Supplementary materials: Vaccine effectiveness against infection with the Delta (B.1.617.2) variant, Norway, April to August 2021

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Part 1. Data sources and definition of medium and high risk for severe course of COVID-19

The national identity number was essential to link data from all registries used in the analysis (Table S1).

Table S1. Data sources in the Norwegian preparedness registry BeredtC19 used in this study and individualized data retrieved from each source.

| Data source                                                                 | Data content                                                                 |
|-----------------------------------------------------------------------------|-----------------------------------------------------------------------------|
| Norwegian Surveillance System for Communicable Diseases (MSIS)              | Confirmed cases of COVID-19, COVID-19 associated deaths                      |
| MSIS laboratory database                                                    | Results of PCR screening assays or whole genome sequencing of samples positive for SARS-CoV-2 |
| The Norwegian Intensive Care and Pandemic Registry                         | Hospitalisations with confirmed COVID-19 as main cause of hospitalisation   |
| The Norwegian Immunisation Registry (SYSVAK)                                | COVID-19 vaccine doses given                                                 |
| The National Population Register                                            | Registration status (alive/dead)                                            |
| Norwegian Patient Registry (NPR) and Norway Control and Payment of Health Reimbursement database (KUHR) | ICD-10 and ICPC-2 codes on underlying comorbidities                         |

Some people have underlying comorbidities that cause them to have a moderate or high risk of severe COVID-19 regardless of age. These individuals have been prioritized early for vaccination.

The underlying comorbidities that have been defined as increasing the risk of severe COVID-19 are divided into two groups:

Risk group 1 (high risk) includes people with diseases/conditions that carry a high risk of severe COVID-19, also in younger individuals. These comorbidities include having received an organ transplant, immunodeficiency, hematological cancer in the last five years, other active cancers, ongoing or recently discontinued treatment for cancer (especially immunosuppressive therapy, radiation therapy to the lungs or cytotoxic drugs), neurological or neuromuscular diseases that cause impaired cough or lung function (e.g., ALS and cerebral palsy), Down syndrome and chronic kidney disease, or significant renal impairment.

Risk group 2 (medium risk) includes people with diseases/conditions that entail a moderate risk of severe COVID-19. This includes chronic liver disease or significant hepatic impairment, immunosuppressive therapy as in autoimmune diseases, diabetes, chronic lung disease including cystic fibrosis and severe asthma which have required the use of high dose inhaled or oral steroids within the past year, obesity with a body mass index (BMI) of ≥35 kg/m², dementia, chronic heart and vascular disease (with the exception of high blood pressure) and stroke.
Part 2. Vaccination status at the end of study

In this rapid communication, we have defined vaccination status as:

- Unvaccinated: unvaccinated, < 21 days after 1\textsuperscript{st} vaccine dose
- Partly vaccinated: \geq 21 days after 1\textsuperscript{st} vaccine dose, < 7 days after 2\textsuperscript{nd} vaccine dose
- Fully vaccinated: \geq 7 days after 2\textsuperscript{nd} vaccine dose

Table S2 shows the vaccination status for different subgroups of the study population. Here, we defined vaccination status at the end of the study period – i.e. it does not take into account the vaccination status at the time of infection of individuals who tested positive for SARS-CoV-2 during the study period.

Table S2. Vaccination status by sex, age group, country of birth, county of residence and risk for severe COVID-19, and types of vaccines administered, Norway, 15 April – 15 August 2021.
Type of vaccine

| Type of Vaccine         | N       | %     | N       | %     | % of all reported |
|-------------------------|---------|-------|---------|-------|-------------------|
| Comirnaty               | 2,974,727 | 81.1  | 1,104,046 | 81.4 | 1,574,945         |
| Spikevax                | 441,038  | 14.4  | 195,348  | 9.7   | 188,284           |
| Vaxzevria               | 4,450    | 0.3   | 3,347    | 0.1   | 1,078             |
| Vaxzevria+ mRNA         | 131,324  | 0.2   | 252      | 6.8   | 131,071           |
| mRNA mixed              | 97,400   | 4.3   | 57,779   | 2.0   | 39,534            |

Risk for severe disease based on underlying comorbidities that are associated with a moderate or high risk of serious illness regardless of age (further details provided in this supplement, part 1).

For types of vaccines, percentages have been calculated per column, and not per row as for the other characteristics presented in the table.

Comirnaty: BioNTech-Pfizer, Mainz, Germany/New York, United States; Vaxzevria: AstraZeneca, Cambridge, United Kingdom; Spikevax: mRNA-1273, Moderna, Cambridge, United States.

Vaxzevria was discontinued in Norway on 11 March 2021 and those who received their first dose were offered a second dose of either Comirnaty or Spikevax.

In Norway the combination of vaccine doses of Comirnaty and Spikevax has been administered.

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Part 3. Assessment of representativeness of screened cases with available variant data

We assessed the representativeness of the screened cases by comparing the characteristics of the screened cases and notified cases among our study population.

We found differences between cases who were screened for virus variants with regards to county of residence, sampling week, and hospitalisation (Table S3). Differences in county and sampling week reflect the evolution of the outbreak as well as the introduction of PCR screening methodology for virus variants at the primary diagnostic laboratories. Differences in the sampling week are also influenced by the latest weeks not being fully updated regarding the information on detected variants since there is a delay in analysing the samples (and expected to be more updated in the coming weeks). The proportion of cases screened among hospitalised cases was slightly higher than among those not hospitalised (77% vs 72%) and slightly higher among non-Norwegian born (74 vs 72%). The above differences were considered minor for our study aim.

Table S3. Characteristics of reported and screened cases of SARS-CoV-2, Norway, 15 April to 15 August 2021.

| Characteristics | All reported cases | Screened cases | % of all reported |
|-----------------|--------------------|----------------|-------------------|
|                 | N  | %   | N  | %  |                     |
| Total           | 27,284 | 100 | 19,721 | 100 | 72 %                |
| Sex             |      |     |      |     |                     |
| Female          | 12,560 | 46  | 9,146 | 46  | 73 %                |
| Male            | 14,724 | 54  | 10,575 | 54  | 72 %                |
| P-value=0.067   |      |     |      |     |                     |
| Age group       |      |     |      |     |                     |
| 18-24           | 8,513 | 31  | 6,175 | 31  | 73 %                |
| 25-34           | 6,795 | 25  | 4,921 | 25  | 72 %                |
| 35-44           | 4,968 | 18  | 3,567 | 18  | 72 %                |
| 45-54           | 4,237 | 15  | 3,073 | 16  | 73 %                |
| 55-64           | 1,851 | 6.8 | 1,311 | 6.7 | 71 %                |
| 65-74           | 578   | 2.1 | 439   | 2.2 | 76 %                |
| 75-84           | 212   | 0.8 | 145   | 0.7 | 68 %                |
| >=85            | 130   | 0.5 | 90    | 0.5 | 69 %                |
| P-value=0.246   |      |     |      |     |                     |
| Norwegian born  |      |     |      |     |                     |
| Yes             | 17,218 | 63  | 12,489 | 63  | 73 %                |
| No              | 10,057 | 37  | 7,223 | 37  | 72 %                |
**Part 4. Vaccine effectiveness estimates for age groups 18-44, 45-64 and 65+ years**

Here we present vaccine effectiveness estimates against infection with the Delta and Alpha variants separately for the age groups 18-44, 45-64 and 65+ years. As for the analyses presented in the main text, we used vaccination status as a time-dependent covariate, and explicit time to account for changes in the baseline hazard over time in a Cox proportional hazards model, adjusting for sex, county of birth, county of residence, and underlying comorbidities associated with increased risk of severe COVID-19. The results should be interpreted with caution due to data paucity.

**Table S4.** Crude and adjusted vaccine effectiveness (VE) against infection with the Delta and Alpha variants of SARS-CoV-2 for each age group, Norway, 15 April - 15 August 2021 (n = 18,431).

| Variant group | Age group | Vaccination status          | Events | Rate\(^a\) | VE (%) | 95% CI | Crude VE | Adjusted VE\(^b\) |
|---------------|-----------|-----------------------------|--------|------------|--------|--------|----------|----------------------|
| Delta         | 18-44     | Unvaccinated                | 2924   | 16.02      | 14.0   | 8.0 – 20.3 | Ref.     | 18.3 – 29.7           |
|               |           | Partly vaccinated           | 1147   | 41.95      | 14.4   | 8.0 – 20.3 |          |                      |
Part 5. Sensitivity analysis of vaccine effectiveness estimates

In this rapid communication, we have defined vaccination status as:

- Unvaccinated: unvaccinated, <21 days after 1st vaccine dose
- Partly vaccinated: ≥21 days after 1st vaccine dose, <7 days after 2nd vaccine dose
- Fully vaccinated: ≥7 days after 2nd vaccine dose

These definitions, while widely used in analyses of VE, might bias the VE estimate downwards if the vaccines induce some protection prior to day 21 after first dose. As a sensitivity analysis, we looked at whether this potential bias could change our results and conclusion. In this analysis, we kept all study participants, but excluded all follow-up time between the day of the first dose and 21 days after the first dose. This excluded 925 Delta infection events and 910 Alpha infection events. This approach slightly increased the VE estimates, and the resulting crude and adjusted VE estimates are presented in Table S5.

Table S5. Crude and adjusted vaccine effectiveness (VE) against infection with the Delta and Alpha variants of SARS-CoV-2, Norway, 15 April - 15 August 2021 (n = 16,596).

| Variant | Vaccination status | Events | Ratea | Crude VE | Adjusted VEb |
|---------|--------------------|--------|-------|----------|--------------|
|         |                    |        |       | %        | %            |            |
|         |                    |        |       | 95% CI   | 95% CI       |            |
|         |                    |        |       |          |              |            |
| Delta   | Unvaccinated       | 2,338  | 9.70  | Ref.     | Ref.         |            |
|         | Partly vaccinated  | 1,609  | 18.85 | 46.2     | 42.5 – 49.7  | 32.2        | 27.1 – 37.0 |
|         | Fully vaccinated   | 558    | 4.09  | 87.7     | 86.5 – 88.8  | 68.8        | 65.2 – 72.0  |
| Alpha   | Unvaccinated       | 11,288 | 46.84 | Ref.     | Ref.         |            |
|         | Partly vaccinated  | 596    | 6.98  | 76.1     | 74.0 – 78.0  | 56.9        | 52.9 – 60.6  |
|         | Fully vaccinated   | 207    | 1.52  | 93.4     | 92.4 – 94.2  | 85.4        | 82.9 – 87.4  |
Alpha: Phylogenetic Assignment of Named Global Outbreak (Pango) lineage designation B.1.1.7; CI: confidence interval; Delta: B.1.617.2; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2; VE: vaccine effectiveness.

\(^{a}\) Incidence rate per 1,000,000 person-days

\(^{b}\) Adjusted for age, sex, county of residence, country of birth and underlying comorbidities increasing the risk for severe COVID-19.

Cox proportional hazard models were implemented using explicit time accounting for changes in the baseline hazard over time.