COVID-19 Vaccine Effectiveness Among Adolescents

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abstract

BACKGROUND: For adolescents, data on the long-term effectiveness of the BNT162b2 and mRNA-1273 vaccines against severe COVID-19 outcomes are scarce. Additionally, only a few studies have evaluated vaccine effectiveness (VE) for mRNA-1273 or heterologous mRNA vaccine schedules (ie, mixing BNT162b2 and mRNA-1273).

METHODS: Nationwide register-based 1-to-1 matched cohort analyses were conducted in Denmark, Finland, Norway, and Sweden between May 28, 2021, and April 30, 2023, to estimate VE for primary COVID-19 vaccine (2-dose) schedules among adolescents aged 12 to 17 years. Cumulative incidences of COVID-19–related hospitalization (primary outcome) and laboratory-confirmed SARS-CoV-2 infection (secondary outcome) were compared for vaccinated and unvaccinated at 6 months of follow-up using the Kaplan-Meier estimator. Country-specific VE (1-risk ratio) and risk differences (RD) were combined by random-effects meta-analyses.

RESULTS: The study included 526 966 primary schedule vaccinated adolescents. VE against COVID-19–related hospitalization was 72.6% (95% confidence interval [CI], 62.5–82.7) and RD was −2.8 (95% CI, −4.5 to −1.0) per 10 000 vaccinated for BNT162b2 at 6 months of follow-up compared with unvaccinated. The corresponding VE and RD were 86.0% (95% CI, 56.8–100.0) and −2.1 (95% CI, −4.0 to −0.2) per 10 000 vaccinated for mRNA-1273 and 80.7% (95% CI, 58.0–100.0) and −5.5 (95% CI, −15.5 to 4.6) per 10 000 vaccinated for heterologous mRNA vaccine schedules. Estimates were comparable when restricting to a period of omicron predominance and extending follow-up to 12 months.

CONCLUSIONS: Across 4 Nordic countries, severe COVID-19 in adolescents was a rare event. Compared with unvaccinated, BNT162b2, mRNA-1273, and heterologous mRNA vaccination schedules provided high protection against COVID-19–related hospitalization, including hospitalizations during the omicron period.

WHAT'S KNOWN ON THIS SUBJECT: Data on vaccine effectiveness against severe COVID-19 among adolescents aged 12 to 17 years are scarce, especially with long-term follow-up. Additionally, few studies have evaluated effectiveness for mRNA-1273 and heterologous mRNA vaccine schedules (ie, mixing BNT162b2 and mRNA-1273).

WHAT THIS STUDY ADDS: Among adolescents aged 12 to 17 years, BNT162b2, mRNA-1273, and heterologous vaccine schedules provided high protection against COVID-19 hospitalization, with vaccine effectiveness ranging between 72.6% and 86.0% at 6 months of follow-up, including COVID-19–related hospitalizations caused by omicron.

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The mRNA vaccines, BNT162b2 (Pfizer-BioNTech) and mRNA-1273 (Moderna), have been primarily used against COVID-19 among adolescents aged 12 to 17 years in the Western countries. In the Nordic countries, COVID-19 vaccinations were introduced for adolescents aged 12 years or older during the summer and autumn of 2021.[1] Both mRNA vaccines were rolled out for the adolescent populations, but mRNA-1273 vaccination was halted on October 6, 2021, for young males in Denmark, Finland, and Norway and for all individuals younger than age 30 years in Sweden because of safety concerns.[2] Initially, when the first adolescents aged 12 to 17 years were vaccinated, the δ variant was the dominant strain of SARS-CoV-2 in the Nordic countries. Subsequently, the δ variant was replaced by the *o* variant in late 2021 (initially, sublineages BA.1 and BA.2 and later BA.5), which caused an unprecedented high number of SARS-CoV-2 infections.

In randomized controlled trials conducted before the emergence of omicron, both primary schedules with the BNT162b2 and mRNA-1273 were highly effective against symptomatic SARS-CoV-2 infection among adolescents aged 12 to 15 years.[3,4] In previous observational studies, effectiveness for BNT162b2 has varied from moderate[5–7] to high[8–15] against COVID-19–related hospitalization among adolescents. However, data on long-term effectiveness against severe COVID-19 among adolescents are scarce, and, previously, signs of rapid waning has been observed following a primary schedule.[7] Additionally, studies evaluating vaccine effectiveness (VE) for mRNA-1273 or heterologous mRNA vaccine schedules (mixing BNT162b2 and mRNA-1273) among adolescents are limited.

In nationwide cohorts in Denmark, Finland, Norway, and Sweden, effectiveness for primary BNT162b2, mRNA-1273, and heterologous mRNA vaccine schedules were evaluated among adolescents aged 12 to 17 years against COVID-19–related hospitalization at 6 months after vaccination. Secondary analyses included extending follow-up to 12 months, estimating VE in a period of omicron predominance, and assessing VE against SARS-CoV-2 infection.

METHODS

Setting and Study Design

Nationwide register-based 1-to-1 matched cohort analyses were conducted in Denmark, Finland, Norway, and Sweden during a study period from May 28, 2021, to April 30, 2023, by using several national registers within each country (Supplemental Tables 3–4). Country-specific cohorts of adolescents aged 12 to 17 years without previous COVID-19–related hospitalization were constructed and adolescents who had received a COVID-19 vaccination before the study period or who were not known residents within the respective participating countries were excluded from the cohorts. The δ, and later, the omicron variants were the dominant strains of SARS-CoV-2 during the study period (Supplemental Fig 2).

A target trial was emulated similarly as in previous studies.[16–19] At the day an individual received a second COVID-19 vaccine dose (the index date), the vaccinated individual was matched with an individual who was unvaccinated at that time (Supplemental Fig 3). The day the second dose was administered within each matched pair served as the index date for both individuals. Vaccinated and unvaccinated individuals were matched on age (in years) and a propensity score taking demographic and clinical characteristics into account (see Statistical Analysis). Matched unvaccinated (at the assigned index date) that later became vaccinated were allowed to potentially reenter the cohort as vaccinated as part of an additional matched pair. BNT162b2, mRNA-1273, and heterologous mRNA vaccine schedules (ie, mixing BNT162b2 and mRNA-1273) were included in the study, whereas schedules with other COVID-19 vaccines were few and excluded.

Outcomes

The primary outcome of interest was COVID-19-related hospitalization. A COVID-19 hospitalization had to fulfill all the following criteria:

1. Inpatient hospital contact or hospital contact with a duration of at least 12 hours.
2. Hospitalization with a COVID-19–related diagnosis (Supplemental Table 4).
3. Positive SARS-CoV-2 polymerase chain reaction (PCR) test during the period starting 14 days before and ending 2 days after the date of hospital admission.

In addition, a secondary outcome of laboratory-confirmed SARS-CoV-2 infection was included, which was defined as any PCR-confirmed infection with SARS-CoV-2 (Supplemental Table 4).

Statistical Analysis

Follow-up for an individual started on day 14 after the index date and ended on the day of the outcome of interest, day 180 after start of follow-up, death, emigration, a booster COVID-19 vaccination, or end of the study period (April 30, 2023), whichever occurred first. In addition, a matched pair was censored if the unvaccinated received COVID-19 vaccination during follow-up.[18,19]

Cumulative incidences for vaccinated and unvaccinated individuals were estimated using the Kaplan-Meier estimator. VE (1 – the risk ratio) and risk difference (RD) were estimated using the cumulative incidences at day 180 since start of the follow-up with corresponding 95% confidence intervals (CI), which were calculated by the δ method. Propensity scores estimating the conditional probability of vaccination with a particular schedule given sex, region of

residency, selected comorbidities, vaccination priority group and previous SARS-CoV-2 infection status (no previous SARS-CoV-2 infection, pre-omicron infection, or omicron infection) were calculated using logistic regression (Supplemental Table 4). Secondary analyses included: (1) extending follow-up to 12 months since vaccination, (2) restricting follow-up to period of omicron variant predominance by stratification on calendar period (Supplemental Table 5), and (3) examining the effectiveness among one-dose recipients as compared with unvaccinated.

Country-specific estimates were combined by meta-analyses implemented using the mixmeta package in R. To take into account any heterogeneity in effects between countries, we used random effects meta-analyses. Country-specific estimates were weighted by the inverse of the variance of the estimate. The analyses were performed with R 4.1.2 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Cohorts of Adolescents Aged 12 to 17 Years

The study cohorts comprised 526 966 primary schedule (2-dose) vaccinated adolescents and as many 1:1 matched unvaccinated adolescents. BNT162b2 was the most common vaccine schedule (a total of 419 168 recipients) across the 4 countries (Table 1). In Finland, mRNA-1273 and heterologous mRNA vaccine schedules were more commonly used compared with the other countries. Mean age ranged from 13.9 to 16.8 years across the 4 countries. Most vaccine schedules were administered between July and November 2021 (Supplemental Figs 4–7). The prevalence of comorbidities was low in all study cohorts (Table 1).

Vaccine Effectiveness Among Adolescents in Nordic Countries

Across all the 4 Nordic countries, COVID-19–related hospitalization was a rare event among the adolescents during the follow-up. Among the study subjects, the number of COVID-19–related hospitalizations ranged during the 180-day follow-up period from <5 to 37 and from 8 to 140 among vaccinated and unvaccinated, respectively (Table 2). During follow-up, the cumulative incidences of COVID-19–related hospitalizations were higher among unvaccinated (Fig 1, Supplemental Figs 8–10). Analysis could not be conducted in Norway for COVID-19–related hospitalization because no events were observed among the vaccinated in the matched cohorts.

Primary BNT162b2, mRNA-1273, and heterologous mRNA vaccination schedule was associated with a country-combined VE against COVID-19 hospitalization of 72.6% (95% CI, 62.5–82.7), 86.0% (95% CI, 56.8–100.0), and 80.7% (95% CI, 58.0–100.0) at day 180 of follow-up, respectively (Table 2). The corresponding RDs were −2.8 (95% CI, −4.5 to −1.0), −2.1 (95% CI, −4.0 to −0.2), and −5.5 (95% CI, −15.5 to 4.6) per 10 000 person-years, respectively.

Extending follow-up to day 365 in secondary analyses showed comparable results; the country-combined VE against COVID-19 hospitalization was 65.6% (95% CI, 55.4–75.8) for BNT162b2, 91.0% (95% CI, 72.6–100.0) for mRNA-1273, and 82.5% (95% CI, 63.6–100.0) for heterologous schedules (Table 2). Restricting the analyses to a period of *o* predominance did not alter the findings (Table 2). Effectiveness estimates for 1-dose vaccination were influenced by low number of cases (Supplemental Table 6).

The day 180 country-combined VE against laboratory-confirmed SARS-CoV-2 infection was 22.2% (95% CI, 4.5–39.8) for BNT162b2, 3.6% (95% CI, −37.0 to 44.1) for mRNA-1273, and 27.8% (95% CI, −1.1 to 56.7) for heterologous vaccination (Supplemental Table 7). Findings were similar when extending follow-up to day 365 as well as when restricting to a period of omicron predominance. VE for 1-dose schedules was low (Supplemental Table 8).

DISCUSSION

In this multinational study comprising matched cohort analyses of adolescents aged 12 to 17 years in Nordic countries, BNT162b2, mRNA-1273, and heterologous schedules were associated with high protection against COVID-19–related hospitalization with VE ranging between 72.6% and 86.0% at 6 months of follow-up. Similar VE estimates were observed when extending follow-up to 12 months as well as after stratifying by the omicron period of predominance.

The findings are in line with previous studies reporting VE for BNT162b2 between 37% and 85% against COVID-19–related hospitalization among adolescents.[5–7,9–15] However, only a few studies have estimated the VE after 6 months from the primary schedule. One of these studies, conducted in Hong Kong, reported waning shortly after the primary schedule and lower levels of protection after 180 days (VE, 33.6%; 95% CI, 5.5–53.3) among children and adolescents aged 5 to 17 years.[7] However, another study from Singapore observed maintained levels of protection up to 8 months of follow-up among adolescents aged 12 to 17 years.[10] This current study with extended follow-up to 12 months indicated that the protection is sustained after 6 months. Additionally, in this study, both mRNA-1273 and heterologous mRNA vaccine schedules conferred high protection against COVID-19 hospitalization in adolescents, including in a period of omicron predominance. Currently, little research exists on the effectiveness of these schedules against severe COVID-19 among adolescents, although among adults, mRNA-1273 and heterologous mRNA vaccine schedules have provided comparable to slightly higher VE against severe COVID-19 to that of BNT162b2 vaccination.[18,20]

Estimates of COVID-19 vaccination VE should be appreciated together with the absolute reductions in cases.

TABLE 1 Descriptive Data of 2-Dose Vaccinated and Matched Unvaccinated Individuals						
	2-Dose Schedules					
	BNT162b2	**Matched**	**mRNA-1273**	**Matched**	**Heterologous**	**Matched**
No. of participants	419 168	419 168	46 321	46 321	61 477	61 477
Denmark	106 462	106 462	653	653	NA	NA
Finland	84 172	84 172	42 559	42 559	42 517	42 517
Norway	44 883	44 883	883	883	10 984	10 984
Sweden	183 651	183 651	2226	2226	7976	7976
Mean age (SD)[a]						
Denmark	14.5 (1.7)	14.4 (1.7)	14.8 (1.6)	14.8 (1.6)	NA	NA
Finland	14.9 (1.8)	14.8 (1.8)	14.1 (1.3)	14.1 (1.3)	14.3 (1.5)	14.3 (1.5)
Norway	15.5 (1.5)	15.5 (1.5)	16.8 (0.6)	16.8 (0.6)	16.7 (0.6)	16.7 (0.6)
Sweden	13.9 (1.5)	13.9 (1.5)	16.4 (0.6)	16.4 (0.6)	16.4 (0.7)	16.4 (0.7)
Female						
Denmark	49.1%	48.2%	46.1%	49.9%	NA	NA
Finland	51.3%	44.2%	70.8%	45.0%	30.8%	44.6%
Norway	50.4%	45.9%	51.5%	41.1%	49.3%	44.0%
Sweden	49.0%	47.3%	47.8%	44.9%	47.1%	44.4%
Calendar period (min-max)						
Denmark	7/1/21–4/30/23	7/1/21–4/30/23	7/27/21–1/23/23	7/27/21–11/10/22	NA	NA
Finland	10/7/21–11/22/22	7/10/21–4/30/23	8/16/21–4/30/23	8/16/21–4/30/23	7/3/21–4/30/23	7/3/21–4/30/23
Norway	7/1/21–4/30/23	7/1/21–4/30/23	7/25/21–4/30/23	7/25/21–4/30/23	7/14/21–4/30/23	7/14/21–4/30/23
Sweden	10/4/21–4/30/23	10/4/21–4/30/23	10/6/21–4/30/23	10/6/21–4/30/23	10/5/21–4/30/23	10/5/21–4/30/23
COVID-19 vaccine priority group - vulnerable individuals[b]						
Denmark	39 (0.0%)	39 (0.0%)	<5	<5	NA	NA
Finland	44 (0.1%)	93 (0.1%)	7 (0.0%)	51 (0.1%)	29 (0.1%)	49 (0.1%)
Norway	0	0	0	0	0	0
Sweden	<5	0	0	0	0	0
COVID-19 vaccine priority group – health care workers						
Denmark	275 (0.3%)	168 (0.2%)	<5	<5	NA	NA
Finland	<5	<5	0	0	0	0
Norway	510 (1.1%)	496 (1.1%)	19 (2.2%)	6 (0.7%)	202 (1.8%)	200 (1.8%)
Sweden	0	0	0	0	0	0
Autoimmune-related condition						
Denmark	1020 (1.0%)	952 (0.9%)	6 (0.9%)	8 (1.2%)	NA	NA
Finland	736 (0.9%)	553 (0.7%)	189 (0.4%)	294 (0.7%)	175 (0.4%)	288 (0.7%)
Norway	371 (0.8%)	368 (0.8%)	11 (1.2%)	8 (0.9%)	77 (0.7%)	67 (0.6%)
Sweden	925 (0.5%)	729 (0.4%)	24 (1.1%)	<5	86 (1.1%)	27 (0.3%)
Cancer						
Denmark	68 (0.1%)	75 (0.1%)	<5	0	NA	NA
Finland	147 (0.2%)	163 (0.2%)	60 (0.1%)	64 (0.2%)	81 (0.2%)	68 (0.2%)
Norway	146 (0.3%)	108 (0.2%)	0	<5	28 (0.3%)	17 (0.2%)
Sweden	144 (0.1%)	179 (0.1%)	7 (0.3%)	<5	12 (0.2%)	7 (0.1%)
Chronic pulmonary disease						
Denmark	2019 (1.9%)	1561 (1.5%)	11 (1.7%)	11 (1.7%)	NA	NA
Finland	41 (0.0%)	20 (0.0%)	10 (0.0%)	10 (0.0%)	7 (0.0%)	9 (0.0%)
Norway	3623 (8.1%)	2403 (5.4%)	56 (6.3%)	29 (3.3%)	744 (6.8%)	517 (4.7%)
Sweden	4734 (2.6%)	5071 (2.8%)	123 (5.5%)	27 (1.2%)	424 (5.3%)	85 (1.1%)
Cardiovascular condition or diabetes						
Denmark	548 (0.5%)	381 (0.4%)	<5	<5	NA	NA
Finland	1308 (1.6%)	699 (0.8%)	197 (0.5%)	345 (0.8%)	264 (0.6%)	333 (0.8%)
Norway	625 (1.4%)	442 (1.0%)	16 (1.8%)	6 (0.7%)	130 (1.2%)	94 (0.9%)
Sweden	891 (0.5%)	686 (0.4%)	19 (0.9%)	6 (0.3%)	84 (1.1%)	27 (0.3%)
Renal disease						
Denmark	143 (0.1%)	130 (0.1%)	0	<5	NA	NA

TABLE 1 Continued						
	2-Dose Schedules					
	BNT162b2	Matched	mRNA-1273	Matched	Heterologous	Matched
Finland	102 (0.1%)	85 (0.1%)	34 (0.1%)	42 (0.1%)	33 (0.1%)	43 (0.1%)
Norway	20 (0.0%)	9 (0.0%)	0	0	<5	<5
Sweden	225 (0.1%)	254 (0.1%)	7 (0.3%)	5 (0.2%)	21 (0.3%)	12 (0.2%)

NA, not available; heterologous, primary schedule (2 doses) with mix of BNT162b2 and mRNA-1273; SD, standard deviation.
[a] Age was defined by birth year in Norway and Sweden (the specific birthdates were not available in these countries). Use of mRNA-1273 was halted in Sweden for adolescents in autumn 2021.
[b] For definition, see Supplemental Table 4.

In this study, vaccination prevented approximately 3.5 to 6.2 COVID-19–related hospitalizations per 10 000 adolescents over a 12-month follow-up period. For comparison, in Finland 10-valent pneumococcal vaccine was previously estimated to prevent 27.1 (95% CI, 0.9–53.3) hospital-diagnosed pneumonia per 10 000 person-years among children aged 6 weeks to 18 months.[21] Therefore, the impact of primary vaccine schedules for COVID-19 seemed to be modest among the healthy adolescents in terms of absolute numbers.

As opposed to the COVID-19 hospitalization findings, VE against SARS-CoV-2 infection was notably lower during the 6- and 12-month follow-up periods. VE also varied widely across countries and schedules causing imprecision of the estimates. However, similar findings of lower VE against SARS-CoV-2 infection for BNT162b2 have been reported in previous studies.[1,7,9,10,13,22] Additionally, a test-negative study conducted in Argentina also reported low VE for mRNA-1273 (VE, 17.9%; 95% CI, 14.0–21.5) and the heterologous mRNA vaccine schedule (VE, 40.6%; 95% CI, 29.4–50.0 for BNT162b2 followed by mRNA-1273, and VE, 31.5%; 95% CI, 26.3–36.4 for mRNA-1273 followed by BNT162b2) among adolescents during the omicron period.[13]

This study has several strengths and limitations. The study was conducted in the 4 largest Nordic countries with similar nationwide linkable registers. These registers have a well-documented track record in the monitoring of VE and safety in all participating countries[1,2,18,19] and include data on comorbidities that might be confounders, which affect the vaccine uptake, immunogenicity, and probability of SARS-CoV-2 testing together with the probability of developing the outcomes under study. Although most comorbidity information can be obtained from the registers, some potential confounding factors, such as obesity, were not available. Therefore, and also because of the observational nature of our study, residual confounding cannot be fully excluded. Another strength is the specificity of the COVID-19–related hospitalization outcome definition. By using hospital admission data, hospitalizations resulting from COVID-19 were captured (ascertained by COVID-19–related diagnoses and concurrent positive SARS-CoV-2 PCR test) while excluding most of those admissions where SARS-CoV-2 infection was more likely to simply co-occur at time of admission (ie, hospitalized with COVID-19 such as a positive SARS-CoV-2 test sampled during routine screening while hospitalized for another cause).[23] This distinguishing is crucial as VE against hospitalizations with COVID-19 is considerably lower compared with the VE against hospitalizations because of COVID-19.[24] Still,

TABLE 2 Risk Differences and Vaccine Effectiveness for 2-Dose mRNA Vaccine Schedules against COVID-19–Related Hospitalization Among Adolescents Aged 12–17 y

	Vaccinated	Comparison	Measures of Association		
	Events/PYRS	Events/PYRS	RD (95% CI) per 10 000 individuals	VE (95% CI)	Countries Included
Main analysis (6-mo follow-up)					
BNT162b2	37/151 873.2	140/150 773.97	−2.8 (−4.5 to −1.0)	72.6% (62.5 – 82.7)	DK, FI, SE
mRNA-1273	<5/15 535.93	8/14 527.58	−2.1 (−4.0 to −0.2)	86.0% (56.8 – 100.0)	FI
Heterologous	<5/20 304.77	18/19 012.02	−5.5 (−15.5 to 4.6)	80.7% (58.0 – 100.0)	FI, SE
Restricted to period of *o* predominance (6-mo follow-up)					
BNT162b2	35/94 067.96	114/93 273.37	−2.7 (−6.1 to 0.7)	70.4% (46.3 – 94.5)	DK, FI, SE
mRNA-1273	<5/9003.56	<5/8113.45	−1.4 (−3.6 to 0.8)	80.2% (34.5 – 100.0)	FI
Heterologous	<5/14 005.29	14/12 810.11	−9.8 (−21.3 to 1.7)	85.5% (65.1 – 100.0)	FI, SE
Extended follow-up to 12 mo					
BNT162b2	59/276 854.12	182/277 968.97	−3.8 (−5.4 to −2.1)	65.6% (55.4 – 75.8)	DK, FI, SE
mRNA-1273	<5/27 613.46	11/25 610.83	−3.5 (−5.9 to −1.1)	91.0% (72.6 – 100.0)	FI
Heterologous	<5/37 716.39	22/34 680.81	−6.2 (−14.5 to 2.1)	82.5% (63.6 – 100.0)	FI, SE

CI, confidence interval; DK, Denmark; FI, Finland; heterologous, primary schedule (2 doses) with mix of BNT162b2 and mRNA-1273; NO, Norway; PYRS, person-years; RD, risk difference; SE, Sweden; VE, vaccine effectiveness.

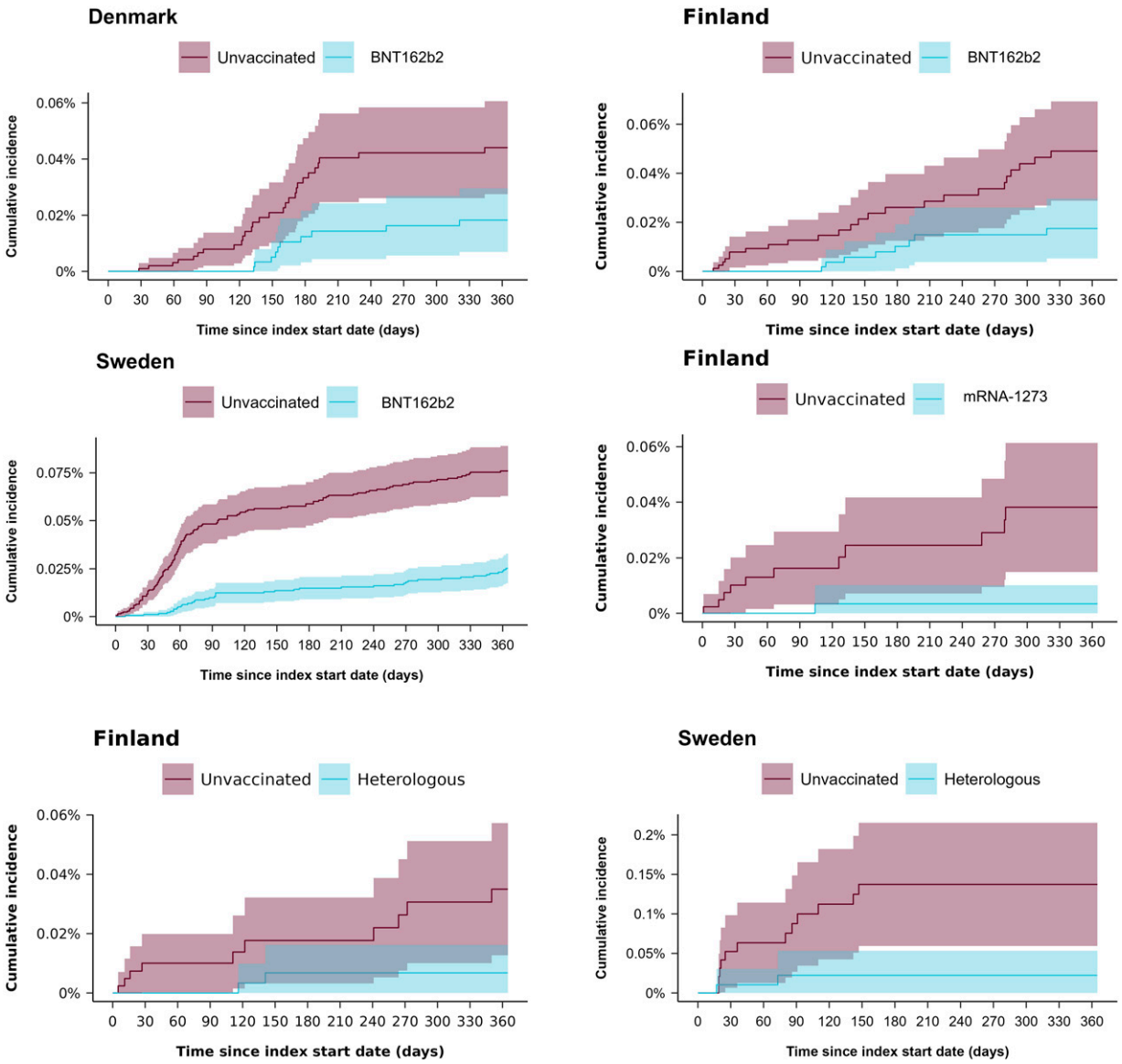

FIGURE 1

Cumulative incidence of COVID-19 hospitalization during 365-day follow-up among matched primary schedule vaccinated and unvaccinated adolescents 12 to 17 years. Analysis could not be conducted in Norway for COVID-19–related hospitalization because no events were observed among the vaccinated in the matched cohorts. Heterologous = primary schedule (2 doses) with mix of BNT162b2 and mRNA-1273.

some hospitalizations with COVID-19 were likely captured by the used outcome definition. Of note, any presence of individuals hospitalized with COVID-19 and instead of because of COVID-19 would most likely tend to skew the estimates toward the null, and thus, provide conservative VE.

To increase the internal validity, a matched target trial emulation was used to estimate VE for the general population. This study design has both strengths and limitations. As per study design, outliers may not have been fully represented in the matched dataset. This was a tradeoff to enhance the generalizability. The matched target emulation design also enabled the estimations of the cumulative incidences directly for both absolute and relative measures of effectiveness, which provides a more comprehensive appreciation of the impact of the COVID-19 vaccination campaigns. Given the matched design, however, estimates from each comparison should primarily be interpreted separately.

The estimation of VE against the secondary outcome of laboratory-confirmed SARS-CoV-2 infection had several limitations. Because the outcome relied on secondary use of national microbiological PCR test results (which were not recommended for individuals with mild respiratory

infections after January–March 2022 in Nordic countries), those individuals infected but not PCR tested would not have been captured in the nationwide surveillance data source (including cases tested SARS-CoV-2 antigen tests only and not PCR confirmed). In addition, home antigen tests for COVID-19 were used widely during the study period and usage varied across the Nordic countries. For example, in Finland, it was made part of the national testing strategy in early 2022, and Norway provided free home antigen tests for students during summer and autumn 2021 that were not recommended to PCR-confirm after January 2022. Thus, that a significant number of infections likely remained undetected together with both difference in proportion of natural immunity because of previous SARS-CoV-2 infection and the possibility of differential testing behavior between vaccinated and unvaccinated adolescents could have influenced the VE estimates against infection substantially. These misclassifications would most likely underestimate VE for of SARS-CoV-2 infection. Additionally, COVID-19 vaccination recommendations differed slightly across the Nordic countries and, for example, Norway offered second doses later for adolescents aged 12 to 15 years compared with other Nordic countries. These factors likely contribute to the substantial variation in RDs for laboratory-confirmed SARS-CoV-2 infection across the countries and interpretation of the results should be done with caution. However, these biases were likely limited for the estimation of VE against COVID-19–related hospitalization.

CONCLUSIONS

In this nationwide cohort analyses of adolescents aged 12 to 17 years in 4 Nordic countries, COVID-19 hospitalization was a rare event. Primary schedules with mRNA vaccines provided high protection against COVID-19 hospitalization (VE ≥72.6%) compared with unvaccinated at 6 months of follow-up. The effectiveness of the COVID-19 vaccines against COVID-19–related hospitalization was sustained when extending follow-up to 12 months as well as during the omicron period. These results may provide further guidance for decision-making with respect to COVID-19 vaccination campaigns among the adolescents.

ETHICAL STATEMENT AND FUNDING

This study was conducted according to ethical regulations within each participating country (Supplemental Table 9).

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ABBREVIATIONS

CI: confidence interval
PCR: polymerase chain reaction
RD: risk difference
VE: vaccine effectiveness

of results, and critically reviewed the manuscript; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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