing 129 fully vaccinated patients (vaccinated with Comirnaty, Spikevax, or Janssen) to unvaccinated patients [14]. Differences in the study cohorts, setting, and design need to be considered. In this study we compare fully vaccinated and unvaccinated patients; however, vaccination programmes are continuing to evolve, and future analyses are necessary to explore how parameters such as vaccine type, number of doses, time since vaccination, and dose intervals affect patient outcomes between groups of vaccinated patients. Although studies have suggested sustained high effectiveness of mRNA vaccines against hospitalization at least 6 months after vaccination [25,26], the duration of protection after the original two-dose schedules for mRNA vaccines and the effects of booster doses [27,28] require ongoing research.

A strength of our study is that all data sources had national coverage. We also had a notably larger cohort of fully vaccinated patients than previous studies [13,14]. Furthermore, hospitals in Norway functioned within capacity during the study period, and criteria for hospitalization and isolation for COVID-19 patients were consistent and not related to vaccination status. Although we did not have access to treatment data, there were no major changes in treatment guidelines for COVID-19 patients in hospital or ICU in Norway during the study period. We also had minimal censoring, with 2.3% of patients still hospitalized at the end of follow-up.

Our study also has limitations. Although we have controlled for several important confounders, the observational nature has the potential for residual confounding. In addition, our estimated proportional decrease in LoS among fully vaccinated patients is likely slightly underestimated for some age groups and LoS outcomes, as ≤5% of patients did not follow an exponential distribution (see supplementary materials A, part 2). Our fully vaccinated cohort is also predominantly representative of patients who received a homologous two-dose Comirnaty regimen. Moreover, some of our reported underlying risk factors do not distinguish potential differences within groups (e.g. whether risk factors are well regulated or treated). Also, 40% of patients had unknown body mass index. Our model may therefore not fully adjust for certain underlying risk factors. Furthermore, our study cohort does not include care home residents who, in Norway, are recommended to receive treatment for severe COVID-19 in their care home, not in hospital. Finally, previous natural infection has been associated with a high level of protection against SARS-CoV-2 reinfection [29,30]. Although we dropped two reported reinfections, there may have been other previously undiagnosed SARS-CoV-2 infections in our unvaccinated cohort. If present, this may underestimate the effect of vaccination.

Our study suggests that mRNA-vaccinated patients hospitalized with COVID-19 in Norway have a shorter LoS and lower risk of ICU admission than unvaccinated patients. These findings can support patient management and ongoing capacity planning in hospitals and underline the importance of vaccination programmes against COVID-19.

Transparency declaration

The authors declare that they have no competing interests. The authors received no specific funding for this work.

Author contributions

RW, ABK, BVS, ES, RK, and EAB conceived the idea for the study. RW drafted the study protocol and coordinated the study. RK and EAB contributed directly to the acquisition of data. RW and ABK contributed to data cleaning, validation, and preparation. RW and ABK led the data analysis. All co-authors contributed to the interpretation of the results. RW and ABK drafted the manuscript. All co-authors contributed to the revision of the manuscript and approved the final version for submission.

Access to data

The dataset analyzed in the study contains individual-level linked data from various central health registries, national clinical registries, and other national administrative registries in Norway. The researchers had access to the data through the national emergency preparedness registry for COVID-19 (Beredt C19), housed at the Norwegian Institute of Public Health (NIPH). In Beredt C19, only fully anonymized data (i.e. data that are neither directly nor potentially indirectly identifiable) are permitted to be shared publicly. Legal restrictions therefore prevent the researchers from publicly sharing the dataset used in the study that would enable others to replicate the study findings. However, external researchers are freely able to request access to linked data from the same registries from outside the structure of Beredt C19, as per normal procedure for conducting health research on registry data in Norway. Further information on Beredt C19, including contact information for the Beredt C19 project manager and information on access to data from each individual data source, is available at https://www.fhi.no/en/id/infectious-diseases/coronavirus/emergency-preparedness-register-for-covid-19/.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cmi.2022.01.033.

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