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Općinsko državno odvjetništvo u Zagrebu
Kazneni odjel
Selska 2
Zagreb

KAZNENA PRIJAVA

Protiv članova Stožera Civilne zaštite Republike Hrvatske: DAVOR BOŽINOVIĆ, potpredsjednik Vlade Republike Hrvatske i ministar unutarnjih poslova, DAMIR TRUT zamjenik načelnika Stožera civilne zaštite Republike Hrvatske, MARIJANA KLANAC, predstavnica Ministarstva unutarnjih poslova, DARKO MAJSTOROVIĆ, predstavnik Ministarstva unutarnjih poslova, NEVEN KARAS, predstavnik Ministarstva unutarnjih poslova, ROKO BAOTIĆ, predstavnik Ministarstva unutarnjih poslova, NIKOLA MILINA, predstavnik Ministarstva unutarnjih poslova, KREŠO TUŠKAN, predstavnik Ministarstva obrane, IVANA JAKIR-BAJO, predstavnica Ministarstva financija, VERA KATALINIĆ-JANKOVIĆ, dr. med., predstavnica Ministarstva zdravstva, KRUNOSLAV KARALIĆ, predstavnik Ministarstva poljoprivrede, IGOR ČIŽMEK, predstavnik Ministarstva zaštite okoliša i energetike, ZDRAVKO VUKIĆ, predstavnik Ministarstva graditeljstva i prostornoga uređenja, DAMIR JUZBAŠIĆ, predstavnik Ministarstva gospodarstva, poduzetništva i obrta, ALEN GOSPOČIĆ, predstavnik Ministarstva mora, prometa i infrastrukture, MARIJAN GAŠPARAC, predstavnik Ministarstva za demografiju, obitelj, mlade i socijalnu politiku, VINKO LJUBIČIĆ, predstavnik Ministarstva vanjskih i europskih poslova, ROBERT PENDE, predstavnik Ministarstva turizma, HRVOJE ŽULJ, predstavnik Ministarstva kulture, GORAN KOLARIĆ, predstavnik Ministarstva znanosti i obrazovanja, SLAVKO TUCAKOVIĆ, predstavnik Hrvatske vatrogasne zajednice, BRANKA IVANČAN-PICEK, predstavnica Državnog hidrometeorološkog zavoda, INES IVANČIĆ, predstavnica Seizmološke službe Hrvatske, ZORAN ĐUROKOVIĆ, predstavnik Hrvatskih voda, ROBERT MARKT, predstavnik Hrvatskog Crvenog križa, JOSIP GRANIĆ, predstavnik Hrvatske gorske službe spašavanja, KRUNOSLAV CAPAK, dr. med., predstavnik Hrvatskog zavoda za javno zdravstvo,

zbog osnovane sumnje da su u svojstvu članova Stožera civilne zaštite Republike Hrvatske počinili kazneno djelo zlouporabe položaja i ovlasti iz članka 291. Kaznenog zakona Republike Hrvatske na način da kao službene osobe nisu obavile dužnost koju su bile dužne obaviti čime su drugima prouzročili znatnu štetu.

Postoji osnovana sumnja da su navedene osobe unatoč činjenici da su znale, odnosno da su morale znati, za postojanje znanstvenih studija i službenih podataka koji ukazuju da osobe koje su cijepljene cjepivima proizvođača Pfizer, Moderna, AstraZeneca i Janssen, prenose virus covid-19 na druge osobe,

propustile donijeti odluku o obveznom testiranju svih pa i cijepljenih osoba kao uvjeta za pristup javnim institucijama, prije svega zdravstvenim ustanovama i ustanovama za skrb o starijima i nemoćnima.

Na taj su način omogućili cijepljenim osobama koje su prenositelji virusa neometan pristup osobama koje su PCR testom ili brzim antigenskim testom dokazali da nisu nositelji virusa Covid-19 kao i bolesnicima, imunkompromitiranima te starijim i nemoćnim osobama,

čime su nanijeli znatnu štetu građanima koji su zbog takve njihove odluke zaraženi virusom Covida-19 te su testirani kao pozitivni, hospitalizirani, završili na respiratoru odnosno preminuli.

Dokazi i obrazloženje

1) Znanstvena studija objavljena u znanstvenom časopisu Lancet, 28. listopada 2021. potvrđuje da cijepljeni prenose virus Covid-19 i da cijepljenje nije jamstvo niti dokaz da osoba nije prenositelj virusa Covida-19. Istraživanje je utvrdilo da su cijepljene osobe zarazile 25% svojih kontakata, dok su necijepljene osobe zarazile 38% svojih kontakata unutar kućanstva. Time je na znanstven način dokazano da cijepljene osobe prenose virus drugim osobama te ih dovode u izravnu opasnost razvijanja bolesti SARS-COV-2 te hospitalizacije i smrti.
Prilog:
https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00648-4/fulltext

2) Iz dokumenta Agencije za zdravstvenu sigurnost Ujedinjenog Kraljevstva objavljenog 7. listopada 2021. godine pod nazivom „Izvješće o nadzoru cjepiva protiv COVID-19“ vidljivo je iz tablice 2 objavljenoj na stranici br. 13 da cijepljene osobe prenose virus Covid-19. Iz navedene tablice pod nazivom „Slučajevi COVID-19 prema statusu cijepljenja između 36. i 39. tjedna 2021.“ je vidljivo da je u promatranom razdoblju virusom Covid-19 zaraženo 266.094 osoba nakon primitka druge doze cjepiva, 32.028 osoba nakon prve doze cjepiva (prvu dozu primili 21 ili više dana prije testiranja) i 7.204 nakon primitka prve doze cjepiva (prvu dozu primili 20 ili manje dana prije testiranja).
Prilog:
https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1023849/Vaccine_surveillance_report_-_week_40.pdf

3) Iz službenih podataka o testiranjima i učinkovitosti cjepiva koje su proizvođači prezentirali European Medicines Agency (EMA) do dana 9. studenoga 2021. proizlazi **da je razlika u postotku razvijanja simptoma bolesti COVID 19 između cijepljenih i necijepljenih osoba kod cjepiva BIONTECH I PFIZER 0,84%, kod cjepiva MODERNA 1,23%, kod cjepiva ASTRAZENECA 1,74% i kod cjepiva JANSSEN 1,18%.** Takve minorne razlike ukazuju na činjenicu da su stope zaraze cijepljenih osoba, a onda i stope prijenosa virusa covid-19 neznatno manje od stope zaraza i prijenosa virusa Covida-19 kod necijepljenih osoba.

Citati iz EMA dokumenta o odobravanju cjepiva i opaske podnositelja prijave
BIONTECH I PFIZER Comirnaty (COVID-19 mRNA vaccine [nucleoside modified])
„..Ispitivanje je pokazalo 95-postotno smanjenje broja simptomatskih slučajeva zaraze u osoba koje su primile cjepivo (8 od 18.198 ispitanika dobilo je simptome bolesti COVID-19) u usporedbi s ispitanicima koji su primili placebo (162 slučaja od 18.325 ispitanika dobilo je simptome bolesti COVID-19)...“
Opaska:
(8/18.198 = 0,04%, odnosno 99,96% cijepljenih nije razvilo simptome bolesti)
(162/18.325 = 0,88%, odnosno 99,12% necijepljenih (placebo) nije razvilo simptome bolesti)
Razlika u postotku razvijanja simptoma bolesti cijepljenih i necijepljenih iznosi 0,84%

MODERNASpikevax1 (COVID-19 mRNA vaccine [nucleoside modified]
„..Ispitivanje je pokazalo smanjenje broja simptomatskih slučajeva zaraze u osoba koje su primile cjepivo od 94,1% (11 od 14.134) ispitanika dobilo je simptome bolesti COVID-19) u usporedbi s ispitanicima koji su primili placebo (185 od 14.073) ispitanika dobilo je simptome bolesti COVID-19). Navedeno pokazuje da je cjepivo pokazalo djelotvornost od 94,1% u kliničkim ispitivanjima...“
Opaska:
(11/14.134 = 0,08%, odnosno 99,92% cijepljenih nije razvilo simptome bolesti)
(185/14.073 = 1,31%, odnosno 98,69% necijepljenih (placebo) nije razvilo simptome bolesti).
Razlika u postotku razvijanja simptoma bolesti cijepljenih i necijepljenih iznosi 1,23%

ASTRAZENECA Vaxzevria1 (COVID-19 Vaccine (ChAdOx1-S [recombinant])
„..Predmetna dva klinička ispitivanja (COV002 i COV003) pokazala su smanjenje broja simptomatskih slučajeva zaraze u osoba koje su primile cjepivo od 59,5% (64 od 5.258 ispitanika dobilo je simptome

bolesti COVID-19) u usporedbi s ispitanicima koji su primili placebo (154 od 5.210) ispitanika dobilo je simptome bolesti COVID-19). Navedeni rezultati
upućuju na to da je cjepivo pokazalo djelotvornost od oko 60% u kliničkim ispitivanjima...“
Opaska:
(64/5.258 = 1,22%, odnosno 98,78% cijepljenih nije razvilo simptome bolesti)
(154/5.210 = 2,96%, odnosno 97,04% necijepljenih (placebo) nije razvilo simptome bolesti)
Razlika u postotku razvijanja simptoma bolesti cijepljenih i necijepljenih iznosi 1,74%

JANSSEN (Ad26.COV2-S [recombinant])
„..Ispitivanje je pokazalo smanjenje broja simptomatskih slučajeva zaraze u osoba koje su primile cjepivo od 67% (116 od 19.630 ispitanika dobilo je simptome bolesti COVID-19) u
usporedbi s ispitanicima koji su primili placebo (348 od 19.691 ispitanika dobilo je simptome bolesti COVID-19). Navedeno pokazuje da je cjepivo pokazalo djelotvornost od 67%...“
Opaska:
(116/19.630 = 0,59%, odnosno 99,41% cijepljenih nije razvilo simptome bolesti)
(348/19.691 = 1,77%, odnosno 98,23% necijepljenih (placebo) nije razvilo simptome bolesti)
Razlika u postotku razvijanja simptoma bolesti cijepljenih i necijepljenih iznosi 1,18%

Prilog:
https://www.ema.europa.eu/en/human-regulatory/overview/public-health-threats/coronavirus-disease-covid-19/treatments-vaccines/covid-19-vaccines

4) Znanstveno istraživanje pod nazivom "Correlation Between 3790 Quantitative Polymerase Chain Reaction–Positives Samples and Positive Cell Cultures, Including 1941 Severe Acute Respiratory Syndrome Coronavirus 2 Isolates" objavljeno 28. rujna 2020. godine u Clinical Infectious Diseases dokazalo je da je pouzdanost PCR testova u izravnoj vezi s brojem ciklusa ponavljanja. Studija je utvrdila da je pouzdanost PCR testova koji se provode pri 35 ciklusa ponavljanja samo 3%. S obzirom da većina hrvatskih i europskih laboratorija provodi PCR testiranje pri 45 ciklusa ponavljanja, PCR testove koji se provode pri 35 i više ciklusa ponavljanja ne može se smatrati pouzdanom metodom utvrđivanja prisutnosti koronavirusa kod testirane osobe. S obzirom da je odlukom Stožera Civilne zaštite osobama koje su testirane kao pozitivne na prisutnost koronavirusa priznat status preboljenja istima je omogućeno neometano kretanje iako ne postoji dokaz da su one uistinu preboljele bolest SARS-Cov-2 te ne postoji dokaz da oni ne prenose virus na druge osobe.
Prilog:
https://doi.org/10.1093/cid/ciaa1491

5) Slijedom navedenog potpuno je razvidno da je jedini razlog uvođenja kovid potvrda u javni život prisila građana na cijepljenje, a ne zaštita života i zdravlja građana. Iz izvješća CDC WONDER od 3. rujna 2021. u SAD-u je u sustav prijavljeno **1.315.380 nuspojava,** od čega je za 4 kovid cjepiva prijavljeno 615.703 nuspojave, odnosno 46,81% ukupno prijavljenih nuspojava za sva cjepiva od 1990. u SAD-u. Iz izvješća Selected Adverse Events Reported after COVID-19 Vaccination od 10. studenog 2021. proizlazi da je prijavljeno **9.549 nuspojava smrti**.
Prilog:
https://wonder.cdc.gov/controller/saved/D8/D217F160

U prilogu tiskana izdanja studija i dokumentacija na kojoj se prijava temelji

U Briselu, 16. studeni 2021.

Mislav Kolakušić
Nezavisni zastupnik u
Europskom parlamentu

Community transmission and viral load kinetics of the SARS-CoV-2 delta (B.1.617.2) variant in vaccinated and unvaccinated individuals in the UK: a prospective, longitudinal, cohort study

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Summary

Background The SARS-CoV-2 delta (B.1.617.2) variant is highly transmissible and spreading globally, including in populations with high vaccination rates. We aimed to investigate transmission and viral load kinetics in vaccinated and unvaccinated individuals with mild delta variant infection in the community.

Methods Between Sept 13, 2020, and Sept 15, 2021, 602 community contacts (identified via the UK contract-tracing system) of 471 UK COVID-19 index cases were recruited to the Assessment of Transmission and Contagiousness of COVID-19 in Contacts cohort study and contributed 8145 upper respiratory tract samples from daily sampling for up to 20 days. Household and non-household exposed contacts aged 5 years or older were eligible for recruitment if they could provide informed consent and agree to self-swabbing of the upper respiratory tract. We analysed transmission risk by vaccination status for 231 contacts exposed to 162 epidemiologically linked delta variant-infected index cases. We compared viral load trajectories from fully vaccinated individuals with delta infection (n=29) with unvaccinated individuals with delta (n=16), alpha (B.1.1.7; n=39), and pre-alpha (n=49) infections. Primary outcomes for the epidemiological analysis were to assess the secondary attack rate (SAR) in household contacts stratified by contact vaccination status and the index cases' vaccination status. Primary outcomes for the viral load kinetics analysis were to detect differences in the peak viral load, viral growth rate, and viral decline rate between participants according to SARS-CoV-2 variant and vaccination status.

Findings The SAR in household contacts exposed to the delta variant was 25% (95% CI 18–33) for fully vaccinated individuals compared with 38% (24–53) in unvaccinated individuals. The median time between second vaccine dose and study recruitment in fully vaccinated contacts was longer for infected individuals (median 101 days [IQR 74–120]) than for uninfected individuals (64 days [32–97], p=0·001). SAR among household contacts exposed to fully vaccinated index cases was similar to household contacts exposed to unvaccinated index cases (25% [95% CI 15–35] for vaccinated *vs* 23% [15–31] for unvaccinated). 12 (39%) of 31 infections in fully vaccinated household contacts arose from fully vaccinated epidemiologically linked index cases, further confirmed by genomic and virological analysis in three index case–contact pairs. Although peak viral load did not differ by vaccination status or variant type, it increased modestly with age (difference of 0·39 [95% credible interval –0·03 to 0·79] in peak $\log_{10}$ viral load per mL between those aged 10 years and 50 years). Fully vaccinated individuals with delta variant infection had a faster (posterior probability >0·84) mean rate of viral load decline (0·95 $\log_{10}$ copies per mL per day) than did unvaccinated individuals with pre-alpha (0·69), alpha (0·82), or delta (0·79) variant infections. Within individuals, faster viral load growth was correlated with higher peak viral load (correlation 0·42 [95% credible interval 0·13 to 0·65]) and slower decline (–0·44 [–0·67 to –0·18]).

Interpretation Vaccination reduces the risk of delta variant infection and accelerates viral clearance. Nonetheless, fully vaccinated individuals with breakthrough infections have peak viral load similar to unvaccinated cases and can efficiently transmit infection in household settings, including to fully vaccinated contacts. Host–virus interactions early in infection may shape the entire viral trajectory.

Funding National Institute for Health Research.

Introduction

While the primary aim of vaccination is to protect individuals against severe COVID-19 disease and its consequences, the extent to which vaccines reduce onward transmission of SARS-CoV-2 is key to containing the pandemic. This outcome depends on the ability of

Lancet Infect Dis 2021

Published **Online** October 28, 2021 https://doi.org/10.1016/S1473-3099(21)00648-4

This online publication has been corrected. The corrected version first appeared at thelancet.com/infection on November 2, 2021

See **Online/Comment** https://doi.org/10.1016/S1473-3099(21)00690-3

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Research in context

Evidence before this study

The SARS-CoV-2 delta variant is spreading globally, including in populations with high vaccination coverage. While vaccination remains highly effective at attenuating disease severity and preventing death, vaccine effectiveness against infection is reduced for delta. Determining the extent of transmission from vaccinated delta-infected individuals to their vaccinated contacts is a public health priority. Comparing the upper respiratory tract (URT) viral load kinetics of delta infections with those of other variants gives insight into potential mechanisms for its increased transmissibility. We searched PubMed and *medRxiv* for articles published between database inception and Sept 20, 2021, using search terms describing "SARS-CoV-2, delta variant, viral load, and transmission". Two studies longitudinally sampled the URT in vaccinated and unvaccinated delta variant-infected individuals to compare viral load kinetics. In a retrospective study of a cohort of hospitalised patients in Singapore, more rapid viral load decline was found in vaccinated individuals than unvaccinated cases. However, the unvaccinated cases in this study had moderate-to-severe infection, which is known to be associated with prolonged shedding. The second study longitudinally sampled professional USA sports players. Again, clearance of delta viral RNA in vaccinated cases was faster than in unvaccinated cases, but only 8% of unvaccinated cases had delta variant infection, complicating interpretation. Lastly, a report of a single-source nosocomial outbreak of a distinct delta sub-lineage in Vietnamese health-care workers plotted viral load kinetics (without comparison with unvaccinated delta infections) and demonstrated transmission between fully vaccinated health-care workers in the nosocomial setting. The findings might therefore not be generalisable beyond the particular setting and distinct viral sub-lineage investigated.

Added value of this study

The majority of SARS-CoV-2 transmission occurs in households, but transmission between fully vaccinated individuals in this setting has not been shown to date. To ascertain secondary transmission with high sensitivity, we longitudinally followed index cases and their contacts (regardless of symptoms) in the community early after exposure to the delta variant of SARS-CoV-2, performing daily quantitative RT-PCR on URT samples for 14–20 days. We found that the secondary attack rate in fully vaccinated household contacts was high at 25%, but this value was lower than that of unvaccinated contacts (38%). Risk of infection increased with time in the 2–3 months since the second dose of vaccine. The proportion of infected contacts was similar regardless of the index cases' vaccination status. We observed transmission of the delta variant between fully vaccinated index cases and their fully vaccinated contacts in several households, confirmed by whole-genome sequencing. Peak viral load did not differ by vaccination status or variant type but did increase modestly with age. Vaccinated delta cases experienced faster viral load decline than did unvaccinated alpha or delta cases. Across study participants, faster viral load growth was correlated with higher peak viral load and slower decline, suggesting that host–virus interactions early in infection shape the entire viral trajectory. Since our findings are derived from community household contacts in a real-life setting, they are probably generalisable to the general population.

Implications of all the available evidence

Although vaccines remain highly effective at preventing severe disease and deaths from COVID-19, our findings suggest that vaccination is not sufficient to prevent transmission of the delta variant in household settings with prolonged exposures. Our findings highlight the importance of community studies to characterise the epidemiological phenotype of new SARS-CoV-2 variants in increasingly highly vaccinated populations. Continued public health and social measures to curb transmission of the delta variant remain important, even in vaccinated individuals.

vaccines to protect against infection and the extent to which vaccination reduces the infectiousness of breakthrough infections.

Vaccination was found to be effective in reducing household transmission of the alpha variant (B.1.1.7) by 40–50%,[1] and infected, vaccinated individuals had lower viral load in the upper respiratory tract (URT) than infections in unvaccinated individuals,[2] which is indicative of reduced infectiousness.[3,4] However, the delta variant (B.1.617.2), which is more transmissible than the alpha variant,[5,6] is now the dominant strain worldwide. After a large outbreak in India, the UK was one of the first countries to report a sharp rise in delta variant infection. Current vaccines remain highly effective at preventing admission to hospital and death from delta infection.[7] However, vaccine effectiveness against infection is reduced for delta, compared with alpha,[8,9] and the delta variant continues to cause a high burden of cases even in countries with high vaccination coverage. Data are scarce on the risk of community transmission of delta from vaccinated individuals with mild infections.

Here, we report data from a UK community-based study, the Assessment of Transmission and Contagiousness of COVID-19 in Contacts (ATACCC) study, in which ambulatory close contacts of confirmed COVID-19 cases underwent daily, longitudinal URT sampling, with collection of associated clinical and epidemiological data. We aimed to quantify household transmission of the delta variant and assess the effect of vaccination status on contacts' risk of infection and index cases' infectiousness, including (1) households with unvaccinated contacts and index cases and (2) households with fully vaccinated contacts and fully vaccinated index cases. We also compared sequentially sampled

URT viral RNA trajectories from individuals with non-severe delta, alpha, and pre-alpha SARS-CoV-2 infections to infer the effects of SARS-CoV-2 variant status—and, for delta infections, vaccination status—on transmission potential.

Methods

Study design and participants

ATACCC is an observational longitudinal cohort study of community contacts of SARS-CoV-2 cases. Contacts of symptomatic PCR-confirmed index cases notified to the UK contact-tracing system (National Health Service Test and Trace) were asked if they would be willing to be contacted by Public Health England to discuss participation in the study. All contacts notified within 5 days of index case symptom onset were selected to be contacted within our recruitment capacity. Household and non-household contacts aged 5 years or older were eligible for recruitment if they could provide written informed consent and agree to self-swabbing of the URT. Further details on URT sampling are given in the appendix (p 13).

The ATACCC study is separated into two study arms, ATACCC1 and ATACCC2, which were designed to capture different waves of the SARS-CoV-2 pandemic. In ATACCC1, which investigated alpha variant and pre-alpha cases in Greater London, only contacts were recruited between Sept 13, 2020, and March 13, 2021. ATACCC1 included a pre-alpha wave (September to November, 2020) and an alpha wave (December, 2020, to March, 2021). In ATACCC2, the study was relaunched specifically to investigate delta variant cases in Greater London and Bolton, and both index cases and contacts were recruited between May 25, and Sept 15, 2021. Early recruitment was focused in West London and Bolton because UK incidence of the delta variant was highest in these areas.[10] Based on national and regional surveillance data, community transmission was moderate-to-high throughout most of our recruitment period.

This study was approved by the Health Research Authority. Written informed consent was obtained from all participants before enrolment. Parents and caregivers gave consent for children.

Data collection

Demographic information was collected by the study team on enrolment. The date of exposure for non-household contacts was obtained from Public Health England. COVID-19 vaccination history was determined from the UK National Immunisation Management System, general practitioner records, and self-reporting by study participants. We defined a participant as unvaccinated if they had not received a single dose of a COVID-19 vaccine at least 7 days before enrolment, partially vaccinated if they had received one vaccine dose at least 7 days before study enrolment, and fully vaccinated if they had received two doses of a COVID-19 vaccine at least 7 days before study enrolment. Previous literature was used to determine the 7-day threshold for defining vaccination status.[11–13] We also did sensitivity analyses using a 14-day threshold. The time interval between vaccination and study recruitment was calculated. We used WHO criteria[14] to define symptomatic status up to the day of study recruitment. Symptomatic status for incident cases—participants who were PCR-negative at enrolment and subsequently tested positive—was defined from the day of the first PCR-positive result.

Laboratory procedures

SARS-CoV-2 quantitative RT-PCR, conversion of ORF1ab and envelope (E-gene) cycle threshold values to viral genome copies, whole-genome sequencing, and lineage assignments are described in the appendix (pp 13–14).

Outcomes

Primary outcomes for the epidemiological analysis were to assess the secondary attack rate (SAR) in household contacts stratified by contact vaccination status and the index cases' vaccination status. Primary outcomes for the viral load kinetics analysis were to detect differences in the peak viral load, viral growth rate, and viral decline rate between participants infected with pre-alpha versus alpha versus delta variants and between unvaccinated delta-infected participants and vaccinated delta-infected participants.

See Online for appendix

We assessed vaccine effectiveness and susceptibility to SARS-CoV-2 infection stratified by time elapsed since receipt of second vaccination as exploratory analyses.

Statistical analysis

To model viral kinetics, we used a simple phenomenological model of viral titre[15] during disease pathogenesis. Viral kinetic parameters were estimated on a participant-specific basis using a Bayesian hierarchical model to fit this model to the entire dataset of sequential cycle threshold values measured for all participants. For the 19 participants who were non-household contacts of index cases and had a unique date of exposure, the cycle threshold data were supplemented by a pseudo-absence data point (ie, undetectable virus) on the date of exposure. Test accuracy and model misspecification were modelled with a mixture model by assuming there was a probability p of a test giving an observation drawn from a (normal) error distribution and probability $1-p$ of it being drawn from the true distribution.

The hierarchical structure was represented by grouping participants based on the infecting variant and their vaccination status. A single-group model was fitted, which implicitly assumes that viral kinetic parameters vary by individual but not by variant or vaccination status. A four-group model was also explored, where groups 1, 2, 3, and 4 represent pre-alpha, alpha, unvaccinated delta, and fully vaccinated delta, respectively. We fitted a correlation matrix between

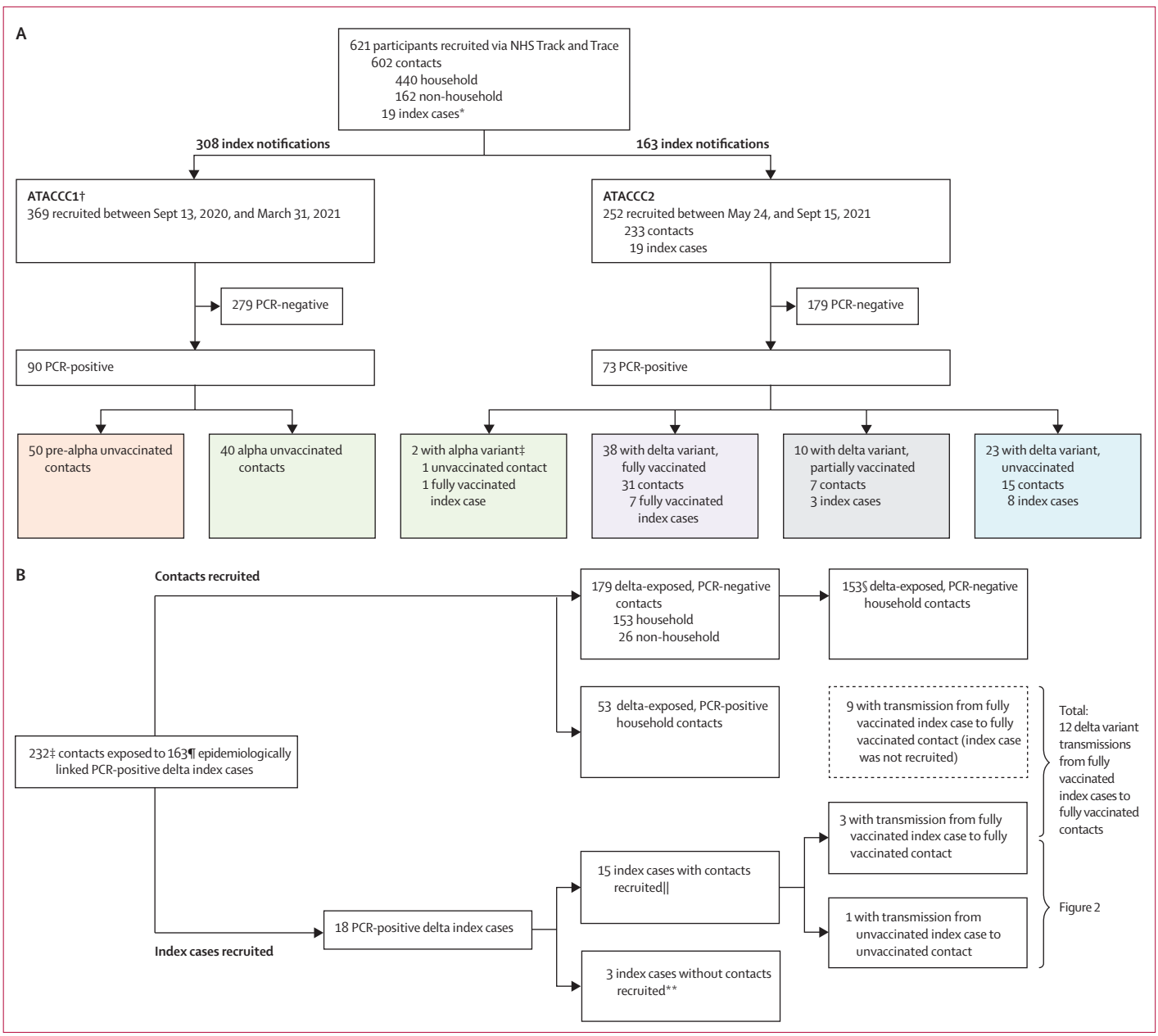


Figure 1: **Recruitment, SARS-CoV-2 infection, variant status, and vaccination history for ATACCC study participants**
(A) Study recruitment and variant status confirmed by whole-genome sequencing (ATACCC1 and ATACCC2 combined). (B) ATACCC2: delta-exposed contacts included in secondary attack rate calculation (table 1) and transmission assessment (table 2). NHS=National Health Service. *All index cases were from ATACCC2. †All contacts. ‡The two earliest PCR-positive cases from the ATACCC2 cohort (one index case and one contact) were confirmed as having the alpha variant on whole-genome sequencing (recruited on May 28, 2021). This alpha variant-exposed, PCR-positive contact is excluded from figure 1B. §One PCR-negative contact had no vaccination status data available and one PCR-negative contact's index case had no vaccination data available. ¶Vaccination data were available for 138 index cases of 163. ||The contacts of these 15 index cases are included within the 232 total contacts. **These three index cases without contacts are only included in the viral load kinetics analysis (figure 3) and are not included in tables 1 and 2.

participant-specific kinetic parameters to allow us to examine whether there is within-group correlation between peak viral titre, viral growth rate, and viral decline rate. Our initial model selection, using leave-one-out cross-validation, selected a four-group hierarchical model with fitted correlation coefficients between individual-level parameters determining peak viral load and viral load growth and decline rates (appendix p 5). However, resulting participant-specific estimates of peak viral load (but not growth and decline rates) showed a marked and significant correlation with age in the exploratory analysis, which motivated examination of models where mean peak viral load could vary with age. The most predictive model overall allowed mean viral

load growth and decline rates to vary across the four groups, with mean peak viral load common to all groups but assumed to vary linearly with the logarithm of age (appendix p 5). We present peak viral loads for the reference age of 50 years with 95% credible intervals (95% CrIs). 50 years was chosen as the reference age as it is typical of the ages of the cases in the whole dataset and the choice of reference age made no difference in the model fits or judgment of differences between the groups.

We computed group-level population means and within-sample group means of log peak viral titre, viral growth rate, and viral decline rate. Since posterior estimates of each of these variables are correlated across groups, overlap in the credible intervals of an estimate for one group with that for another group does not necessarily indicate no significant difference between those groups. We, therefore, computed posterior probabilities, *pp*, that these variables were larger for one group than another. For our model, Bayes factors can be computed as *pp*/(1–*pp*). We only report population (group-level) posterior probabilities greater than 0·75 (corresponding to Bayes factors >3) as indicating at least moderate evidence of a difference.

For vaccine effectiveness, we defined the estimated effectiveness at preventing infection, regardless of symptoms, with delta in the household setting as 1 – SAR (fully vaccinated) / SAR (unvaccinated).

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Between Sept 13, 2020, and Sept 15, 2021, 621 community-based participants (602 contacts and 19 index cases) from 471 index notifications were prospectively enrolled in the ATACCC1 and ATACCC2 studies, and contributed 8145 URT samples. Of these, ATACCC1 enrolled 369 contacts (arising from 308 index notifications), and ATACCC2 enrolled 233 contacts (arising from 163 index notifications) and 19 index cases. SARS-CoV-2 RNA was detected in 163 (26%) of the 621 participants. Whole-genome sequencing of PCR-positive cases confirmed that 71 participants had delta variant infection (18 index cases and 53 contacts), 42 had alpha variant infection (one index case and 41 contacts), and 50 had pre-alpha variant infection (all contacts; figure 1A).

Of 163 PCR-positive participants, 89 (55%) were female and 133 (82%) were White. Median age was 36 years (IQR 26–50). Sex, age, ethnicity, body-mass index (BMI) distribution, and the frequency of comorbidities were similar among those with delta, alpha, and pre-alpha infection, and for vaccinated and unvaccinated delta-infected participants, except for age and sex (appendix pp 2–3). There were fewer unvaccinated females than males (p=0·04) and, as expected from the age-prioritisation of the UK vaccine roll-out, unvaccinated participants infected with the delta variant were significantly younger (p<0·001; appendix p 3). Median time between exposure to the index case and study enrolment was 4 days (IQR 4–5). All participants had non-severe ambulatory illness or were asymptomatic. The proportion of asymptomatic cases did not differ among fully vaccinated, partially vaccinated, and unvaccinated delta groups (appendix p 3).

No pre-alpha-infected and only one alpha-infected participant had received a COVID-19 vaccine before study enrolment. Of 71 delta-infected participants (of whom 18 were index cases), 23 (32%) were unvaccinated, ten (14%) were partially vaccinated, and 38 (54%) were fully vaccinated (figure 1A; appendix p 3). Of the 38 fully vaccinated delta-infected participants, 14 had received the BNT162b2 mRNA vaccine (Pfizer–BioNTech), 23 the ChAdOx1 nCoV-19 adenovirus vector vaccine (Oxford–AstraZeneca), and one the CoronaVac inactivated whole-virion vaccine (Sinovac).

It is highly probable that all but one of the 233 ATACCC2 contacts were exposed to the delta variant because they were recruited when the regional prevalence of delta was at least 90%, and mostly 95–99% (figure 1B).[10] Of these, 206 (89%) were household contacts (in 127 households), and 26 (11%) were non-household contacts. Distributions of age, ethnicity, BMI, smoking status, and comorbidities were similar between PCR-positive and PCR-negative contacts (appendix p 4). The median time between second vaccine dose and study recruitment in fully vaccinated contacts with delta variant infection was 74 days (IQR 35–105; range 16–201), and this was significantly longer in PCR-positive contacts than in PCR-negative contacts (101 days [IQR 74–120] *vs* 64 days [32–97], respectively, p=0·001; appendix p 4). All 53 PCR-positive contacts were exposed in household settings and the SAR for all delta variant-exposed household contacts was 26% (95% CI 20–32). SAR was

	Total	PCR positive	PCR negative	SAR (95% CI)	p value
Contacts					
All	231	53	178	23 (18–29)	NA
Fully vaccinated	140	31	109	22 (16–30)	0·16
Unvaccinated	44	15	29	34 (22–49)	..
Partially vaccinated	47	7	40	15 (7–28)	NA
Household contacts					
All	205	53	152	26 (20–32)	NA
Fully vaccinated	126	31	95	25 (18–33)	0·17
Unvaccinated	40	15	25	38 (24–53)	..
Partially vaccinated	39	7	32	18 (9–33)	NA

χ^2 test was performed to calculate p values for differences in SAR between fully vaccinated and unvaccinated cases. One PCR-negative contact who withdrew from the study without vaccination status information was excluded. NA=not applicable. SAR=secondary attack rate.

Table 1: **SAR in contacts of delta-exposed index cases recruited to the ATACCC2 study**

	All household contacts (n=204)*	Fully vaccinated contacts (n=125)		Partially vaccinated contacts (n=39)		Unvaccinated contacts (n=40)	
		PCR positive (n=31)	PCR negative (n=94)	PCR positive (n=7)	PCR negative (n=32)	PCR positive (n=15)	PCR negative (n=25)
Fully vaccinated index cases (n=50)	69	12	31	1	8	4	13
Partially vaccinated index cases (n=25)	35	7	12	3	10	3	0
Unvaccinated index cases (n=63)	100	12	51	3	14	8	12

Non-household exposed contacts (n=24, all PCR negative) were excluded. One PCR-negative household contact who withdrew from the study without vaccination status information was excluded. One PCR-negative household contact who could not be linked to their index case was also excluded. *The rows below show the number of contacts exposed to each category of index case.

Table 2: **Comparison of vaccination status of the 138 epidemiologically linked PCR-positive index cases for 204 delta variant-exposed household contacts**

not significantly higher in unvaccinated (38%, 95% CI 24–53) than fully vaccinated (25%, 18–33) household contacts (table 1). We estimated vaccine effectiveness at preventing infection (regardless of symptoms) with delta in the household setting to be 34% (bootstrap 95% CI –15 to 60). Sensitivity analyses using a 14 day threshold for time since second vaccination to study recruitment to denote fully vaccinated did not materially affect our estimates of vaccine effectiveness or SAR (data not shown). Although precision is restricted by the small sample size, this estimate is broadly consistent with vaccine effectiveness estimates for delta variant infection based on larger datasets.[9,16,17]

The vaccination status of 138 epidemiologically linked index cases of 204 delta variant-exposed household contacts was available (figure 1B, table 2). The SAR in household contacts exposed to fully vaccinated index cases was 25% (95% CI 15–35; 17 of 69), which is similar to the SAR in household contacts exposed to unvaccinated index cases (23% [15–31]; 23 of 100; table 2). The 53 PCR-positive contacts arose from household exposure to 39 PCR-positive index cases. Of these index cases who gave rise to secondary transmission, the proportion who were fully vaccinated (15 [38%] of 39) was similar to the proportion who were unvaccinated (16 [41%] of 39). The median number of days from the index cases' second vaccination to the day of recruitment for their respective contacts was 73 days (IQR 38–116). Time interval did not differ between index cases who transmitted infection to their contacts and those who did not (94 days [IQR 62–112] and 63 days [35–117], respectively; p=0·43).

18 of the 163 delta variant-infected index cases that led to contact enrolment were themselves recruited to ATACCC2 and serial URT samples were collected from them, allowing for more detailed virology and genome analyses. For 15 of these, their contacts were also recruited (13 household contacts and two non-household contacts). A corresponding PCR-positive household contact was identified for four of these 15 index cases (figure 1B). Genomic analysis showed that index–contact pairs were infected with the same delta variant sub-lineage in these instances, with one exception (figure 2A). In one household (number 4), an unvaccinated index case transmitted the delta variant to an unvaccinated contact, while another partially vaccinated contact was infected with a different delta sub-lineage (which was probably acquired outside the household). In the other three households (numbers 1–3), fully vaccinated index cases transmitted the delta variant to fully vaccinated household contacts, with high viral load in all cases, and temporal relationships between the viral load kinetics that were consistent with transmission from the index cases to their respective contacts (figure 2B).

Inclusion criteria for the modelling analysis selected 133 participant's viral load RNA trajectories from 163 PCR-positive participants (49 with the pre-alpha variant, 39 alpha, and 45 delta; appendix p 14). Of the 45 delta cases, 29 were fully vaccinated and 16 were unvaccinated; partially vaccinated cases were excluded. Of the 133 included cases, 29 (22%) were incident (ie, PCR negative at enrolment converting to PCR positive subsequently) and 104 (78%) were prevalent (ie, already PCR positive at enrolment). 15 of the prevalent cases had a clearly resolvable peak viral load. Figure 3 shows modelled viral RNA (ORF1ab) trajectories together with the viral RNA copy numbers measured for individual participants. The E-gene equivalent is shown in the appendix (p 2). Estimates derived from E-gene cycle threshold value data (appendix pp 5, 7, 9, 11) were similar to those for ORF1ab.

Although viral kinetics appear visually similar for all four groups of cases, we found quantitative differences in estimated viral growth rates and decline rates (tables 3, 4). Population (group-level) estimates of mean viral load decline rates based on ORF1ab cycle threshold value data varied in the range of 0·69–0·95 $\log_{10}$ units per mL per daxes 4; appendix p 10), indicating that a typical 10-day period was required for viral load to decline from peak to undetectable. A faster decline was seen in the alpha (*pp*=0·93), unvaccinated delta (*pp*=0·79), and fully vaccinated delta (*pp*=0·99) groups than in the pre-alpha group. The mean viral load decline rate of the fully vaccinated delta group was also faster than those of the alpha group (*pp*=0·84) and the unvaccinated delta group (*pp*=0·85). The differences in decline rates translate into a difference of about 3 days in the mean duration of the decline phase between the pre-alpha and delta vaccinated groups.

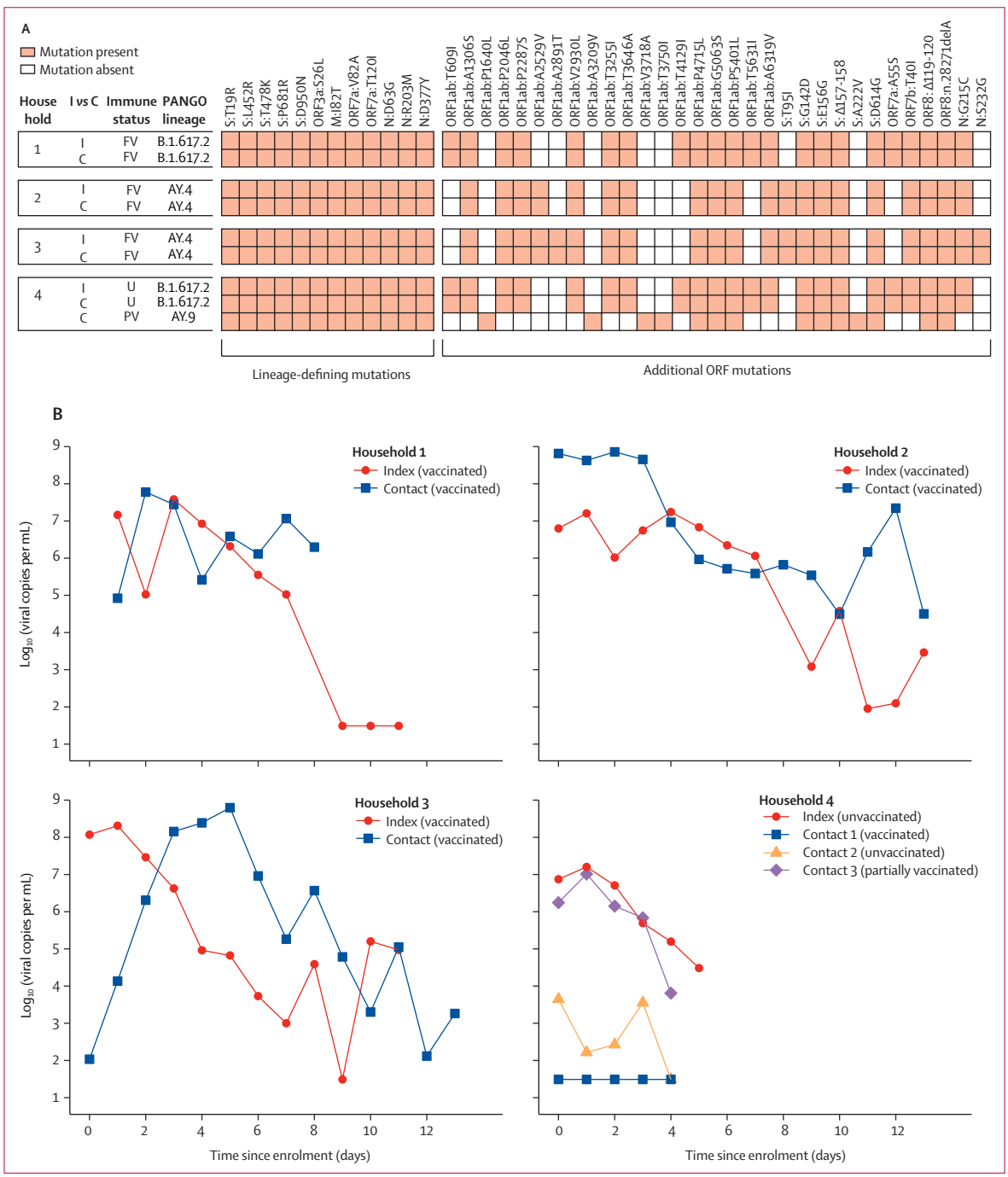
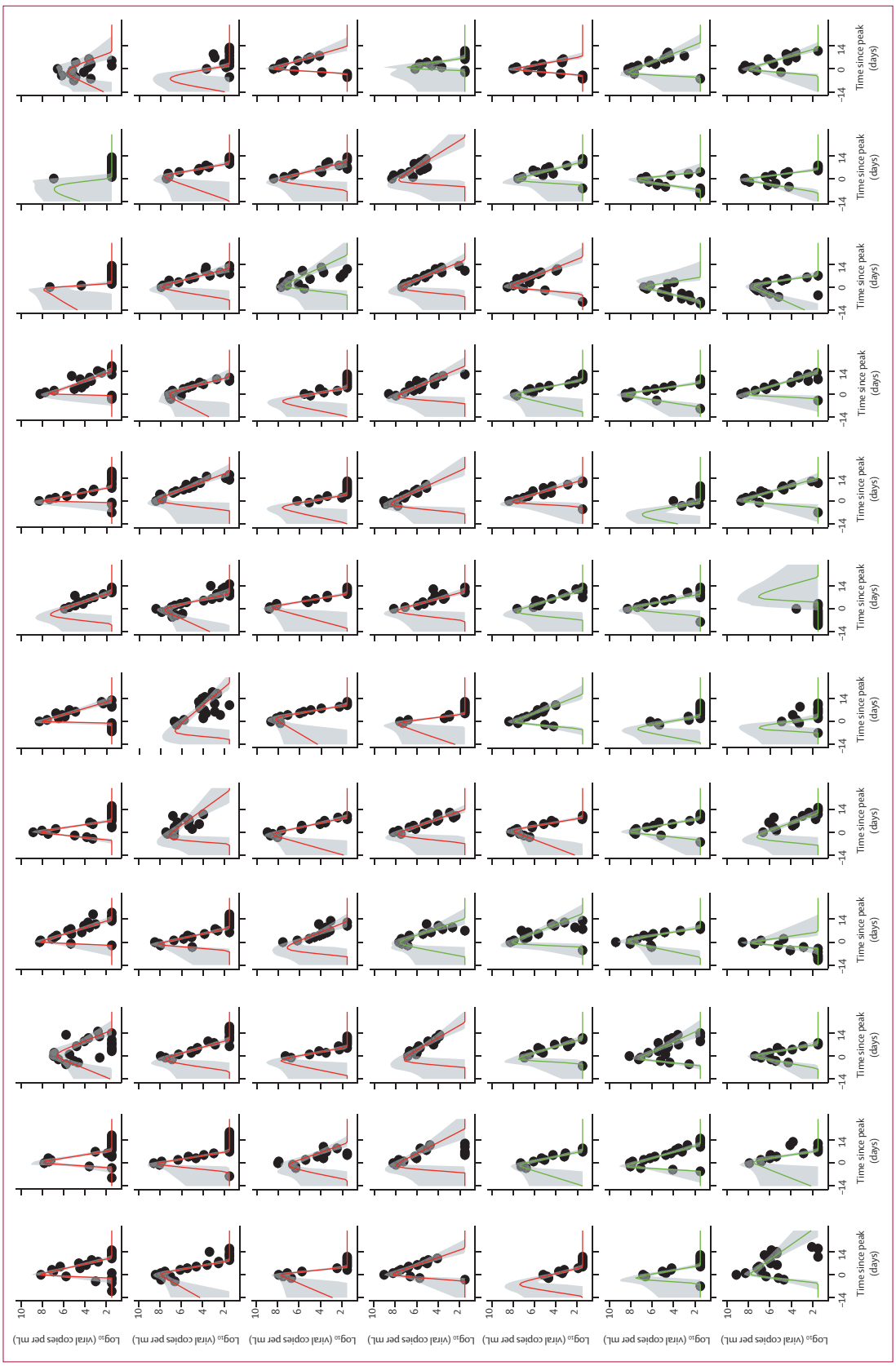


Figure 2: **Virological, epidemiological, and genomic evidence for transmission of the SARS-CoV-2 delta variant (B.1.617.2) in households**
(A) Genomic analysis of the four households with lineage-defining mutations for delta[18] and additional mutations within ORFs displayed to give insight into whether strains from individuals within the household are closely related. Lineages AY.4 and AY.9 are sub-lineages of delta. (B) Viral trajectories and vaccination status of the four index cases infected with the delta variant for whom infection was detected in their epidemiologically linked household contacts. All individuals had non-severe disease. Each plot shows an index case and their household contacts. Undetectable viral load measurements are plotted at the limit of detection ($10^{1\cdot49}$). C=contact. I=index case. FV=fully vaccinated. ORF=open reading frame. PV=partially vaccinated. U=unvaccinated.

Viral load growth rates were substantially faster than decline rates, varying in the range of 2·69–3·24 $\log_{10}$ units per mL per day between groups, indicating that a typical 3-day period was required for viral load to grow from undetectable to peak. Our power to infer differences in growth rates between groups was more restricted than for viral decline, but there was moderate evidence (*pp*=0·79) that growth rates were lower for



(Figure 3 continues on next page)

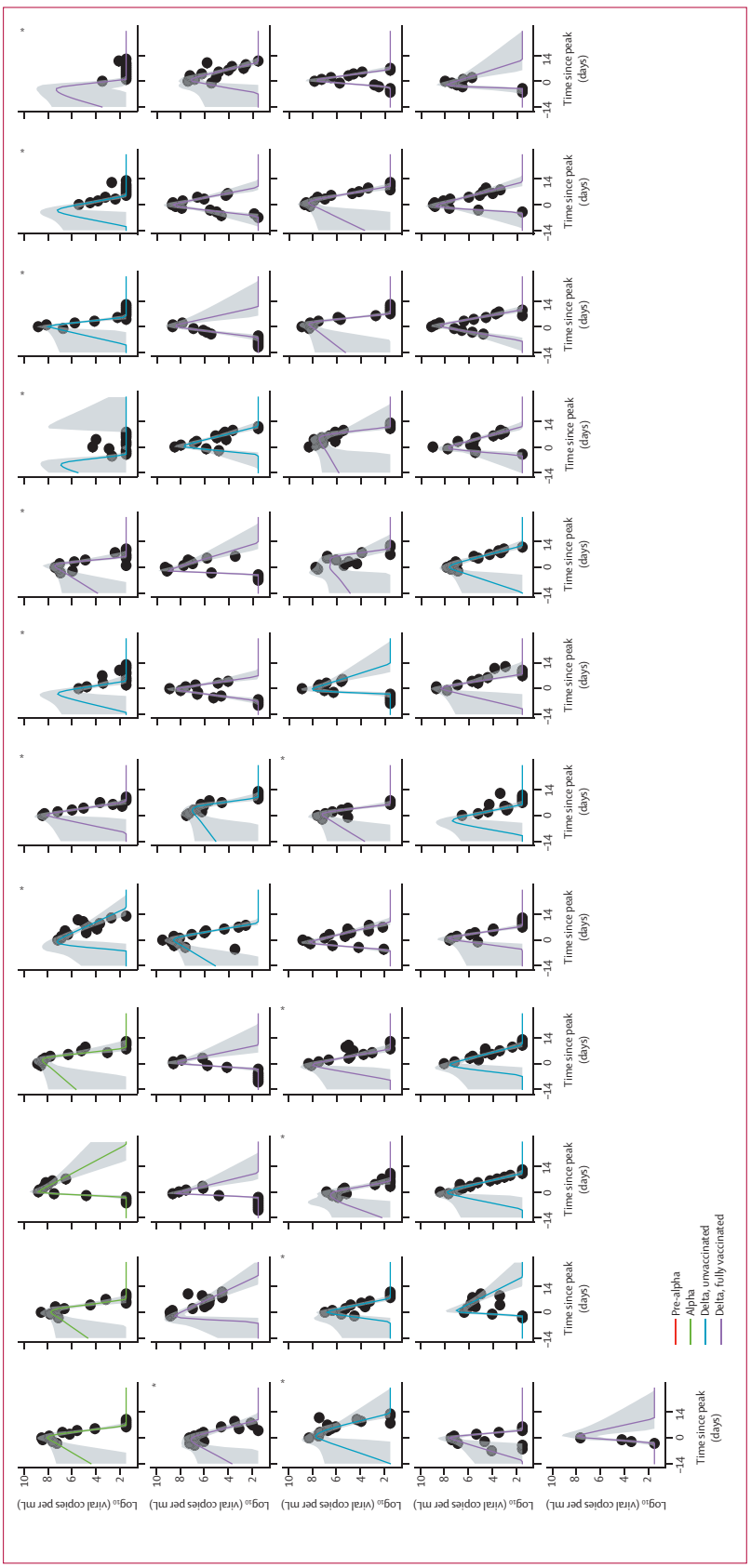


Figure 3: **ORF1ab viral load trajectories from 14 days before to 28 days after peak for 133 participants infected with pre-alpha or alpha variants (uncaccinated), or the delta variant (vaccinated and unvaccinated) variants**
Black circles are measured values, with the first datapoint for each participant being taken to the day of enrolment. Plots are rooted on the day of peak viral load for each participant, denoted as day 0 on the x-axis. Curves show the model posterior median estimate, with a 95% credible interval shading. 133 infected participants, comprising 114 contacts and 19 index cases. *Index cases.

	VL growth rate (95% CrI), log_{10} units per day	Posterior probability estimate is less than pre-alpha	Posterior probability estimate is less than alpha	Posterior probability estimate is less than delta (unvaccinated)	Posterior probability estimate is less than delta (fully vaccinated)
Pre-alpha (n=49)	3·24 (1·78–6·14)	..	0·44	0·27	0·21
Alpha (n=39)	3·13 (1·76–5·94)	0·56	..	0·32	0·25
Delta, unvaccinated (n=16)	2·81 (1·47–5·47)	0·73	0·68	..	0·44
Delta, fully vaccinated (n=29)	2·69 (1·51–5·17)	0·79	0·75	0·56	..

VL growth rates are shown as within-sample posterior mean estimates. Remaining columns show population (group-level) posterior probabilities that the estimate on that row is less than an estimate for a different group. Posterior probabilities are derived from 20 000 posterior samples and have sampling errors of <0·01. VL=viral load. CrI=credible interval.

Table 3: **Estimates of VL growth rates for pre-alpha, alpha, and delta (unvaccinated and fully vaccinated) cases, derived from ORF1ab cycle threshold data**

	VL decline rate (95% CrI), log_{10} units per day	Posterior probability estimate is larger than pre-alpha	Posterior probability estimate is larger than alpha	Posterior probability estimate is larger than delta (unvaccinated)	Posterior probability estimate is larger than delta (fully vaccinated)
Pre-alpha (n=49)	0·69 (0·58–0·81)	..	0·07	0·21	0·01
Alpha (n=39)	0·82 (0·67–1·01)	0·93	..	0·60	0·16
Delta, unvaccinated (n=16)	0·79 (0·59–1·04)	0·79	0·40	..	0·15
Delta, fully vaccinated (n=29)	0·95 (0·76–1·18)	0·99	0·84	0·85	..

VL decline rates are shown as within-sample posterior mean estimates. Remaining columns show population (group-level) posterior probabilities that the estimate on that row is less than an estimate for a different group. Posterior probabilities are derived from 20 000 posterior samples and have sampling errors of <0·01. VL=viral load. CrI=credible interval.

Table 4: **Estimates of VL decline rates for pre-alpha, alpha, and delta (unvaccinated and fully vaccinated) cases, derived from ORF1ab cycle threshold data**

those in the vaccinated delta group than in the pre-alpha group.

We estimated mean peak viral load for 50-year-old adults to be 8·14 (95% CrI 7·95 to 8·32) log_{10} copies per mL, but peak viral load did not differ by variant or vaccination status. However, we estimated that peak viral load increases with age (*pp*=0·96 that the slope of peak viral load with log[age] was >0), with an estimated slope of 0·24 (95% CrI –0·02 to 0·49) log_{10} copies per mL per unit change in log(age). This estimate translates to a difference of 0·39 (–0·03 to 0·79) in mean peak log_{10} copies per mL between those aged 10 years and 50 years.

Within-group individual participant estimates of viral load growth rate were positively correlated with peak viral load, with a correlation coefficient estimate of 0·42 (95% CrI 0·13 to 0·65; appendix p 8). Hence, individuals with faster viral load growth tend to have higher peak viral load. The decline rate of viral load was also negatively correlated with viral load growth rate, with a correlation coefficient estimate of –0·44 (95% CrI –0·67 to –0·18), illustrating that individuals with faster viral load growth tend to experience slower viral load decline.

Discussion

Households are the site of most SARS-CoV-2 transmission globally.[19] In our cohort of densely sampled household contacts exposed to the delta variant, SAR was 38% in unvaccinated contacts and 25% in fully vaccinated contacts. This finding is consistent with the known protective effect of COVID-19 vaccination against infection.[8,9] Notwithstanding, these findings indicate continued risk of infection in household contacts despite vaccination. Our estimate of SAR is higher than that reported in fully vaccinated household contacts exposed before the emergence of the delta variant.[1,20,21] The time interval between vaccination and study recruitment was significantly higher in fully vaccinated PCR-positive contacts than fully vaccinated PCR-negative contacts, suggesting that susceptibility to infection increases with time as soon as 2–3 months after vaccination—consistent with waning protective immunity. This potentially important observation is consistent with recent large-scale data and requires further investigation.[17] Household SAR for delta infection, regardless of vaccination status, was 26% (95% CI 20–32), which is higher than estimates of UK national surveillance data (10·8% [10·7–10·9]).[10] However, we sampled contacts daily, regardless of symptomatology, to actively identify infection with high sensitivity. By contrast, symptom-based, single-timepoint surveillance testing probably underestimates the true SAR, and potentially also overestimates vaccine effectiveness against infection.

We identified similar SAR (25%) in household contacts exposed to fully vaccinated index cases as in those exposed to unvaccinated index cases (23%). This finding indicates that breakthrough infections in fully vaccinated people can efficiently transmit infection in the household setting. We identified 12 household transmission events between fully vaccinated index case–contact pairs; for three of these, genomic sequencing confirmed that the index case and

contact were infected by the same delta variant sub-lineage, thus substantiating epidemiological data and temporal relationships of viral load kinetics to provide definitive evidence for secondary transmission. To our knowledge, one other study has reported that transmission of the delta variant between fully vaccinated people was a point-source nosocomial outbreak—a single health-care worker with a particular delta variant sub-lineage in Vietnam.[22]

Daily longitudinal sampling of cases from early (median 4 days) after exposure for up to 20 days allowed us to generate high-resolution trajectories of URT viral load over the course of infection. To date, two studies have sequentially sampled community cases of mild SARS-CoV-2 infection, and these were from highly specific population groups identified through asymptomatic screening programmes (eg, for university staff and students[23] and for professional athletes[24]).

Our most predictive model of viral load kinetics estimated mean peak $\log_{10}$ viral load per mL of 8·14 (95% CrI 7·95–8·32) for adults aged 50 years, which is very similar to the estimate from a 2021 study using routine surveillance data.[25] We found no evidence of variation in peak viral load by variant or vaccination status, but we report some evidence of modest but significant (pp=0·95) increases in peak viral load with age. Previous studies of viral load in children and adults[4,25,26] have not used such dense sequential sampling of viral load and have, therefore, been restricted in their power to resolve age-related differences; the largest such study[25] reported a similar difference between children and adults to the one we estimated. We found the rate of viral load decline was faster for vaccinated individuals with delta infection than all other groups, and was faster for individuals in the alpha and unvaccinated delta groups than those with pre-alpha infection.

For all variant vaccination groups, the variation between participants seen in viral load kinetic parameter estimates was substantially larger than the variation in mean parameters estimated between groups. The modest scale of differences in viral kinetics between fully vaccinated and unvaccinated individuals with delta infection might explain the relatively high rates of transmission seen from vaccinated delta index cases in our study. We found no evidence of lower SARs from fully vaccinated delta index cases than from unvaccinated ones. However, given that index cases were identified through routine symptomatic surveillance, there might have been a selection bias towards identifying untypically symptomatic vaccine breakthrough index cases.

The differences in viral kinetics we found between the pre-alpha, alpha, and delta variant groups suggest some incremental, but potentially adaptive, changes in viral dynamics associated with the evolution of SARS-CoV-2 towards more rapid viral clearance. Our study provides the first evidence that, within each variant or vaccination group, viral growth rate is positively correlated with peak viral load, but is negatively correlated with viral decline rate. This finding suggests that individual infections during which viral replication is initially fastest generate the highest peak viral load and see the slowest viral clearance, with the latter not just being due to the higher peak. Mechanistically, these data suggest that the host and viral factors determining the initial growth rate of SARS-CoV-2 have a fundamental effect on the trajectory throughout infection, with faster replication being more difficult (in terms of both peak viral load and the subsequent decline of viral load) for the immune response to control. Analysis of sequentially sampled immune markers during infection might give insight into the immune correlates of these early differences in infection kinetics. It is also possible that individuals with the fastest viral load growth and highest peaks contribute disproportionately to community transmission, a hypothesis that should be tested in future studies.

Several population-level, single-timepoint sampling studies using routinely available data have found no major differences in cycle threshold values between vaccinated and unvaccinated individuals with delta variant infection.[10,27,28] However, as the timepoint of sampling in the viral trajectory is unknown, this restricts the interpretation of such results. Two other studies longitudinally sampled vaccinated and unvaccinated individuals with delta variant infection.[23,29] A retrospective cohort of hospitalised patients in Singapore[29] also described a faster rate of viral decline in vaccinated versus unvaccinated individuals with delta variant, reporting somewhat larger differences in decline rates than we estimated here. However, this disparity might be accounted for by the higher severity of illness in unvaccinated individuals in the Singaporean study (almost two-thirds having pneumonia, one-third requiring COVID-19 treatment, and a fifth needing oxygen) than in our study, given that longer viral shedding has been reported in patients with more severe illness.[30] A longitudinal sampling study in the USA reported that pre-alpha, alpha, and delta variant infections had similar viral trajectories.[24] The study also compared trajectories in vaccinated and unvaccinated individuals, reporting similar proliferation phases and peak cycle threshold values, but more rapid clearance of virus in vaccinated individuals. However, this study in the USA stratified by vaccination status and variant separately, rather than jointly, meaning vaccinated individuals with delta infection were being compared with, predominantly, unvaccinated individuals with pre-alpha and alpha infection. Moreover, sampling was done as part of a professional sports player occupational health screening programme, making the results not necessarily representative of typical community infections.

Our study has limitations. First, we recruited only contacts of symptomatic index cases as our study recruitment is derived from routine contact-tracing notifications. Second, index cases were defined as the first household member to have a PCR-positive swab, but we cannot exclude the possibility that another household member might already have been infected and transmitted

to the index case. Third, recording of viral load trajectories is subject to left censoring, where the growth phase in prevalent contacts (already PCR-positive at enrolment) was missed for a proportion of participants. However, we captured 29 incident cases and 15 additional cases on the upslope of the viral trajectory, providing valuable, informative data on viral growth rates and peak viral load in a subset of participants. Fourth, owing to the age-stratified rollout of the UK vaccination programme, the age of the unvaccinated, delta variant-infected participants was lower than that of vaccinated participants. Thus, age might be a confounding factor in our results and, as discussed, peak viral load was associated with age. However, it is unlikely that the higher SAR observed in the unvaccinated contacts would have been driven by younger age rather than the absence of vaccination and, to our knowledge, there is no published evidence showing increased susceptibility to SARS-CoV-2 infection with decreasing age.[31] Finally, although we did not perform viral culture here—which is a better proxy for infectiousness than RT-PCR—two other studies[27,32] have shown cultivable virus from around two-thirds of vaccinated individuals infected with the delta variant, consistent with our conclusions that vaccinated individuals still have the potential to infect others, particularly early after infection when viral loads are high and most transmission is thought to occur.[30]

Our findings help to explain how and why the delta variant is being transmitted so effectively in populations with high vaccine coverage. Although current vaccines remain effective at preventing severe disease and deaths from COVID-19, our findings suggest that vaccination alone is not sufficient to prevent all transmission of the delta variant in the household setting, where exposure is close and prolonged. Increasing population immunity via booster programmes and vaccination of teenagers will help to increase the currently limited effect of vaccination on transmission, but our analysis suggests that direct protection of individuals at risk of severe outcomes, via vaccination and non-pharmacological interventions, will remain central to containing the burden of disease caused by the delta variant.

Contributors

AS, JD, MZ, NMF, WB, and ALal conceptualised the study. AS, SH, JD, KJM, AK, JLB, MGW, ND-F, RV, RK, JF, CT, AVK, JC, VQ, EC, JSN, SH, EM, TP, HH, CL, JS, SB, JP, CA, SA, and NMF were responsible for data curation and investigation. AS, SH, KJM, JLB, AC, NMF, and ALal did the formal data analysis. MAC, AB, DJ, SM, JE, PSF, SD, and ALac did the laboratory work. RV, RK, JF, CT, AVK, JC, VQ, EC, JSN, SH, EM, and SE oversaw the project. AS, SH, JD, KJM, JLB, NMF, and ALal accessed and verified the data. JD, MZ, and ALal acquired funding. NMF sourced and oversaw the software. AS and ALal wrote the initial draft of the manuscript. AS, JD, GPT, MZ, NMF, SH, and ALal reviewed and edited the manuscript. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

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Declaration of interests

NMF reports grants from UK Medical Research Council, UK National Institute of Health Research, UK Research and Innovation, Community Jameel, Janssen Pharmaceuticals, the Bill & Melinda Gates Foundation, and Gavi, the Vaccine Alliance; consulting fees from the World Bank; payment or honoraria from the Wellcome Trust; travel expenses from WHO; advisory board participation for Takeda; and is a senior editor of the *eLife* journal. All other authors declare no competing interests.

Data sharing

An anonymised, de-identified version of the dataset can be made available upon request to allow all results to be reproduced. Modelling code will also be made publicly available on the GitHub repository.

Acknowledgments

This work is supported by the National Institute for Health Research (NIHR200927), a Department of Health and Social Care COVID-19 Fighting Fund award, and the NIHR Health Protection Research Units (HPRUs) in Respiratory Infections and in Modelling and Health Economics. NMF acknowledges funding from the MRC Centre for Global Infectious Disease Analysis and the Jameel Institute. PSF and MAC are supported by the UK Dementia Research Institute. JD is supported by the NIHR HPRU in Emerging and Zoonotic Infections. MGW is supported by the NIHR HPRU in Healthcare Associated Infections and Antimicrobial Resistance. GPT is supported by the Imperial NIHR Biomedical Research Centre. We thank all the participants who were involved in the study, Public Health England staff for facilitating recruitment into the study, the staff of the Virus Reference Department for performing PCR and sequencing assays, and the Immunisations Department for assisting with analysis of vaccination data. We also thank Kristel Timcang, Mohammed Essoussi, Holly Grey, Guilia Miserocchi, Harriet Catchpole, Charlotte Williams, Niamh Nichols, Jessica Russell, Sean Nevin, Lulu Wang, Berenice Di Biase, Alice Panes, Esther Barrow, and Lauren Edmunds for their involvement in logistics, conducting data entry, or quality control; and the Molecular Diagnostics Unit at Imperial College London, in particular Lucy Mosscrop, Carolina Rosadas de Oliveira, and Patricia Watber, for performing RNA extraction, quantitative RT-PCR, and preparing samples for sequencing.

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UK Health Security Agency

COVID-19 vaccine surveillance report

Week 40

Contents

Summary

Four coronavirus (COVID-19) vaccines have now been approved for use in the UK. Rigorous clinical trials have been undertaken to understand the immune response, safety profile and efficacy of these vaccines as part of the regulatory process. Ongoing monitoring of the vaccines as they are rolled out in the population is important to continually ensure that clinical and public health guidance on the vaccination programme is built upon the best available evidence.

UK Health Security Agency, UKHSA, formerly Public Health England (PHE), works closely with the Medicines and Healthcare Regulatory Agency (MHRA), NHS England, and other government, devolved administration and academic partners to monitor the COVID-19 vaccination programme. Details of the vaccine surveillance strategy are set on the page COVID-19: vaccine surveillance strategy (1). As with all vaccines, the safety of COVID-19 vaccines is continuously being monitored by the MHRA. They conclude that overall, the benefits of COVID-19 vaccines outweigh any potential risks (2).

Vaccine effectiveness

Several studies of vaccine effectiveness have been conducted in the UK which indicate that 2 doses of vaccine are between 65 and 95% effective at preventing symptomatic disease with COVID-19 with the Delta variant, with higher levels of protection against severe disease including hospitalisation and death. There is some evidence of waning of protection against infection and symptomatic disease over time, though protection against severe disease remains high in most groups at least 5 months after the second dose.

Population impact

The impact of the vaccination programme on the population is assessed by taking into account vaccine coverage, evidence on vaccine effectiveness and the latest COVID-19 disease surveillance indicators. Vaccine coverage tells us about the proportion of the population that have received 1 and 2 doses of COVID-19 vaccines. By 3 October 2021, the overall vaccine uptake in England for dose 1 was 65.3% and 60.1% for dose 2. In line with the programme rollout, coverage is highest in the oldest age groups.

We present data on COVID-19 cases, hospitalisations and deaths by vaccination status.

Based on antibody testing of blood donors, 98.0% of the adult population now have antibodies to COVID-19 from either infection or vaccination compared to 19.0% that have antibodies from infection alone. Over 96% of adults aged 17 or older have antibodies from either infection or vaccination.

Vaccine effectiveness

Large clinical trials have been undertaken for each of the COVID-19 vaccines approved in the UK which found that they are highly efficacious at preventing symptomatic disease in the populations that were studied. The clinical trials have been designed to be able to assess the efficacy of the vaccine against laboratory confirmed symptomatic disease with a relatively short follow up period so that effective vaccines can be introduced as rapidly as possible. Nevertheless, understanding the effectiveness against different outcomes (such as severe disease and onwards transmission), effectiveness in different subgroups of the population and understanding the duration of protection are equally important in decision making around which vaccines should be implemented as the programme evolves, who they should be offered to and whether booster doses are required.

Vaccine effectiveness is estimated by comparing rates of disease in vaccinated individuals to rates in unvaccinated individuals. Below we outline the latest real-world evidence on vaccine effectiveness from studies in UK populations. We focus on data related to the Delta variant which is currently dominant in the UK. The findings are also summarised in Table 1.

Effectiveness against symptomatic disease

Vaccine effectiveness against symptomatic COVID-19 has been assessed in England based on community testing data linked to vaccination data from the National Immunisation Management System (NIMS), cohort studies such as the COVID Infection Survey and GP electronic health record data. After 2 doses, observed vaccine effectiveness against symptomatic disease with the Delta variant reaches approximately 65 to 70% with AstraZeneca Vaxzevria and 80 to 95% with Pfizer-BioNTech Comirnaty and Moderna Spikevax (3, 4) Vaccine effectiveness is generally slightly higher in younger compared to older age groups. With both Vaxzevria and and Comirnaty, there is evidence of waning of protection over time, most notably among older adults. There is not yet enough follow-up with Spikevax to assess waning (3).

Data (based primarily on the Alpha variant) suggest that in most clinical risk groups, immune response to vaccination is maintained and high levels of VE are seen with both the Pfizer and AstraZeneca vaccines. Reduced antibody response and vaccine effectiveness were seen after 1 dose of vaccine among the immunosuppressed group, however, after a second dose the reduction in vaccine effectiveness is smaller (5).

Analyses by dosing interval suggest that immune response to vaccination and vaccine effectiveness against symptomatic disease improves with a longer (greater than 6 week interval) compared to a shorter interval of 3 to 4 weeks (6, 3)

Effectiveness against hospitalisation

Several studies have estimated vaccine effectiveness against hospitalisation in older all of which indicate higher levels of protection against hospitalisation with all vaccines against the Alpha variant (7, 8, 9, 10). Effectiveness against hospitalisation of over 90% is also observed with the Delta variant with all 3 vaccines (3). In most groups there is relatively limited waning of protection against hospitalisation over a period of at least 5 months after the second dose. Greater waning appears to occur among those in clinical risk groups (3).

Effectiveness against mortality

High levels of protection (over 90%) are also seen against mortality with all 3 vaccines and against both the Alpha and Delta variants (7, 11, 3). Relatively limited waning of protection against mortality is seen over a period of at least 5 months.

Effectiveness against infection

Although individuals may not develop symptoms of COVID-19 after vaccination, it is possible that they could still be infected with the virus and could transmit to others. Understanding how effective vaccines are at preventing infection is therefore important to predict the likely impact of the vaccination programme on the wider population. In order to estimate vaccine effectiveness against infection, repeat asymptomatic testing of a defined cohort of individuals is required. Studies have now reported on vaccine effectiveness against infection in healthcare workers, care home residents and the general population (12, 13, 14, 15). With the delta variant, vaccine effectiveness against infection has been estimated at around 65% with Vaxzevria and 80% with Comirnaty (4).

Effectiveness against transmission

As described above, several studies have provided evidence that vaccines are effective at preventing infection. Uninfected individuals cannot transmit; therefore, the vaccines are also effective at preventing transmission. There may be additional benefit, beyond that due to prevention of infection, if some of those individuals who become infected despite vaccination are also at a reduced risk of transmitting (for example, because of reduced duration or level of viral shedding). A household transmission study in England found that household contacts of cases vaccinated with a single dose had approximately 35 to 50% reduced risk of becoming a confirmed case of COVID-19. This study used routine testing data so would only include household contacts that developed symptoms and went on to request a test via pillar 2. It cannot exclude asymptomatic secondary cases or mildly symptomatic cases who chose not to request a COVID-19 test (16). Data from Scotland has also shown that household contacts of vaccinated healthcare workers are at reduced risk of becoming a case, which is in line with the studies on infection (17). Both of these studies relate to a period when the Alpha variant dominated. An analysis from the ONS Community Infection Survey found that contacts of vaccinated index cases had around 65-80% reduced odds of testing positive with the Alpha variant and 35-65% reduced odds of testing positive with the Delta variant compare to contacts of unvaccinated index cases (18).

A summary of vaccine effectiveness evidence can be seen in Table 1.

Table 1. Summary of evidence on vaccine effectiveness against different outcomes Delta

Outcome	Vaccine effectiveness*		
	Pfizer-BioNTech Cominarty	**AstraZeneca Vaxzevria**	**Moderna Spikevax**
Infection	75-85%	60-70%	
Symptomatic disease	80-90%	65-75%	90-99%
Hospitalisation	95-99%	90-99%	95-99%
Mortality	90-99%	90-95%	

High Confidence	Evidence from multiple studies which is consistent and comprehensive
Medium Confidence	Evidence is emerging from a limited number of studies or with a moderately level of uncertainty
Low Confidence	Little evidence is available at present and results are inconclusive

* Estimates of initial vaccine effectiveness in the general population after a 2 dose course. This typically applies for at least the first 3 to 4 months after vaccination. For some outcomes there may be waning of effectiveness beyond this point.

Population impact

Vaccines typically have both direct effects on those who are vaccinated and indirect effects on the wider population due to a reduced probability that people will come into contact with an infected individual. The overall impact of the vaccination programme may therefore extend beyond that estimated through vaccine effectiveness analysis.

Estimating the impact of a vaccination programme is challenging as there is no completely unaffected control group. Furthermore, the effects of the vaccination programme need to be differentiated from that of other interventions (for example, lockdowns or outbreak control measures), changes in behaviour and any seasonal variation in COVID-19 activity.

UKHSA and other government and academic partners monitor the impact of the of the vaccination programme on levels of COVID-19 antibodies in the population and different disease indicators, including hospitalisations and mortality. This is done through population-based testing and through modelling which combines vaccine coverage rates in different populations, estimates of vaccine effectiveness and disease surveillance indicators.

Vaccine coverage

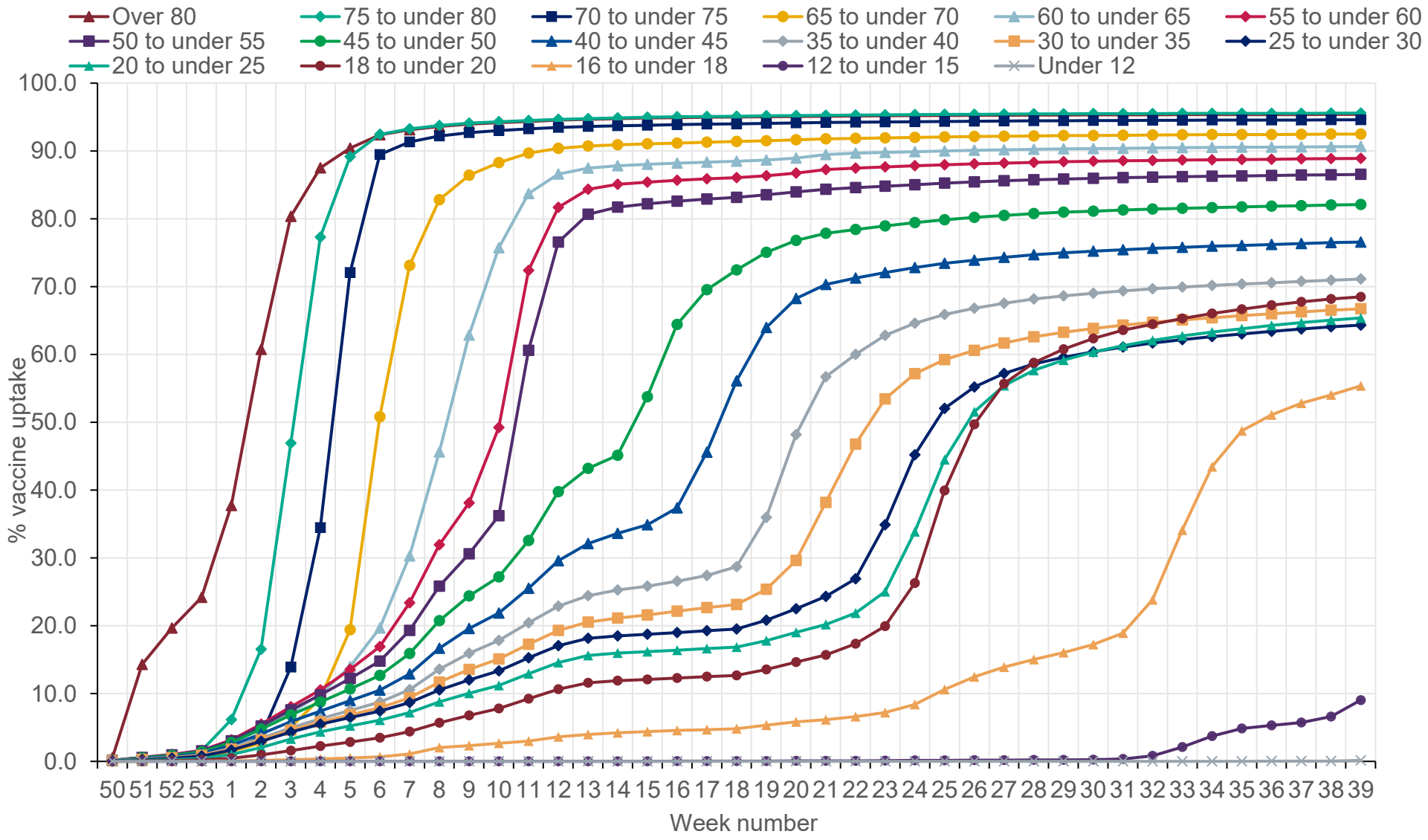
The data in this week's report covers the period from 8 December 2020 to 3 October 2021 (week 39) (Figure 1). It shows the provisional number and percentage of people in England who have had received 1 dose or 2 doses of a COVID-19 vaccination by age group and week since the start of the programme.

Up to 31 August 2021 81,532 women of child-bearing age in England (under 50) who reported that they were pregnant or could be pregnant at the time, received at least 1 dose of COVID-19 vaccination and of these, 65,579 have received their second dose. This is in response to the self-reported pre-screening question "Are you or could you be pregnant?". The true number of pregnant women who have had a COVID-19 vaccination is likely to be greater than this.

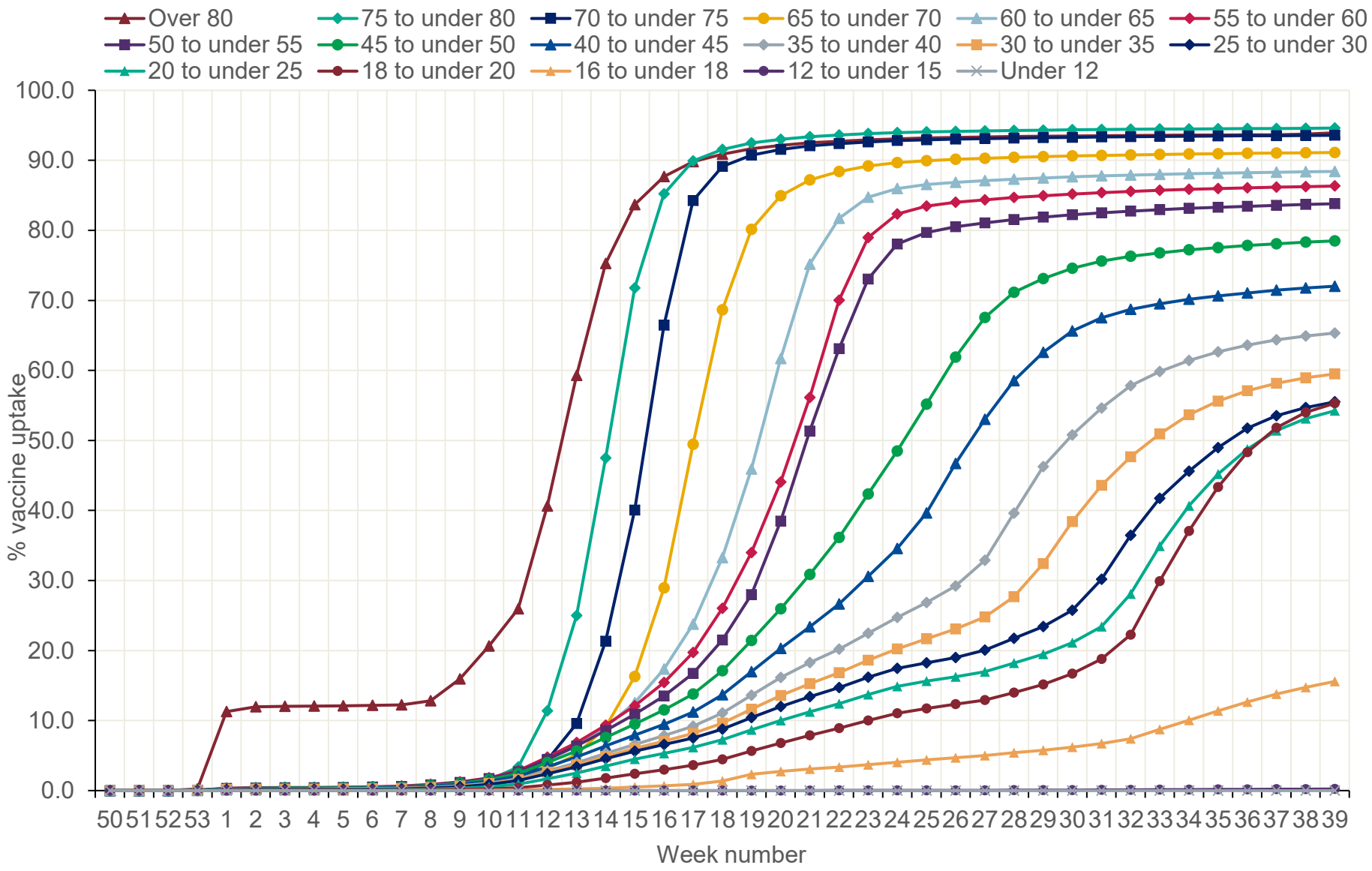
Please note that pregnant women are not a separate priority group as defined by JCVI who have advised that "women who are pregnant should be offered vaccination at the same time as non-pregnant women, based on their age and clinical risk group" therefore comparing vaccine uptake in pregnant women to other vaccination programmes is not currently appropriate. The MHRA closely monitors the safety of COVID-19 vaccine exposures in pregnancy, including Yellow Card reports for COVID-19 vaccines used in pregnancy, for the latest information please see the webpage Coronavirus vaccine – weekly summary of Yellow Card reporting.

Figure 1. Cumulative weekly vaccine uptake by age

a) Dose 1



b) Dose 2


Over 80
75 to under 80
70 to under 75
65 to under 70
60 to under 65
55 to under 60
50 to under 55
45 to under 50
40 to under 45
35 to under 40
30 to under 35
25 to under 30
20 to under 25
18 to under 20
16 to under 18
12 to under 15
Under 12
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
% vaccine uptake
50 51 52 53 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39
Week number

Vaccination status

Vaccination status of COVID-19 cases, deaths and hospitalisations by week of specimen date over the past 4 weeks up to week 39 (up to 3 October 2021) are shown in Table 2 to 4 and Figure 2.

Methods

COVID-19 cases and deaths identified through routine collection from the Second Generation Surveillance System (SGSS) and from UKHSA EpiCell's deaths data as described here, were linked to the National Immunisation Management System (NIMS) to derive vaccination status, using an individual's NHS number as the unique identifier.

Attendance to emergency care at NHS trusts was derived from the Emergency Care DataSet (ECDS) managed by NHS Digital. The same data source was used to identify COVID-19 cases where the attendance to emergency care resulted in admission to an NHS trust.

ECDS is updated weekly, and cases are linked to these data twice weekly. Data from ECDS are subject to reporting delays as, although NHS trusts may update data daily, the mandatory deadline for submission is by the 21st of every month. This means that for weeks immediately following the 21st of a month, numbers may be artificially low and are likely to be higher in later versions of the report.

Data from ECDS also only report on cases who have been presented to emergency care and had a related overnight patient admission and do not show those who are currently in hospital with COVID-19. As such, it is not appropriate for use for surveillance of those currently hospitalised with COVID-19. In addition, these data will not show cases who were directly admitted as inpatients without presenting to emergency care.

The outcome of overnight inpatient admission following presentation to emergency care, was limited to those occurring within 28 days of the earliest specimen date for a COVID-19 case.

Deaths include those who died (a) within 28 days of the earliest specimen date or (b) within 60 days of the first specimen date or more than 60 days after the first specimen date with COVID-19 mentioned on the death certificate.

The rate of COVID-19 cases, hospitalisation, and deaths in fully vaccinated and unvaccinated groups was calculated using vaccine coverage data for each age group extracted from the National Immunisation Management Service.

Results

The rate of a positive COVID-19 test varies by age and vaccination status. The rate of a positive COVID-19 test is substantially lower in vaccinated individuals compared to unvaccinated individuals up to the age of 39. In individuals aged greater than 40, the rate of a positive COVID-19 test is higher in vaccinated individuals compared to unvaccinated. This is likely to be due to a variety of reasons, including differences in the population of vaccinated and unvaccinated people as well as differences in testing patterns.

The rate of hospitalisation within 28 days of a positive COVID-19 test increases with age, and is substantially greater in unvaccinated individuals compared to vaccinated individuals.

The rate of death within 28 days or within 60 days of a positive COVID-19 test increases with age, and again is substantially greater in unvaccinated individuals compared to fully vaccinated individuals.

Interpretation of data

These data should be considered in the context of vaccination status of the population groups shown in the rest of this report. The vaccination status of cases, inpatients and deaths is not the most appropriate method to assess vaccine effectiveness and there is a high risk of misinterpretation. Vaccine effectiveness has been formally estimated from a number of different sources and is described earlier in this report.

In the context of very high vaccine coverage in the population, even with a highly effective vaccine, it is expected that a large proportion of cases, hospitalisations and deaths would occur in vaccinated individuals, simply because a larger proportion of the population are vaccinated than unvaccinated and no vaccine is 100% effective. This is especially true because vaccination has been prioritised in individuals who are more susceptible or more at risk of severe disease. Individuals in risk groups may also be more at risk of hospitalisation or death due to non-COVID-19 causes, and thus may be hospitalised or die with COVID-19 rather than because of COVID-19.

Table 2. COVID-19 cases by vaccination status between week 36 and week 39 2021

Cases reported by specimen date between week 36 and week 39 2021	Total	Unlinked*	Not vaccinated	Received one dose (1-20 days before specimen date)	Received one dose, ≥21 days before specimen date	Second dose ≥14 days before specimen date	Rates among persons vaccinated with 2 doses (per 100,000)	Rates among persons not vaccinated (per 100,000)
Under 18	305,428	20,967	272,981	4,973	5,898	609	278.8	2,325.7
18-29	67,820	8,556	23,440	1,119	12,593	22,112	409.6	688.1
30-39	81,532	7,534	21,449	690	7,468	44,391	763.6	738.4
40-49	101,094	6,839	11,662	297	3,653	78,643	1,281.8	690.2
50-59	70,731	4,668	5,144	89	1,464	59,366	839.5	502.5
60-69	36,953	2,585	1,798	26	546	31,998	563.1	332.9
70-79	22,142	1,367	693	6	207	19,869	428.9	281.4
80+	10,581	869	403	4	199	9,106	354.4	319.5

*individuals whose NHS numbers were unavailable to link to the NIMS

** Interpretation of the case rates in vaccinated and unvaccinated population is particularly susceptible to changes in denominators and should be interpreted with extra caution.

Table 3. COVID-19 cases presenting to emergency care (within 28 days of a positive specimen) resulting in an overnight inpatient admission by vaccination status between week 36 and week 39 2021

Cases presenting to emergency care (within 28 days of a positive test) resulting in overnight inpatient admission, by specimen date between week 36 and week 39 2021	Total	Unlinked*	Not vaccinated	Received one dose (1-20 days before specimen date)	Received one dose, ≥21 days before specimen date	Second dose ≥14 days before specimen date	Rates among persons vaccinated with 2 doses (per 100,000)	Rates among persons not vaccinated (per 100,000)
Under 18	486	20	455	3	7	1	0.5	3.9
18-29	348	6	241	6	35	60	1.1	7.1
30-39	588	15	396	5	46	126	2.2	13.6
40-49	769	15	388	9	46	311	5.1	23.0
50-59	870	6	359	3	36	466	6.6	35.1
60-69	963	8	274	4	29	648	11.4	50.7
70-79	1,246	2	173	2	30	1,039	22.4	70.2
80+	1,421	2	125	1	34	1,259	49.0	99.1

*individuals whose NHS numbers were unavailable to link to the NIMS

Table 4. COVID-19 deaths (a) within 28 days and (b) within 60 days of positive specimen or with COVID-19 reported on death certificate, by vaccination status between week 36 and week 39 2021

(a)

Death within 28 days of positive COVID-19 test by date of death between week 36 and week 39 2021	Total	Unlinked*	Not vaccinated	Received one dose (1-20 days before specimen date)	Received one dose, ≥21 days before specimen date	Second dose ≥14 days before specimen date	Rates among persons vaccinated with 2 doses (per 100,000)	Rates among persons not vaccinated (per 100,000)
Under 18	6	3	2	1	0	0	0.0	0.0
18-29	18	1	12	0	0	5	0.1	0.4
30-39	38	2	29	0	0	7	0.1	1.0
40-49	77	3	46	0	5	23	0.4	2.7
50-59	238	6	113	1	12	106	1.5	11.0
60-69	414	7	114	0	22	271	4.8	21.1
70-79	786	3	127	0	22	634	13.7	51.6
80+	1,449	8	168	1	37	1,235	48.1	133.2

(b)

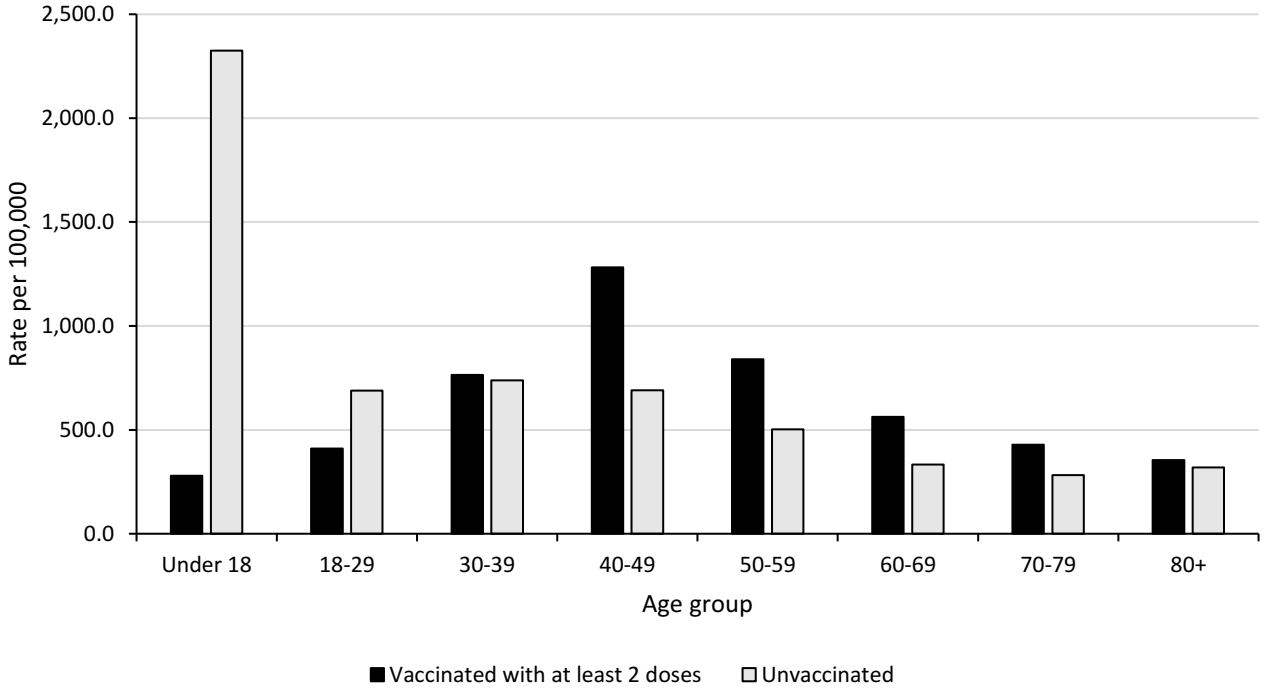
Death within 60 days of positive COVID-19 test by date of death between week 36 and week 39 2021	Total	Unlinked*	Not vaccinated	Received one dose (1-20 days before specimen date)	Received one dose, ≥21 days before specimen date	Second dose ≥14 days before specimen date	Rates among persons vaccinated with 2 doses (per 100,000)	Rates among persons not vaccinated (per 100,000)
Under 18	8	4	3	1	0	0	0.0	0.0
18-29	25	1	16	0	1	7	0.1	0.5
30-39	49	3	34	0	1	11	0.2	1.2
40-49	116	3	73	0	8	32	0.5	4.3
50-59	305	7	146	1	15	136	1.9	14.3
60-69	519	9	150	0	28	332	5.8	27.8
70-79	938	4	147	0	29	758	16.4	59.7
80+	1,711	8	183	1	45	1,474	57.4	145.1

*individuals whose NHS numbers were unavailable to link to the NIMS

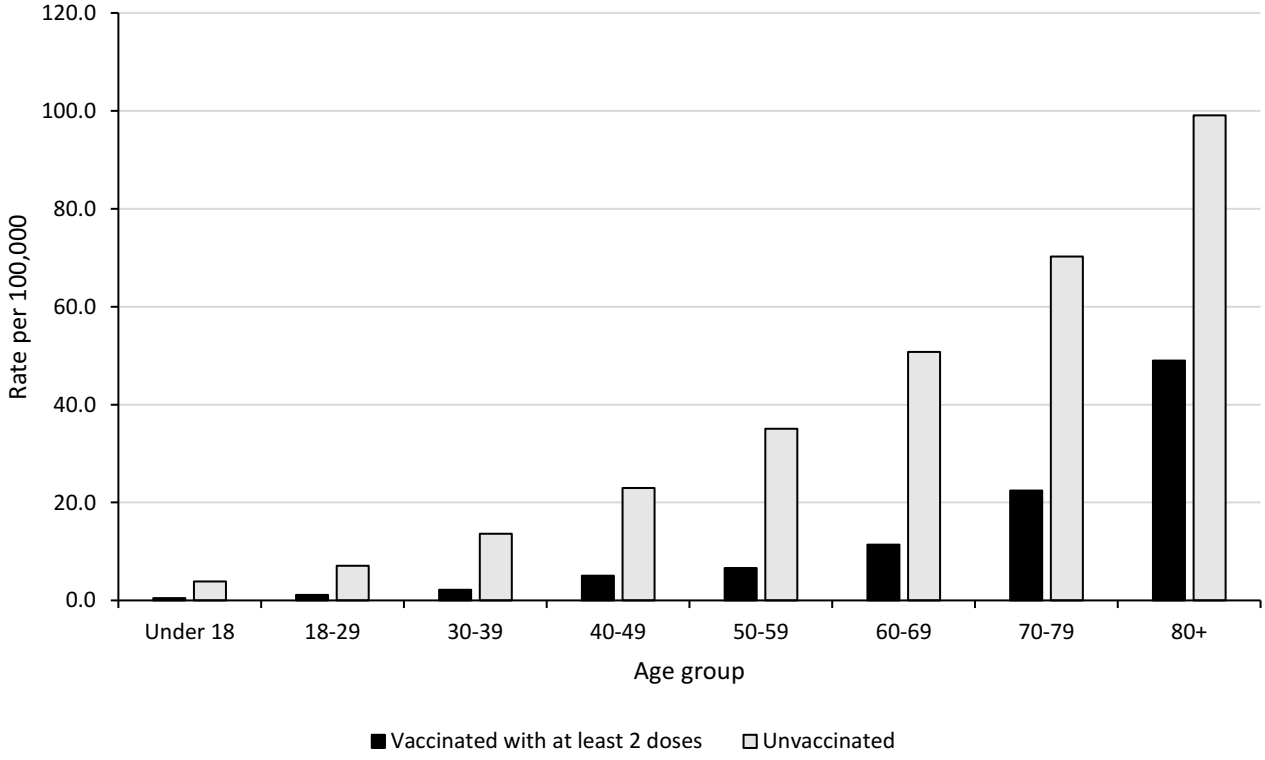
** Number of deaths of people who had had a positive test result for COVID-19 and either died within 60 days of the first positive test or have COVID-19 mentioned on their death certificate

Figure 2. Rates (per 100,000) by vaccination status from week 36 to week 39 2021

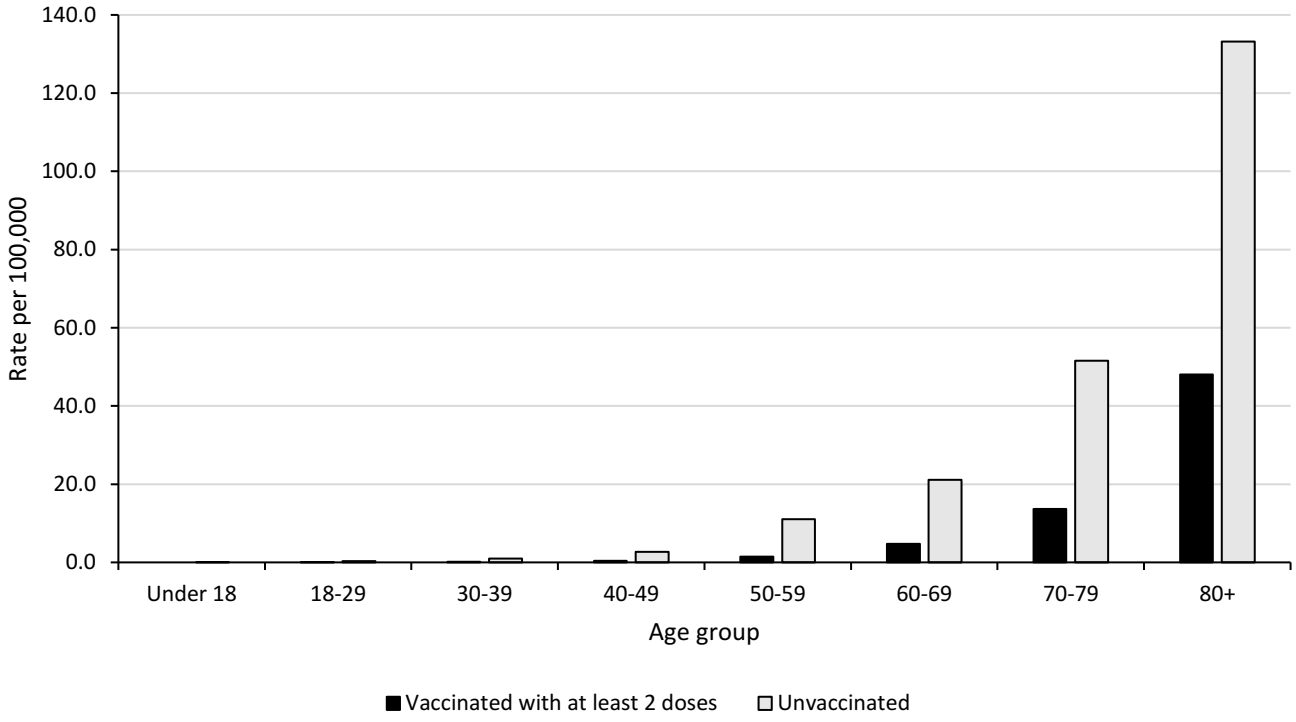
(a) COVID-19 cases



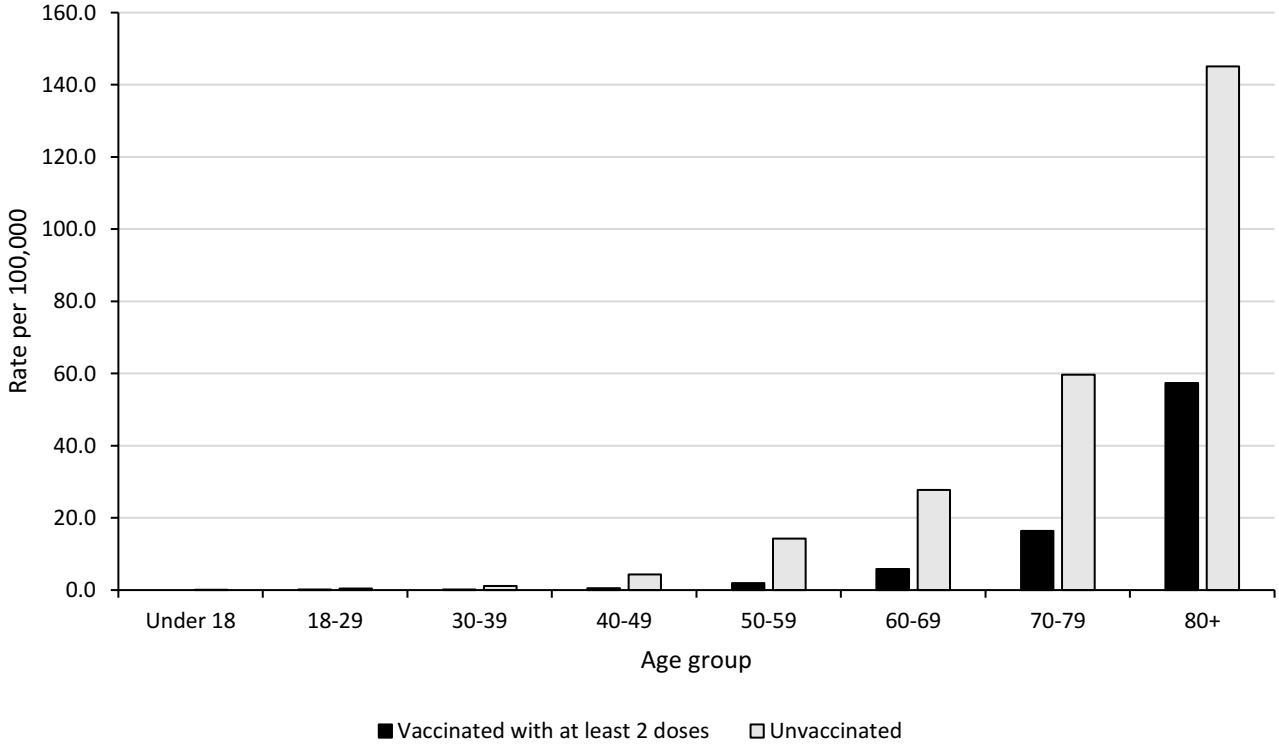
(b) Cases presenting to emergency care (within 28 days of a positive test) resulting in overnight inpatient admission



(c) Death within 28 days of positive COVID-19 test



(d) Death within 60 days of positive COVID-19 test



Vaccine impact on proportion of population with antibodies to COVID-19

UKHSA monitors the proportion of the population with antibodies to COVID-19 by testing samples provided by healthy adult blood donors aged 17 years and older, supplied by the NHS Blood and Transplant (NHS BT collection). This is important in helping to understand the extent of spread of COVID-19 infection (including asymptomatic infection) in the population and the impact of the vaccine programme. 250 samples from every geographic region in England are tested each week using 2 different laboratory tests, the Roche nucleoprotein (N) and Roche spike (S) antibody assays. This dual testing helps to distinguish between antibodies that are produced following natural COVID-19 infection and those that develop after vaccination. Nucleoprotein (Roche N) assays only detect post-infection antibodies, whereas spike (Roche S) assays will detect both post-infection antibodies and vaccine-induced antibodies. Thus, changes in the proportion of samples testing positive on the Roche N assay will reflect the effect of natural infection and spread of COVID-19 in the population. Increases in the proportion positive as measured by S antibody will reflect both infection and vaccination. Antibody responses reflect infection or vaccination occurring at least 2 to 3 weeks previously given the time taken to generate an antibody response.

In week 40, errors were identified and corrected in some historical sample records within week 30, first reported in week 32. These records had resulted in some minor variations in age specific Roche N estimates between report weeks 32 and 39, although these were unlikely to alter the interpretation of any trends. Data reported in this week's report have been corrected and the updated historical Roche N seropositivity can be seen in figure 4.

In this report, we present the results using a 4-weekly average, of testing samples up to 24 September 2021, which takes account of the age and geographical distribution of the English population. Overall, the proportion of the population with antibodies using the Roche N and Roche S assays respectively were 19.0% and 98.0% for the period 30 August to 24 September (weeks 35 to 38) (Figure 3). This compares with 18.6% Roche N seropositivity and 97.8% Roche S seropositivity for the period of 02 August to 29 August (weeks 31 to 34).

The continuing increase in seropositivity using the Roche S assay reflects the growing proportion of adults who have developed antibodies following vaccination.

Figure 4a and 4b show the proportion of the population with antibodies by age group. Recent increases in N seropositivity has been observed in some age groups. Roche N seropositivity has increased slightly in the 30 to 39 year olds from 20.9% in weeks 31 to 34 to 24.5% in weeks 35 to 38. Similarly, small increases were observed in individuals aged 60 to 69 from 11.3% in weeks 31 to 34 to 12.3% in weeks 35 to 38. Prevalence in those aged 40 to 49 years old has decreased from 19.4% in weeks 31 to 34 to 18.4% in weeks 35 to 38. Similarly, decreases were also observed in 50 to 59 year olds from 19.1% in weeks 31 to 34 to 17.7% in weeks 35 to 38. Prevalence in individuals aged 17 to 29 has remained stable at 28.0% in weeks 31 to 34 and 27.9% in weeks 35 to 38 as well as in individuals aged 70 to 84 between 7.6% in weeks 31 to 34 and 7.5% in weeks 35 to 38. Decreases in Roche N seropositivity may be due to waning of

the N antibody response over time, however it's important to note that confidence intervals overlap.

The pattern of increases in Roche S seropositivity which are observed follow the roll out of the vaccination programme with the oldest age groups offered vaccine first. (Figure 4b). Roche S seropositivity increased first in donors aged 70 to 84 and has plateaued since week 13, reaching 99.2% in weeks 35 to 38. Seropositivity has also plateaued since week 16 for those aged 60 to 69 reaching 98.7% in weeks 35 to 38. Plateauing in Roche S seropositivity has been observed since week 19 in those aged 50 to 59 reaching 98.8% in weeks 35 to 38 2021. A plateauing in seropositivity has been observed in the 40 to 49-year olds since week 23 reaching 98.6% in weeks 35 to 38. Plateauing has been observed in the 30 to 39 year olds from week 28 reaching 97.4% in weeks 35 to 38. A plateauing in seropositivity has recently been observed in the 17 to 29 year olds reaching 96.3% in weeks 35 to 38 2021.

The impact of the vaccination programme is clearly evident from the increases in the proportion of the adult population with antibodies based on Roche S testing. This was evident initially amongst individuals aged 50 years and above who were prioritised for vaccination as part of the phase 1 programme and since week 15 in younger adults and below as part of phase 2 of the vaccination programme. Roche S seropositivity is now >95% across all adult age groups.

Figure 3. Overall population weighted 4-weekly rolling SARS-CoV-2 antibody seroprevalence (% seropositive) in blood donors from the Roche S and Roche N assays.

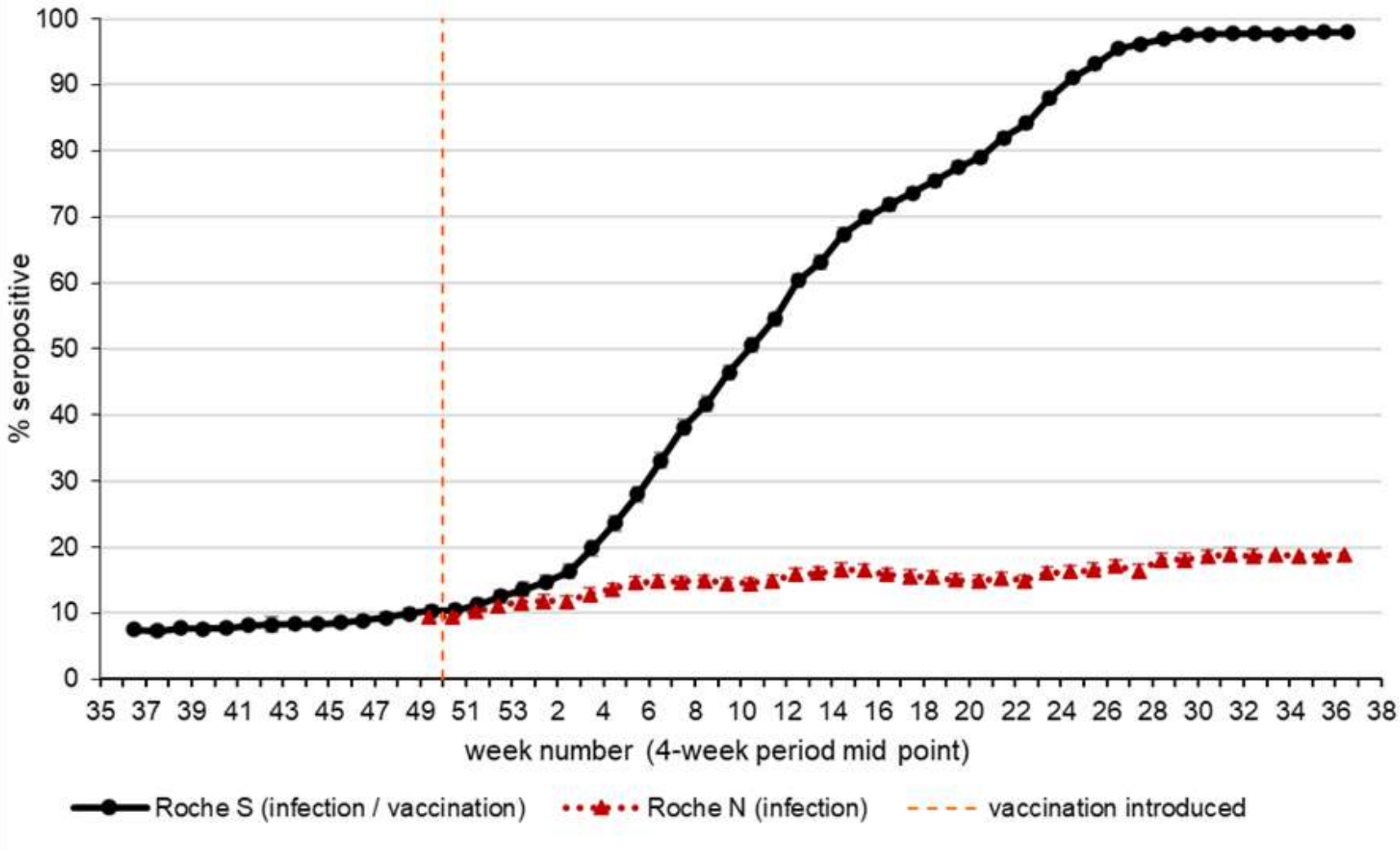
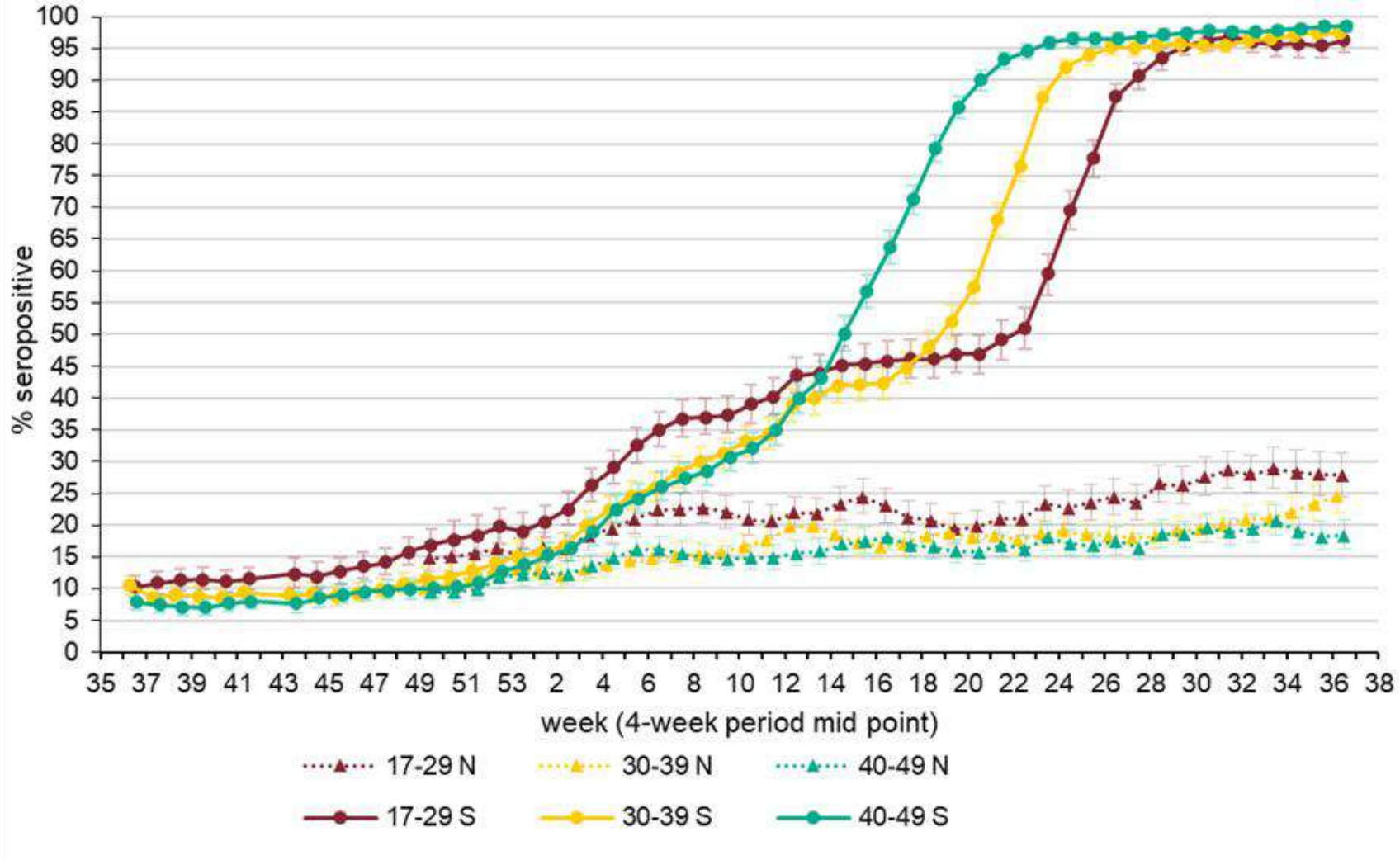
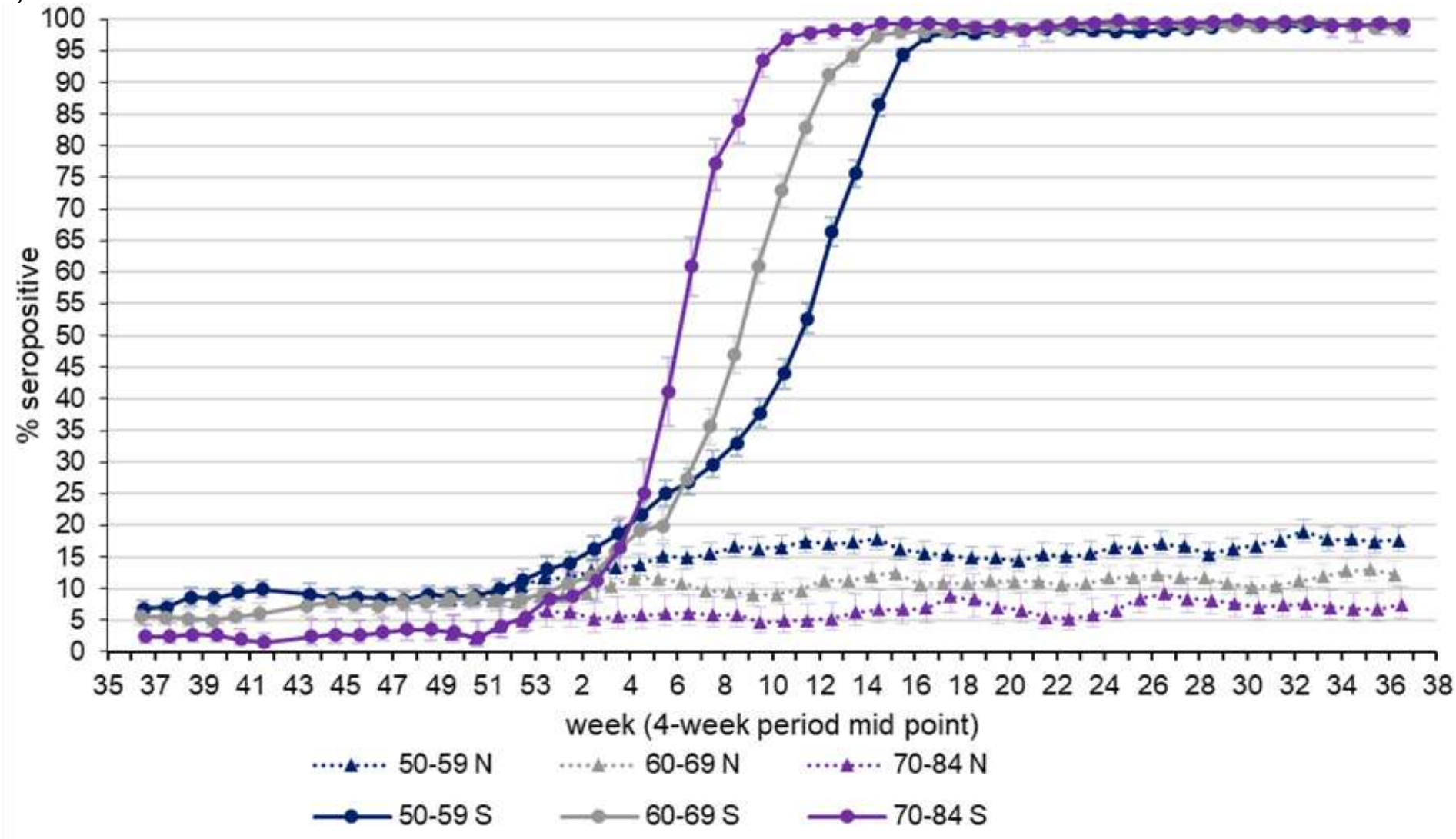


Figure 4. Population weighted 4-weekly rolling SARS-CoV-2 antibody seroprevalence (% seropositive) in blood donors from the Roche S and Roche N assays by a) age groups 17 to 29, 30 to 39 and 40 to 49, b) age group 50 to 59, 60 to 69 and 70 to 84.

a)



b)


% seropositive
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
35 37 39 41 43 45 47 49 51 53 2 4 6 8 10 12 14 16 18 20 22 24 26 28 30 32 34 36 38
week (4-week period mid point)
50-59 N
60-69 N
70-84 N
50-59 S
60-69 S
70-84 S

Summary of impact on hospitalisations, infections and mortality

UKHSA previously reported on the number of hospitalisations directly averted by vaccination. In total, around 261,500 hospitalisations have been prevented in those aged 45 years and over up to 19 September 2021.

UKHSA and University of Cambridge MRC Biostatistics Unit previously reported on the direct and indirect impact of the vaccination programme on infections and mortality. Estimates suggest that 127,500 deaths and 24,144,000 infections have been prevented as a result of the COVID-19 vaccination programme, up to 24 September.

Neither of these models will be updated going forward. This is due to these models being unable to account for the interventions that would have been implemented in the absence of vaccination. Consequently, over time the state of the actual pandemic and the no-vaccination pandemic scenario have become increasingly less comparable. For further context surrounding this figure and for previous estimates, please see previous vaccine surveillance reports.

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About the UK Health Security Agency

The UK Health Security Agency is an executive agency, sponsored by the Department of Health and Social Care.

www.ukhsa.gov.uk

Published: 7 October 2021
Publishing reference: GOV-10076

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EMEA/H/C/005735

Comirnaty (*COVID-19 mRNA vaccine [nucleoside modified]*)

An overview of Comirnaty and why it is authorised in the EU

What is Comirnaty and what is it used for?

Comirnaty is a vaccine for preventing coronavirus disease 2019 (COVID-19) in people aged 12 years and older.

Comirnaty contains a molecule called messenger RNA (mRNA) with instructions for producing a protein from SARS-CoV-2, the virus that causes COVID-19. Comirnaty does not contain the virus itself and cannot cause COVID-19.

How is Comirnaty used?

Comirnaty is given as two injections, usually into the muscle of the upper arm, 3 weeks apart.

An additional dose may be given to people with a severely weakened immune system, at least 28 days after their second dose.

A booster dose may be given at least 6 months after the second dose for people aged 18 years and older. At national level, public health bodies may issue official recommendations, taking into account emerging effectiveness data and the limited safety data.

For more information about using Comirnaty, see the package leaflet or consult a healthcare professional.

How does Comirnaty work?

Comirnaty works by preparing the body to defend itself against COVID-19. It contains a molecule called mRNA which has instructions for making the spike protein. This is a protein on the surface of the SARS-CoV-2 virus which the virus needs to enter the body's cells.

When a person is given the vaccine, some of their cells will read the mRNA instructions and temporarily produce the spike protein. The person's immune system will then recognise this protein as foreign and produce antibodies and activate T cells (white blood cells) to attack it.

If, later on, the person comes into contact with SARS-CoV-2 virus, their immune system will recognise it and be ready to defend the body against it.

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The mRNA from the vaccine does not stay in the body but is broken down shortly after vaccination.

What benefits of Comirnaty have been shown in studies?

A very large clinical trial showed that Comirnaty, given as a two-dose regimen, was effective at preventing COVID-19 in people from 12 years of age.

The trial involved around 44,000 people aged 16 and above in total. Half received the vaccine and half were given a dummy injection. People did not know whether they received the vaccine or the dummy injection.

Efficacy in people aged 16 and above was calculated in over 36,000 participants (including people over 75 years of age) who had no sign of previous infection. The study showed a 95% reduction in the number of symptomatic COVID-19 cases in the people who received the vaccine (8 cases out of 18,198 got COVID-19 symptoms) compared with people who received a dummy injection (162 cases out of 18,325 got COVID-19 symptoms). This means that the vaccine demonstrated a 95% efficacy in the trial.

The trial in people aged 16 years and older also showed around 95% efficacy in the participants at risk of severe COVID-19, including those with asthma, chronic lung disease, diabetes, high blood pressure or obesity.

The trial was extended to include 2,260 children aged 12 to 15. It showed that the immune response to Comirnaty in this group was comparable to the immune response in the 16 to 25 age group (as measured by the level of antibodies against SARS-CoV-2). The efficacy of Comirnaty was calculated in close to 2,000 children from 12 to 15 who had no sign of previous infection. These received either the vaccine or a placebo (a dummy injection), without knowing which one they were given. Of the 1,005 children receiving the vaccine, none developed COVID-19 compared to 16 children out of the 978 who received the dummy injection. This means that, in this study, the vaccine was 100% effective at preventing COVID-19 (although the true rate could be between 75% and 100%).

Another study showed that an additional dose of Comirnaty increased the ability to produce antibodies against SARS-CoV-2 in organ transplant patients with severely weakened immune systems.

Further data showed a rise in antibody levels when a booster dose was given after the second dose in people from 18 to 55 years old with a normal immune system.

Can people who have already had COVID-19 be vaccinated with Comirnaty?

There were no additional side effects in the 545 people who received Comirnaty in the trial and had previously had COVID-19.

There were not enough data from the trial to conclude on how well Comirnaty works for people who have already had COVID-19.

Can Comirnaty reduce transmission of the virus from one person to another?

The impact of vaccination with Comirnaty on the spread of the SARS-CoV-2 virus in the community is not yet known. It is not yet known how much vaccinated people may still be able to carry and spread the virus.

How long does protection from Comirnaty last?

It is not currently known how long protection given by Comirnaty lasts. The people vaccinated in the clinical trial will continue to be followed for 2 years to gather more information on the duration of protection.

Can children be vaccinated with Comirnaty?

Comirnaty is not currently authorised for children below 12 years of age.

Can immunocompromised people be vaccinated with Comirnaty?

There are limited data on immunocompromised people. Although immunocompromised people may not respond as well to the vaccine, there are no particular safety concerns. Immunocompromised people can still be vaccinated as they may be at higher risk from COVID-19.

Severely immunocompromised people may be given an additional dose of Comirnaty, at least 28 days after their second dose.

Can pregnant or breast-feeding women be vaccinated with Comirnaty?

Animal studies do not show any harmful effects in pregnancy, however data on the use of Comirnaty during pregnancy are very limited. Although there are no studies on breast-feeding, no risk for breast-feeding is expected.

The decision on whether to use the vaccine in pregnant women should be made in close consultation with a healthcare professional after considering the benefits and risks.

Can people with allergies be vaccinated with Comirnaty?

People who already know they have an allergy to one of the components of the vaccine listed in section 6 of the package leaflet should not receive the vaccine.

Allergic reactions (hypersensitivity) have been seen in people receiving the vaccine. A very small number of cases of anaphylaxis (severe allergic reaction) have occurred since the vaccine started being used in vaccination campaigns. Therefore, as for all vaccines, Comirnaty should be given under close medical supervision, with the appropriate medical treatment available. People who have a severe allergic reaction when they are given the first dose of Comirnaty should not receive the second dose.

How well does Comirnaty work for people of different ethnicities and genders?

The main trial included people of different ethnicities and genders. Efficacy of around 95% was maintained across genders and ethnic groups.

What are the risks associated with Comirnaty?

The most common side effects with Comirnaty were usually mild or moderate and got better within a few days after vaccination. These included pain and swelling at the injection site, tiredness, headache, muscle and joint pain, chills, fever and diarrhoea. They affected more than 1 in 10 people.

Redness at the injection site, nausea and vomiting occurred in less than 1 in 10 people. Itching at the injection site, pain in the arm where the vaccine was injected, enlarged lymph nodes, difficulty sleeping, feeling unwell, decreased appetite, lethargy (lack of energy), hyperhidrosis (excessive

sweating), night sweats, asthenia (weakness), and allergic reactions (such as rash, itching, itchy rash, and rapid swelling under the skin) were uncommon side effects (affecting less than 1 in 100 people). Weakness in muscles on one side of face (acute peripheral facial paralysis or palsy) occurred rarely in less than 1 in 1,000 people.

A very small number of cases of myocarditis (inflammation of the heart muscle) and pericarditis (inflammation of the membrane around the heart) have occurred with Comirnaty. Allergic reactions have also occurred with Comirnaty, including a very small number of cases of severe allergic reactions (anaphylaxis). As for all vaccines, Comirnaty should be given under close supervision with appropriate medical treatment available.

Why is Comirnaty authorised in the EU?

Comirnaty offers a high level of protection against COVID-19 which is a critical need in the current pandemic. The main trial showed that the vaccine has a 95% efficacy. Most side effects are mild to moderate in severity and are gone within a few days.

The Agency therefore decided that Comirnaty's benefits are greater than its risks and that it can be authorised for use in the EU.

Comirnaty has been granted a conditional marketing authorisation. This means that there is more evidence to come about the vaccine (see below), which the company is required to provide. The Agency will review any new information that becomes available and this overview will be updated as necessary.

What information is still awaited for Comirnaty?

As Comirnaty received a conditional marketing authorisation, the company that markets Comirnaty will continue to provide results from the main trial, which is ongoing for 2 years. This trial and additional studies will provide information on how long protection lasts, how well the vaccine prevents severe COVID-19, how well it protects immunocompromised people, pregnant women, and whether it prevents asymptomatic cases.

In addition, independent studies of COVID-19 vaccines coordinated by EU authorities will also give more information on the vaccine's long-term safety and benefit in the general population.

The company will also carry out studies to provide additional assurance on the pharmaceutical quality of the vaccine as the manufacturing continues to be scaled up.

What measures are being taken to ensure the safe and effective use of Comirnaty?

Recommendations and precautions to be followed by healthcare professionals and patients for the safe and effective use of Comirnaty have been included in the summary of product characteristics and the package leaflet.

A risk management plan (RMP) for Comirnaty is also in place and contains important information about the vaccine's safety, how to collect further information and how to minimise any potential risks.

Safety measures will be implemented for Comirnaty in line with the EU safety monitoring plan for COVID-19 vaccines to ensure that new safety information is rapidly collected and analysed. The company that markets Comirnaty will provide monthly safety reports.

As for all medicines, data on the use of Comirnaty are continuously monitored. Suspected side effects reported with Comirnaty are carefully evaluated and any necessary action taken to protect patients.

Other information about Comirnaty

Comirnaty received a conditional marketing authorisation valid throughout the EU on 21 December 2020.

Further information on Comirnaty can be found on the Agency's website: ema.europa.eu/medicines/human/EPAR/comirnaty

This overview was last updated in 10-2021.

EMA/564427/2021
EMEA/H/C/005791

Spikevax[1] (*COVID-19 mRNA vaccine [nucleoside modified]*)

An overview of Spikevax and why it is authorised in the EU

What is Spikevax and what is it used for?

Spikevax is a vaccine for preventing coronavirus disease 2019 (COVID-19) in people aged 12 years and older.

Spikevax contains a molecule called messenger RNA (mRNA) with instructions for producing a protein from SARS-CoV-2, the virus that causes COVID-19. Spikevax does not contain the virus itself and cannot cause COVID-19.

How is Spikevax used?

Spikevax is given as two injections, usually into the muscle of the upper arm, 28 days apart. An additional dose may be given to people with a severely weakened immune system, at least 28 days after their second dose.

For more information about using Spikevax, see the package leaflet or consult a healthcare professional.

How does Spikevax work?

Spikevax works by preparing the body to defend itself against COVID-19. It contains a molecule called mRNA which has instructions for making the spike protein. This is a protein on the surface of the SARS-CoV-2 virus which the virus needs to enter the body's cells.

When a person is given the vaccine, some of their cells will read the mRNA instructions and temporarily produce the spike protein. The person's immune system will then recognise this protein as foreign and produce antibodies and activate T cells (white blood cells) to attack it.

If, later on, the person comes into contact with SARS-CoV-2 virus, their immune system will recognise it and be ready to defend the body against it.

The mRNA from the vaccine does not stay in the body but is broken down shortly after vaccination.

[1] Previously known as COVID-19 Vaccine Moderna

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What benefits of Spikevax have been shown in studies?

A very large clinical trial showed that Spikevax, given as a two-dose regimen, was effective at preventing COVID-19 in people from 18 years of age. The trial involved around 30,000 people in total. Half received the vaccine and half were given dummy injections. People did not know whether they received the vaccine or the dummy injections.

Efficacy was calculated in around 28,000 people from 18 to 94 years of age who had no sign of previous infection.

The trial showed a 94.1% reduction in the number of symptomatic COVID-19 cases in the people who received the vaccine (11 out of 14,134 vaccinated people got COVID-19 with symptoms) compared with people who received dummy injections (185 out of 14,073 people who received dummy injections got COVID-19 with symptoms). This means that the vaccine demonstrated a 94.1% efficacy in the trial. The trial also showed 90.9% efficacy in participants at risk of severe COVID-19, including those with chronic lung disease, heart disease, obesity, liver disease, diabetes or HIV infection.

The effects of Spikevax were also investigated in a study involving over 3,000 children aged 12 to 17 years. The study showed that Spikevax produced a comparable antibody response in 12- to 17-year-olds to that seen in young adults (aged 18 to 25 years), as measured by the level of antibodies against SARS-CoV-2. In addition, none of 2,163 children receiving the vaccine developed COVID-19, compared with four of 1,073 children given a dummy injection. These results allowed to conclude that the efficacy of Spikevax in children 12 to 17 years old is similar to that in adults.

Another study showed that an additional dose of Spikevax increased the ability to produce antibodies against SARS-CoV-2 in organ transplant patients with severely weakened immune systems.

Can people who have already had COVID-19 be vaccinated with Spikevax?

There were no additional side effects in the 343 people who received Spikevax in the trial and had previously had COVID-19.

There were not enough data from the trial to conclude on how well Spikevax works for people who have already had COVID-19.

Can Spikevax reduce transmission of the virus from one person to another?

The impact of vaccination with Spikevax on the spread of the SARS-CoV-2 virus in the community is not yet known. It is not yet known how much vaccinated people may still be able to carry and spread the virus.

How long does protection from Spikevax last?

It is not currently known how long protection given by Spikevax lasts. The people vaccinated in the clinical trial will continue to be followed for 2 years to gather more information on the duration of protection.

Can children be vaccinated with Spikevax?

Spikevax is not currently authorised for children below 12 years of age.

Can immunocompromised people be vaccinated with Spikevax?

There are limited data on immunocompromised people. Although immunocompromised people may not respond as well to the vaccine, there are no particular safety concerns. Immunocompromised people can still be vaccinated as they may be at higher risk from COVID-19.

Severely immunocompromised people may be given an additional dose of Spikevax, at least 28 days after their second dose.

Can pregnant or breast-feeding women be vaccinated with Spikevax?

Animal studies do not show any harmful effects in pregnancy, however data on the use of Spikevax during pregnancy are very limited. Although there are no studies on breast-feeding, no risk from breast-feeding is expected.

The decision on whether to use the vaccine in pregnant women should be made in close consultation with a healthcare professional after considering the benefits and risks.

Can people with allergies be vaccinated with Spikevax?

People who already know they have an allergy to one of the components of the vaccine listed in section 6 of the package leaflet should not receive the vaccine.

Allergic reactions (hypersensitivity) have been seen in people receiving the vaccine. A very small number of cases of anaphylaxis (severe allergic reaction) have occurred. Therefore, as for all vaccines, Spikevax should be given under close medical supervision, with the appropriate medical treatment available in case of allergic reactions. People who have a severe allergic reaction when they are given the first dose of Spikevax should not receive the second dose.

How well does Spikevax work for people of different ethnicities and genders?

The clinical trials included people of different ethnicities and genders. The high efficacy was maintained across genders and ethnic groups.

What are the risks associated with Spikevax?

The most common side effects with Spikevax in the trials were usually mild or moderate and got better within a few days after vaccination.

The most common side effects are pain and swelling at the injection site, tiredness, chills, fever, swollen or tender lymph nodes under the arm, headache, muscle and joint pain, nausea (feeling sick) and vomiting. They may affect more than 1 in 10 people.

Redness, hives and rash at the injection site, sometimes occurring more than a week after injection, and rash may affect less than 1 in 10 people. Itching at the injection site and dizziness may affect less than 1 in 100 people. Swelling of the face, which may affect people who had facial cosmetic injections in the past, weakness in muscles on one side of the face (acute peripheral facial paralysis or palsy) and hypoaesthesia (reduced sensation to touch, pain and temperature) may affect less than 1 in 1,000 people.

A very small number of cases of myocarditis (inflammation of the heart muscle) and pericarditis (inflammation of the membrane around the heart) have occurred with Spikevax. Allergic reactions have also occurred in people receiving the vaccine, including a very small number of cases of severe

allergic reactions (anaphylaxis). As for all vaccines, Spikevax should be given under close supervision with appropriate medical treatment available.

Why is Spikevax authorised in the EU?

Spikevax offers a high level of protection against COVID-19 which is a critical need in the current pandemic. The main trial showed that the vaccine has a 94.1% efficacy in adults; the efficacy of Spikevax in children 12 to 17 years old is similar to that in adults. Most side effects are mild to moderate in severity and are gone within a few days.

The European Medicines Agency therefore decided that Spikevax's benefits are greater than its risks and it can be authorised for use in the EU.

Spikevax has been given 'conditional marketing authorisation'. This means that there is more evidence to come about the vaccine (see below), which the company is required to provide. The Agency will review any new information that becomes available and this overview will be updated as necessary.

What information is still awaited for Spikevax?

Since Spikevax has been given conditional marketing authorisation, the company that markets Spikevax will provide final results from the two clinical trials, which will continue until the end of 2022. These trials and additional studies will provide information on how long protection lasts, how well the vaccine prevents severe COVID-19, how well it protects immunocompromised people, pregnant women, and whether it prevents asymptomatic cases.

In addition, independent studies of COVID-19 vaccines coordinated by EU authorities will also give more information on the vaccine's long-term safety and benefit in the general population.

The company will also carry out studies to provide additional assurance on the pharmaceutical quality of the vaccine as the manufacturing continues to be scaled up.

What measures are being taken to ensure the safe and effective use of Spikevax?

Recommendations and precautions to be followed by healthcare professionals and patients for the safe and effective use of Spikevax have been included in the summary of product characteristics and the package leaflet.

A risk management plan (RMP) for Spikevax is also in place and contains important information about the vaccine's safety, how to collect further information and how to minimise any potential risks.

Safety measures will be implemented for Spikevax in line with the EU safety monitoring plan for COVID-19 vaccines to ensure that new safety information is rapidly collected and analysed. The company that markets Spikevax will provide monthly safety reports.

As for all medicines, data on the use of Spikevax are continuously monitored. Suspected side effects reported with Spikevax are carefully evaluated and any necessary action taken to protect patients.

Other information about Spikevax

COVID-19 Vaccine Moderna received a conditional marketing authorisation valid throughout the EU on 6 January 2021.

The name of the vaccine was changed to Spikevax on 22 June 2021.

Further information on Spikevax can be found on the Agency's website: ema.europa.eu/medicines/human/EPAR/spikevax-previously-covid-19-vaccine-moderna

This overview was last updated in 10-2021.

EMA/542013/2021
EMEA/H/C/005675

Vaxzevria[1] *(COVID-19 Vaccine (ChAdOx1-S [recombinant]))*

An overview of Vaxzevria and why it is authorised in the EU

What is Vaxzevria and what is it used for?

Vaxzevria is a vaccine for preventing coronavirus disease 2019 (COVID-19) in people aged 18 years and older. COVID-19 is caused by SARS-CoV-2 virus.

Vaxzevria is made up of another virus (of the adenovirus family) that has been modified to contain the gene for making a protein from SARS-CoV-2.

Vaxzevria does not contain the virus itself and cannot cause COVID-19.

Detailed information about this vaccine is available in the product information, which includes the package leaflet.

How is Vaxzevria used?

Vaxzevria is given as two injections, usually into the muscle of the upper arm. The second dose should be given between 4 and 12 weeks after the first dose.

Arrangements for the supply of the vaccine are the responsibility of national authorities. For more information about using Vaxzevria, see the package leaflet or talk to a healthcare professional.

How does Vaxzevria work?

Vaxzevria works by preparing the body to defend itself against COVID-19. It is made up of another virus (adenovirus) that has been modified to contain the gene for making the SARS-CoV-2 spike protein. This is a protein on the surface of the SARS-CoV-2 virus which the virus needs to enter the body's cells.

Once it has been given, the vaccine delivers the SARS-CoV-2 gene into cells in the body. The cells will use the gene to produce the spike protein. The person's immune system will then recognise this protein as foreign and produce antibodies and activate T cells (white blood cells) to attack it.

[1] Previously known as COVID-19 Vaccine AstraZeneca

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If, later on, the person comes into contact with SARS-CoV-2 virus, their immune system will recognise it and be ready to defend the body against it.

The adenovirus in the vaccine cannot reproduce and does not cause disease.

What benefits of Vaxzevria have been shown in studies?

Combined results from 4 clinical trials in the United Kingdom, Brazil and South Africa showed that Vaxzevria was safe and effective at preventing COVID-19 in people from 18 years of age. These studies involved around 24,000 people altogether. Half received the vaccine and half were given a control injection, either a dummy injection or another non-COVID vaccine. People did not know if they had been given the test vaccine or the control injection.

The Agency based its calculation of how well the vaccine worked on the results from study COV002 (conducted in the UK) and study COV003 (conducted in Brazil). The other two studies had fewer than 6 COVID-19 cases occurring in each, which was not enough to measure the preventive effect of the vaccine. In addition, as the vaccine is to be given as two standard doses, and the second dose should be given between 4 and 12 weeks after the first, the Agency concentrated on results involving people who received this standard regimen.

These showed a 59.5% reduction in the number of symptomatic COVID-19 cases in people given the vaccine (64 of 5,258 got COVID-19 with symptoms) compared with people given control injections (154 of 5,210 got COVID-19 with symptoms). This means that the vaccine demonstrated around a 60% efficacy in the clinical trials.

Most of the participants in these studies were between 18 and 55 years old. There were not enough results in older participants (over 55 years old) to provide a figure for how well the vaccine will work in this group. However, protection is expected, given that an immune response is seen in this age group and based on experience with other vaccines; as there is reliable information on safety in this population, EMA's scientific experts considered that the vaccine can be used in older adults. More information is expected from ongoing studies, which include a higher proportion of elderly participants.

Can people who have already had COVID-19 be vaccinated with Vaxzevria?

There were no additional side effects in the 345 people who received Vaxzevria in the trial and had previously had COVID-19.

There were not enough data from the trial to conclude on how well Vaxzevria works for people who have already had COVID-19.

Can Vaxzevria reduce transmission of the virus from one person to another?

The impact of vaccination with Vaxzevria on the spread of the SARS-CoV-2 virus in the community is not yet known. It is not yet known how much vaccinated people may still be able to carry and spread the virus.

How long does protection from Vaxzevria last?

It is not currently known how long protection given by Vaxzevria lasts. The people vaccinated in the clinical trials will continue to be followed for 1 year to gather more information on the duration of protection.

Can children be vaccinated with Vaxzevria?

Vaxzevria is not currently authorised for use in children. EMA has agreed with the company on a plan to conduct trials involving children at a later stage.

Can immunocompromised people be vaccinated with Vaxzevria?

There are limited data on immunocompromised people (people with weakened immune systems). Although immunocompromised people may not respond as well to the vaccine, there are no particular safety concerns. Immunocompromised people can still be vaccinated as they may be at higher risk from COVID-19.

Can pregnant or breast-feeding women be vaccinated with Vaxzevria?

Preliminary animal studies do not show any harmful effects in pregnancy, however data on the use of Vaxzevria during pregnancy are very limited. Although there are no studies on breast-feeding, no risk from breast-feeding is expected.

The decision on whether to use the vaccine in pregnant women should be made in close consultation with a healthcare professional after considering the benefits and risks.

Can people with allergies be vaccinated with Vaxzevria?

People who already know they have an allergy to one of the components of the vaccine listed in section 6 of the package leaflet should not receive the vaccine.

Allergic reactions (hypersensitivity) have been seen in people receiving the vaccine. Cases of anaphylaxis (severe allergic reaction) have also occurred. As for all vaccines, Vaxzevria should be given under close medical supervision, with the appropriate medical treatment available in case of allergic reactions. People who have a severe allergic reaction when they are given the first dose of Vaxzevria should not receive the second dose.

How well does Vaxzevria work for people of different ethnicities and genders?

The clinical trial included people of different ethnicities and genders. The efficacy was maintained across genders and ethnic groups.

What are the risks associated with Vaxzevria?

The most common side effects with Vaxzevria in the trials were usually mild or moderate and got better within a few days after vaccination. When compared with the first dose, side effects reported after the second dose were milder and reported less frequently. People receiving Vaxzevria may experience more than one side effect at the same time.

The most common side effects are tenderness, pain and bruising at the injection site, headache, tiredness, muscle pain, general feeling of being unwell, chills, fever, joint pain and nausea (feeling sick). They may affect more than 1 in 10 people.

Thrombocytopenia (low levels of blood platelets), vomiting, diarrhoea, pain in legs or arms, swelling and redness at the injection site, flu-like illness and asthenia (weakness) may affect up to 1 in 10 people. Lymphadenopathy (enlarged lymph nodes), decreased appetite, dizziness, sleepiness, lethargy (lack of energy), sweating, abdominal (belly) pain, itching, rash and urticaria (itchy rash) may affect

up to 1 in 100 people. Thrombosis (formation of blood clots in the blood vessels) in combination with thrombocytopenia (thrombosis with thrombocytopenia syndrome, TTS) and Guillain-Barré syndrome (a neurological disorder in which the body's immune system damages nerve cells) may affect up to 1 in 10,000 people.

A very small number of cases of angioedema (rapid swelling under the skin) have occurred with Vaxzevria, as well as a very small number of cases of capillary leak syndrome (fluid leakage from small blood vessels causing tissue swelling and a drop in blood pressure).

Allergic reactions have occurred in people receiving the vaccine, including some cases of severe allergic reactions (anaphylaxis). As for all vaccines, Vaxzevria should be given under close supervision with appropriate medical treatment available.

Vaxzevria must not be given to people who have had thrombosis with thrombocytopenia syndrome (TTS) after receiving the vaccine. Vaxzevria must also not be given to people who have previously had capillary leak syndrome.

Why is Vaxzevria authorised in the EU?

Vaxzevria offers a good level of protection against COVID-19 which is a critical need in the current pandemic. The main trials showed that the vaccine has around 60% efficacy. Most side effects are mild to moderate in severity and are gone within a few days.

The European Medicines Agency decided that Vaxzevria's benefits are greater than its risks and it can be authorised for use in the EU.

Vaxzevria has been given 'conditional authorisation'. This means that there is more evidence to come about the vaccine (see below), which the company is required to provide. The Agency will review any new information that becomes available and this overview will be updated as necessary.

What information is still awaited for Vaxzevria?

Since Vaxzevria has been given conditional authorisation, the company that markets the vaccine will continue to provide results from the clinical trials, which are ongoing. These trials and additional studies will provide information on how long protection lasts, including against new variants of the virus, how well the vaccine prevents severe COVID-19, how well it protects older people, immunocompromised people, children and pregnant women, and whether it prevents asymptomatic cases.

In addition, independent studies of COVID-19 vaccines coordinated by EU authorities will also give more information on the vaccine's long-term safety and benefit in the general population.

The company will also carry out studies to provide additional assurance on the pharmaceutical quality and testing of the vaccine as the manufacturing continues to be scaled up.

What measures are being taken to ensure the safe and effective use of Vaxzevria?

Recommendations and precautions to be followed by healthcare professionals and patients for the safe and effective use of Vaxzevria have been included in the summary of product characteristics and the package leaflet.

A risk management plan for Vaxzevria is also in place and contains important information about the vaccine's safety, how to collect further information and how to minimise any potential risks. A summary of the RMP is available.

Safety measures will be implemented for Vaxzevria in line with the EU safety monitoring plan for COVID-19 vaccines to ensure that new safety information is rapidly collected and analysed. The company that markets Vaxzevria will provide monthly safety reports.

As for all medicines, data on the use of Vaxzevria are continuously monitored. Suspected side effects reported with Vaxzevria are carefully evaluated and any necessary action taken to protect patients.

Other information about Vaxzevria

COVID-19 Vaccine AstraZeneca received a conditional marketing authorisation valid throughout the EU on 29 January 2021.

The name of the vaccine was changed to Vaxzevria on 25 March 2021.

Further information on Vaxzevria can be found on the Agency's website: ema.europa.eu/medicines/human/EPAR/vaxzevria.

This overview was last updated in 09-2021.

EMA/565324/2021
EMEA/H/C/005737

COVID-19 Vaccine Janssen (*COVID-19 vaccine (Ad26.COV2-S [recombinant])*)

An overview of COVID-19 Vaccine Janssen and why it is authorised in the EU

What is COVID-19 Vaccine Janssen and what is it used for?

COVID-19 Vaccine Janssen is a vaccine for preventing coronavirus disease 2019 (COVID-19) in people aged 18 years and older. COVID-19 is caused by SARS-CoV-2 virus.

COVID-19 Vaccine Janssen is made up of another virus (of the adenovirus family) that has been modified to contain the gene for making a protein found on SARS-CoV-2.

COVID-19 Vaccine Janssen does not contain SARS-CoV-2 itself and cannot cause COVID-19.

Detailed information about this vaccine is available in the product information, which includes the package leaflet.

How is COVID-19 Vaccine Janssen used?

COVID-19 Vaccine Janssen is given as a single injection, usually into the muscle of the upper arm.

Arrangements for the supply of the vaccine are the responsibility of national authorities. For more information about using COVID-19 Vaccine Janssen, see the package leaflet or talk to a healthcare professional.

How does COVID-19 Vaccine Janssen work?

COVID-19 Vaccine Janssen works by preparing the body to defend itself against COVID-19. It is made up of another virus (an adenovirus) that has been modified to contain the gene for making the SARS-CoV-2 spike protein. This is a protein on the SARS-CoV-2 virus which it needs to enter the body's cells.

The adenovirus passes the SARS-CoV-2 gene into the vaccinated person's cells. The cells can then use the gene to produce the spike protein. The person's immune system will recognise the spike protein as foreign and produce antibodies and activate T cells (white blood cells) to target it.

Later, if the person comes into contact with SARS-CoV-2 virus, the person's immune system will recognise the spike protein on the virus and be ready to defend the body against it.

The adenovirus in the vaccine cannot reproduce and does not cause the disease.

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What benefits of COVID-19 Vaccine Janssen have been shown in studies?

Results from a clinical trial involving people in the United States, South Africa and Latin American countries found that COVID-19 Vaccine Janssen was effective at preventing COVID-19 in people from 18 years of age. This study involved over 44,000 people. Half received a single dose of the vaccine and half were given placebo (a dummy injection). People did not know if they had been given COVID-19 Vaccine Janssen or placebo.

The trial found a 67% reduction in the number of symptomatic COVID-19 cases after 2 weeks in people who received COVID-19 Vaccine Janssen (116 cases out of 19,630 people) compared with people given placebo (348 of 19,691 people). This means that the vaccine had a 67% efficacy.

Can people who have already had COVID-19 be vaccinated with COVID-19 Vaccine Janssen?

There were no additional side effects in 2,151 people who received COVID-19 Vaccine Janssen in the trials and had previously had COVID-19.

There were not enough data from the trials to conclude on how well COVID-19 Vaccine Janssen works for people who have already had COVID-19.

Can COVID-19 Vaccine Janssen reduce transmission of the virus from one person to another?

The effect of COVID-19 Vaccine Janssen on the spread of the SARS-CoV-2 virus in the community is not yet known. It is not yet known to what extent vaccinated people may still be able to carry and spread the virus.

How long does protection from COVID-19 Vaccine Janssen last?

Protection with COVID-19 Vaccine Janssen starts around 14 days after vaccination but it is not currently known how long protection continues. The people vaccinated in the clinical trials will continue to be followed for 2 years to gather more information on the duration of protection.

Can children be vaccinated with COVID-19 Vaccine Janssen?

COVID-19 Vaccine Janssen is not currently authorised for use in children. EMA has agreed with the company on a plan to conduct trials involving children.

Can immunocompromised people be vaccinated with COVID-19 Vaccine Janssen?

There are no data on immunocompromised people (people with weakened immune systems). Although immunocompromised people may not respond as well to the vaccine, there are no particular safety concerns. Immunocompromised people can still be vaccinated as they may be at higher risk from COVID-19.

Can pregnant or breast-feeding women be vaccinated with COVID-19 Vaccine Janssen?

Animal studies do not show any harmful effects of COVID-19 Vaccine Janssen in pregnancy. However, data on the use of COVID-19 Vaccine Janssen during pregnancy are very limited.

There are no studies of COVID-19 Vaccine Janssen on breast-feeding but no risk from breast-feeding is expected.

The decision on whether to use the vaccine in pregnant women should be made in close consultation with a healthcare professional after considering the benefits and risks.

Can people with allergies be vaccinated with COVID-19 Vaccine Janssen?

People who have an allergy to one of the components of the vaccine listed in section 6 of the package leaflet should not receive the vaccine.

Allergic reactions (hypersensitivity) have occurred in people receiving the vaccine. One case of anaphylaxis (severe allergic reaction) has occurred in an ongoing study. As for all vaccines, COVID-19 Vaccine Janssen should be given under close medical supervision, with the appropriate medical treatment available in case of allergic reactions.

How well does COVID-19 Vaccine Janssen work for people of different ethnicities and genders?

The clinical trials included people of different ethnicities and genders. The vaccine worked across genders and ethnic groups.

What are the risks associated with COVID-19 Vaccine Janssen?

The most common side effects with COVID-19 Vaccine Janssen in the trials were usually mild or moderate and got better within 1 or 2 days after vaccination.

The most common side effects are pain at the injection site, headache, tiredness, muscle pain and nausea. They may affect more than 1 in 10 people.

Coughing, joint pain, fever, chills, as well as redness and swelling at injection site may affect up to 1 in 10 people. Sneezing, tremor, dizziness, paraesthesia (unusual sensations like numbness, tingling or pins and needles), throat pain, rash, sweating, diarrhoea, muscle weakness, pain in the arms and legs, backache, weakness and feeling generally unwell may affect up to 1 in 100 people. Rare side effects (which may affect up to 1 in 1,000 people) are venous thromboembolism (formation of blood clots in veins), lymphadenopathy (enlarged lymph nodes), hypoesthesia (reduced sensation to touch, pain and temperature), tinnitus (ringing or buzzing in the ears), vomiting, hypersensitivity (allergy) and itchy rash.

Thrombosis (formation of blood clots in the blood vessels) in combination with thrombocytopenia (low levels of blood platelets) and Guillain-Barré syndrome (a neurological disorder in which the body's immune system damages nerve cells) may affect up to 1 in 10,000 people.

Allergic reactions, including anaphylaxis (severe allergic reaction), have occurred in people receiving the vaccine. As for all vaccines, COVID-19 Vaccine Janssen should be given under close supervision with appropriate medical treatment available.

A very small number of cases of immune thrombocytopenia (a condition in which the immune system mistakenly targets blood platelets reducing their levels and affecting normal blood clotting) and capillary leak syndrome (fluid leakage from small blood vessels causing tissue swelling and a drop in blood pressure) have occurred with COVID-19 Vaccine Janssen.

COVID-19 Vaccine Janssen must not be given to people who have previously had capillary leak syndrome.

Why is COVID-19 Vaccine Janssen authorised in the EU?

COVID-19 Vaccine Janssen offers a good level of protection against COVID-19 which is critical during the current pandemic. The main trial showed that the vaccine has around 67% efficacy. Most side effects are mild to moderate in severity and last only a few days.

The European Medicines Agency therefore decided that COVID-19 Vaccine Janssen's benefits are greater than its risks and it can be authorised for use in the EU.

COVID-19 Vaccine Janssen has been given 'conditional marketing authorisation'. This means that there is more evidence to come about the vaccine (see below), which the company is required to provide. The Agency will review any new information that becomes available and this overview will be updated as necessary.

What information is still awaited for COVID-19 Vaccine Janssen?

Since COVID-19 Vaccine Janssen has been given conditional marketing authorisation, the company that markets the vaccine will provide results from ongoing clinical trials. These trials and additional studies will provide information on how long protection lasts, the vaccine's effectiveness against new variants of the virus, how well it protects older people, people of different ethnicities, immunocompromised people, children and pregnant women, whether it prevents asymptomatic cases, and the effects and timing of a second dose of the vaccine.

In addition, independent studies of COVID-19 vaccines coordinated by EU authorities will also give more information on the vaccine's long-term safety and benefits in the general population.

The company will also carry out studies to provide additional assurance on the pharmaceutical quality and testing of the vaccine as the manufacturing continues to be scaled up.

What measures are being taken to ensure the safe and effective use of COVID-19 Vaccine Janssen?

Recommendations and precautions to be followed by healthcare professionals and patients for the safe and effective use of COVID-19 Vaccine Janssen have been included in the summary of product characteristics and the package leaflet.

A risk management plan for COVID-19 Vaccine Janssen is also in place and contains important information about the vaccine's safety, how to collect further information and how to minimise any potential risks. A summary of the RMP is available.

Safety measures will be implemented for COVID-19 Vaccine Janssen in line with the EU safety monitoring plan for COVID-19 vaccines to ensure that new safety information is rapidly collected and analysed. The company that markets COVID-19 Vaccine Janssen will provide monthly safety reports.

As for all medicines, data on the use of COVID-19 Vaccine Janssen are continuously monitored. Suspected side effects reported with COVID-19 Vaccine Janssen are carefully evaluated and any necessary action taken to protect patients.

Other information about COVID-19 Vaccine Janssen

COVID-19 Vaccine Janssen received a conditional marketing authorisation valid throughout the EU on 11 March 2021.

Further information on COVID-19 Vaccine Janssen can be found on the Agency's website: ema.europa.eu/medicines/human/EPAR/covid-19-vaccine-janssen

This overview was last updated in 10-2021.

6 October 2021

COVID-19 vaccine safety update

COMIRNATY

BioNTech Manufacturing GmbH

The safety of Comirnaty is continuously monitored and safety updates are regularly provided to the public. This document outlines the outcomes from the assessment of emerging worldwide safety data carried out by EMA's Pharmacovigilance Risk Assessment Committee (PRAC) (see section 1). It also contains high-level information from the reporting of suspected adverse reactions, which PRAC takes into account in its assessments (see section 2).

This safety update follows the update of 8 September 2021.

Main outcomes from PRAC's latest safety assessment

Erythema multiforme (red spots/patches on the skin) and unusual or decreased feeling in the skin will be added to the product information as side effects of Comirnaty.

The safety updates are published regularly at COVID-19 vaccines: authorised. All published safety updates for Comirnaty are available at Comirnaty: safety updates.

Since its marketing authorisation in the European Union (EU) on 21 December 2020 until 30 September 2021, more than 420 million doses of Comirnaty have been administered in the EU/EEA[1].

1. Updates on safety assessments for Comirnaty

During its meeting held 27 to 30 September 2021, PRAC assessed new safety data (see section 2 'How safety is monitored').

Erythema multiforme

Update to the Comirnaty product information

PRAC continued its assessment of whether erythema multiforme (EM) may be a side effect of Comirnaty.

EM is a skin reaction that causes red spots or patches on the skin, that may look like a target or "bulls-eye" with a dark red centre surrounded by paler red rings.

124 cases had been spontaneously reported as EM worldwide to EudraVigilance (see section 2) as of 31 July 2021 (around 918 million doses of Comirnaty were estimated to have been administered worldwide by 31 July 2021). In 2 cases EM was ruled out, and in 41 cases the information provided was too limited for assessment. In 26 of the reported cases, EM was reported in close temporal association with the vaccination without apparent plausible alternative explanations for the event. Spontaneously reported cases concern suspected side effects, i.e. medical events that have been observed after vaccination, but which are not necessarily related to or caused by the vaccine.

Based on these case reports and the fact that there is a plausible mechanism for how the vaccine may cause EM, PRAC concluded that the product information should be updated to include EM as a side effect of Comirnaty. The frequency category will be 'unknown frequency', because it is generally difficult to robustly estimate side effect frequencies from

[1] The European Centre for Disease Prevention and Control (ECDC) collects these exposure data from EU Member States as well as from the additional countries of the European Economic Area (EEA) Norway, Iceland and Liechtenstein.

cases of suspected side effects that have been reported spontaneously by healthcare professionals or patients.

Paraesthesia and hypoesthesia

Update to the Comirnaty product information

PRAC concluded that paraesthesia (unusual feeling in the skin, such as tingling or a crawling sensation) and hypoesthesia (decreased feeling or sensitivity in the skin) should be added to the product information as side effects of Comirnaty.

This conclusion was based on a total of 21,793 paraesthesia and/or hypoesthesia cases spontaneously reported worldwide to EudraVigilance (see section 2) by 12 August 2021 (around 1,220 million doses of Comirnaty were estimated to have been administered worldwide by 31 August 2021). Spontaneously reported cases concern suspected side effects, i.e. medical events that have been observed after vaccination, but which are not necessarily related to or caused by the vaccine. Of the reported cases of paraesthesia or hypoesthesia, approximately 75% occurred within the day after vaccination.

Other events: Asthenia, lethargy, decreased appetite and (nocturnal) hyperhidrosis

Update to the Comirnaty product information

In the context of the review of clinical trial data by the Committee for Medicinal Products for Human Use (CHMP)[2], asthenia (lack of energy or strength), lethargy (state of indifference and inactivity), decreased appetite and (nocturnal [nighttime]) hyperhidrosis (excessive sweating) have been added as side effects to the product information of Comirnaty. The frequency category for these events is 'uncommon' (i.e. occurring in less than 1 in 100 persons).

Menstrual disorders

No evidence for causal relationship with Comirnaty

PRAC assessed cases reported as menstrual disorders occurring after vaccination with Comirnaty.

Until 30 August 2021, a total of 16,263 cases had been reported worldwide (16,226 as spontaneous reports; 6,118 as serious), of which 1,665 (10.2%) were medically confirmed by a healthcare professional as menstrual disorder (around 1,220 million doses of Comirnaty were estimated to have been administered worldwide by 31 August 2021). Spontaneously reported cases concern suspected side effects, i.e. medical

[2] See safety update for Comirnaty of 14 July 2021

events that have been observed after vaccination, but which are not necessarily related to or caused by the vaccine.

The assessment of all cases included an analysis of the type of symptoms and their time to onset; no specific pattern of menstrual cycle disturbances could be identified. In about half of the cases, past or current relevant medical conditions or concurrent medication were considered plausible explanations for menstrual disorders. An observed-to-expected (O/E) analysis for the 6,050 cases reported as 'heavy menstrual bleeding' (which was the most frequently reported disorder at 34.7%) resulted in an O/E ratio below 1; this means the number of cases reported after vaccination in relevant time windows was below the number of events expected to occur in an unvaccinated female population of the same size (based on observational data collected from the general population).

Based on the assessment of all data, PRAC concluded that there is currently no evidence suggesting a causal relationship of menstrual disorders with Comirnaty.

Menstrual disorders are very common in the general population and can occur without an underlying medical condition. Causes can range from stress and tiredness to conditions such as fibroids and endometriosis.

An assessment carried out in August 2021 by the Medicines & Healthcare products Regulatory Agency (MHRA) in the United Kingdom (UK) also concluded that the number of case reports in the UK were low in relation to both the number of vaccinated women and how common menstrual disorders are generally, that the symptoms were transient and that the data did not support a causal link between changes to menstrual periods and the COVID-19 vaccines available in the UK, including Comirnaty[3].

Glomerulonephritis and nephrotic syndrome

Close monitoring continues

Following a small number of cases after vaccination with Comirnaty reported in the medical literature[4], PRAC continued its assessment of whether glomerulonephritis (inflammation of tiny filters in the kidneys)

[3] For the latest UK data, see Coronavirus vaccine – weekly summary of Yellow Card reporting

[4] D'Agati et al. Minimal change disease and acute kidney injury following the Pfizer-BioNTech COVID-19 vaccine. Kidney Int. 2021.; Lebedev et al. Minimal change disease following the Pfizer-BioNTech COVID-19 vaccine. Am J Kidney Dis. 2021.; Kervella et al. Minimal change disease relapse following SARS-CoV-2 mRNA vaccine. Kidney Int. 2021.; Komaba et al. Relapse of minimal change disease following the Pfizer-BioNTech COVID-19 Vaccine, Am J Kidney Dis. 2021.; Maas et al. An additional case of minimal change disease following the Pfizer-BioNTech COVID-19 Vaccine. Am J Kidney Dis. 2021.; Mancianiti et al. Minimal change disease following vaccination for SARS-CoV-2. Journal of Nephrology. 2021.; Rahim et al. A case of gross hematuria and IgA nephropathy flare-up following SARS-CoV-2 vaccination. Kidney Int. 2021.; Schwotzer et al. Letter regarding "Minimal change disease relapse following SARS-CoV-2 mRNA vaccine". Kidney Int. 2021.; Tan et al. Is COVID-19 vaccination unmasking glomerulonephritis? Kidney Int. 2021.

and nephrotic syndrome (kidney disorder causing the kidneys to leak too much protein in the urine) may be side effects of Comirnaty.

PRAC assessed 89 cases reported as glomerulonephritis or nephrotic syndrome worldwide to EudraVigilance (see section 2) by 31 July 2021 (around 918 million doses of Comirnaty were estimated to have been administered worldwide by 31 July 2021). Spontaneously reported cases concern suspected side effects, i.e. medical events that have been observed after vaccination, but which are not necessarily related to or caused by the vaccine. After analysis of the cases, no particular patterns could be identified, and information regarding medical history, confounding conditions or risk factors was found to be lacking in many cases.

PRAC concluded that the available data did not establish a causal relationship of glomerulonephritis or nephrotic syndrome with Comirnaty and that an update to the product information of Comirnaty is not warranted at present. However, the topic remains under close monitoring.

PRAC encourages all healthcare professionals and patients to report any cases of glomerulonephritis or nephrotic syndrome occurring in people after vaccination (see section 2). Affected patients may present with bloody or foamy urine, oedema (swelling especially of the eyelids, feet or abdomen), or fatigue.

2. How safety is monitored

As for all COVID-19 vaccines, relevant new information emerging on Comirnaty is collected and promptly reviewed. This is in line with the pharmacovigilance plan for COVID-19 vaccines of the EU regulatory network (comprising the regulatory bodies of the EU Member States, EMA and the European Commission).

Summary safety reports

The pharmacovigilance plan for COVID-19 vaccines includes Monthly Summary Safety Reports (MSSRs) which are compiled by the marketing authorisation holders to support timely and continuous benefit-risk evaluations for COVID-19 vaccines used during the pandemic. MSSRs are intended to be compiled for at least the first six months of marketing (afterwards, pandemic summary safety reports may cover time periods longer than a month). These reports complement the submission of Periodic Safety Update Reports (PSURs).

Case reports of suspected side effects

Collecting reports of medical events and problems that occur following the use of a medicine, and therefore might be side effects, is one of the pillars of the EU safety monitoring system. Healthcare professionals and vaccinated individuals are encouraged to report to their national

competent authorities all suspected side effects individuals may have experienced after receiving a vaccine even if it is unclear whether the vaccine was the cause. For more information on how to report, including the importance of detailing the vaccine product name and the batch, see Reporting suspected side effects.

These spontaneous reports are collected in EudraVigilance, the EU database used for monitoring and analysing suspected side effects. Publicly available information can be accessed via EudraVigilance – European database of suspected drug reaction reports in all EU/EEA languages. Search for "COVID-19 mRNA Vaccine PFIZER-BIONTECH (Tozinameran)" to see all suspected side effect cases reported for Comirnaty.

As of 30 September 2021, a total of 361,767 cases of suspected side effects with Comirnaty were spontaneously reported to EudraVigilance from EU/EEA countries; 5,113 of these reported a fatal outcome[5,6]. By the same date more than 420 million doses of Comirnaty had been given to people in the EU/EEA[7].

These reports describe suspected side effects in individuals, i.e. medical events observed following the use of a vaccine. The fact that someone has had a medical issue or died after vaccination does not necessarily mean that this was caused by the vaccine. This may have been caused, for example, by health problems not related to the vaccination.

The EU regulatory network continuously monitors EudraVigilance to detect any new safety issues. EudraVigilance relies on individual healthcare professionals and patients to report their own experience. The monitoring detects unusual or unexpected patterns in the reports received for further investigation and risk assessment. EMA's detailed assessments take into account all available data from all sources to draw a robust conclusion on the safety of the vaccine. These data include clinical trial results, reports of suspected side effects in EudraVigilance, epidemiological studies monitoring the safety of the vaccine, toxicological investigations and any other relevant information.

[5] These figures have been calculated excluding cases reported from Northern Ireland (EU reporting requirements for suspected adverse reactions to EudraVigilance apply to Northern Ireland in accordance with the Protocol on Ireland/Northern Ireland).
[6] Source: EudraVigilance. These figures cannot be extracted directly from the public database of suspected adverse reactions, which groups information per type of side effects. As more than one suspected side effect may have been included in a single case report, the total number of side effects will never match the number of individual cases. Similarly, this public database does not provide the total number of cases reported with a fatal outcome.
[7] The European Centre for Disease Prevention and Control (ECDC) collects these exposure data from EU Member States as well as from the additional countries of the European Economic Area (EEA) Norway, Iceland and Liechtenstein.

Planned and ongoing studies

The company that markets Comirnaty will continue to provide results from the main clinical trial, which is ongoing for up to two years. It will also conduct additional studies to monitor the safety and effectiveness of the vaccine as it is used in vaccination campaigns and other clinical practice. For the list of planned and ongoing safety studies for Comirnaty, see the risk management plan.

A paediatric investigation plan (PIP) for Comirnaty is in place. This describes how the company collects data on the vaccine's efficacy and safety for its use in children.

In addition, EMA is coordinating observational studies in EU Member States looking at real-world data from clinical practice to monitor the safety and effectiveness of COVID-19 vaccines, including in pregnant women.

3. Other information for Comirnaty

Comirnaty is a vaccine that was authorised in the EU on 21 December 2020 to prevent COVID-19 when infected with the coronavirus SARS-CoV-2. COVID-19 is a potentially severe disease that may result in death. The initial marketing authorisation was for use in people aged 16 years and older; on 31 May 2021, the marketing authorisation was extended to use in individuals aged 12 years and older.

Comirnaty contains a molecule called mRNA, which the body uses to temporarily produce the SARS-CoV-2 spike protein. The mRNA is broken down shortly after vaccination. The spike protein does not cause COVID-19.

Before Comirnaty was granted an EU marketing authorisation, the efficacy and safety of the vaccine were assessed through pre-clinical studies and large clinical trials. More than 18,000 participants had been given the vaccine in clinical trials.

Like all medicines, this vaccine can cause side effects, although not everybody will experience them. The most common side effects known for Comirnaty are usually mild or moderate and get better within a few days after vaccination.

More information on how Comirnaty works and its use is available in all EU/EEA languages in the medicine overview. This includes information on use in pregnant and breastfeeding women and immunocompromised individuals.

The full product information with the summary of product characteristics and the package leaflet is also available in all EU/EEA languages.

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6 October 2021

COVID-19 vaccine safety update

SPIKEVAX

Moderna Biotech Spain, S.L.

The safety of Spikevax is continuously monitored and safety updates are regularly provided to the public. This document outlines the outcomes from the assessment of emerging worldwide safety data carried out by EMA's Pharmacovigilance Risk Assessment Committee (PRAC) (see section 1). It also contains high-level information from the reporting of suspected adverse reactions, which PRAC takes into account in its assessments (see section 2).

This safety update follows the update of 8 September 2021.

Main outcomes from PRAC's latest safety assessment

Erythema multiforme (red spots/patches on the skin) will be added to the product information as a side effect of Spikevax.

The safety updates are published regularly at COVID-19 vaccines: authorised. All published safety updates for Spikevax (previously known as COVID-19 Vaccine Moderna) are available at Spikevax: safety updates.

Since its marketing authorisation in the European Union (EU) on 6 January 2021 until 30 September 2021, more than 59.8 million doses of Spikevax have been administered in the EU/EEA[1].

More than 59.8 million
doses administered in EEA

1. Updates on safety assessments for Spikevax

During its meeting held 27 to 30 September 2021, PRAC assessed new safety data (see section 2 'How safety is monitored').

Erythema multiforme

Update to the Spikevax product information

PRAC continued its assessment of whether erythema multiforme (EM) may be a side effect of Spikevax.

EM is a skin reaction that causes red spots or patches on the skin, that may look like a target or "bulls-eye" with a dark red centre surrounded by paler red rings.

143 cases had been spontaneously reported as EM worldwide to EudraVigilance (see section 2) as of 31 July 2021 (around 207 million doses of Spikevax were estimated to have been administered worldwide by 31 July 2021). Of these, 29 were assessed as confirmed reports of EM; 5 of these were considered to be probably causally related to Spikevax and 20 as possibly causally related to Spikevax. This was determined based on a plausible time to onset of the adverse event following vaccination, the absence of alternative explanations and the level of information available in the case reports. Spontaneously reported cases concern suspected side effects, i.e. medical events that have been observed after vaccination, but which are not necessarily related to or caused by the vaccine.

Based on these case reports and the fact that there is a plausible mechanism for how the vaccine may cause EM, PRAC concluded that the product information should be updated to include erythema multiforme as a side effect of Spikevax. The frequency category will be 'unknown

[1] The European Centre for Disease Prevention and Control (ECDC) collects these exposure data from EU Member States as well as from the additional countries of the European Economic Area (EEA) Norway, Iceland and Liechtenstein.

frequency', because it is generally difficult to robustly estimate side effect frequencies from cases of suspected side effects that have been reported spontaneously by healthcare professionals or patients.

Menstrual disorders

No evidence for causal relationship with Spikevax

PRAC assessed cases reported as menstrual disorders occurring after vaccination with Spikevax as well as a review of the scientific literature.

Until 31 August 2021, a total of 3,619 cases had been reported spontaneously worldwide (118 concerned post-menopausal bleeding), of which 829 (22.9%) were medically confirmed by a healthcare professional as menstrual disorder (117 as serious) (around 230 million doses of Spikevax were estimated to have been administered worldwide by 31 August 2021). Spontaneously reported cases concern suspected side effects, i.e. medical events that have been observed after vaccination, but which are not necessarily related to or caused by the vaccine.

The assessment of all spontaneously reported cases included an analysis of the type of symptoms, their time to onset and duration, as well as concomitant treatment and medical history/current conditions; no specific pattern of menstrual cycle disturbances could be identified. The event duration was short, with an average of 10.3 days and a median of 5.0 days (range 0-179). Observed-to-expected (O/E) analyses for pre- and postmenopausal women resulted in O/E ratios substantially below 1; this means the numbers of cases reported after vaccination in relevant time windows were below the numbers of such events expected to occur in the unvaccinated female populations of the same size (based on observational data collected from the general population), even when assuming that all reported cases would be assessed as possibly causally related. In addition, no statistical differences in reports of menstrual disorder between the vaccinated and unvaccinated groups could be identified from clinical trial data.

PRAC also considered the assessment carried out in August 2021 by the Medicines & Healthcare products Regulatory Agency (MHRA) in the United Kingdom (UK), which concluded that the number of case reports in the UK were low in relation to both the number of vaccinated women and how common menstrual disorders are generally, that the symptoms were transient, and that the data did not support a causal link between changes to menstrual periods and the COVID-19 vaccines available in the UK, including Spikevax[2].

Based on the assessment of all data, PRAC concluded that there is currently no evidence suggesting a causal relationship of menstrual disorders with Spikevax.

[2] For the latest UK data, see Coronavirus vaccine – weekly summary of Yellow Card reporting

Menstrual disorders are very common in the general population and can occur without an underlying medical condition. Causes can range from stress and tiredness to conditions such as fibroids and endometriosis.

Glomerulonephritis and nephrotic syndrome

Close monitoring continues

Following a small number of cases after vaccination with Spikevax reported in the medical literature[3], PRAC continued their assessment of whether glomerulonephritis (inflammation of tiny filters in the kidneys) and nephrotic syndrome (kidney disorder causing the kidneys to leak too much protein in the urine) may be side effects of Spikevax.

PRAC assessed 33 cases which had been spontaneously reported as glomerulonephritis or nephrotic syndrome worldwide to EudraVigilance (see section 2). Of these, 11 cases were assessed as possibly causally related to Spikevax based on a plausible temporal association. The relapsing/remitting forms of this type of disease are common and the cause of relapse or new-onset disease can often not be determined. The remaining cases were considered unlikely to be causally related to Spikevax or could not be assessed due to limited information in the case reports. An observed-to-expected (O/E) analysis (which looked at the number of cases reported worldwide in relation to the number of such events expected to occur in the unvaccinated population of the same size [based on observational data collected from the general population]) did not show statistically significant increases.

PRAC concluded that the currently available data were not sufficient to establish a causal relationship of glomerulonephritis or nephrotic syndrome with Spikevax. However, the topic remains under close monitoring.

PRAC encourages all healthcare professionals and patients to report any cases of glomerulonephritis or nephrotic syndrome occurring in people after vaccination (see section 2). Affected patients may present with bloody or foamy urine, oedema (swelling especially of the eyelids, feet or abdomen), or fatigue.

2. How safety is monitored

As for all COVID-19 vaccines, relevant new information emerging on Spikevax is collected and promptly reviewed. This is in line with the

[3] Anderegg et al. De novo vasculitis after mRNA-1273 (Moderna) vaccination. Kidney Int. 1 Jun 2021.; Holzworth et al. Minimal change disease following the Moderna mRNA-1273 SARS-CoV-2 vaccine Kidney Int. 2021; 100: 463-464.; Kudose et al. Histologic correlates of gross hematuria following Moderna COVID-19 vaccine in patients with IgA nephropathy. Kidney international. 16 June 2021.; Negrea & Rovin. Gross hematuria following vaccination for severe acute respiratory syndrome coronavirus 2 in 2 patients with IgA nephropathy. Kidney Int. 2021; 99: 1487.; Sekar et al. ANCA glomerulonephritis after the Moderna COVID-19 vaccination. Kidney international. 31 May 2021.

pharmacovigilance plan for COVID-19 vaccines of the EU regulatory network (comprising the regulatory bodies of the EU Member States, EMA and the European Commission).

Summary safety reports

The pharmacovigilance plan for COVID-19 vaccines includes Monthly Summary Safety Reports (MSSRs) which are compiled by the marketing authorisation holders to support timely and continuous benefit-risk evaluations for COVID-19 vaccines used during the pandemic. MSSRs are intended to be compiled for at least the first six months of marketing (afterwards, pandemic summary safety reports may cover time periods longer than a month). These reports complement the submission of Periodic Safety Update Reports (PSURs).

Case reports of suspected side effects

Collecting reports of medical events and problems that occur following the use of a medicine, and therefore might be side effects, is one of the pillars of the EU safety monitoring system. Healthcare professionals and vaccinated individuals are encouraged to report to their national competent authorities all suspected side effects individuals may have experienced after receiving a vaccine even if it is unclear whether the vaccine was the cause. For more information on how to report, including the importance of detailing the vaccine product name and the batch, see Reporting suspected side effects.

These spontaneous reports are collected in EudraVigilance, the EU database used for monitoring and analysing suspected side effects. Publicly available information can be accessed via EudraVigilance – European database of suspected drug reaction reports in all EU/EEA languages. Search for "COVID-19 MRNA VACCINE MODERNA (CX-024414)" to see all suspected side effect cases reported for Spikevax.

As of 30 September 2021, a total of 80,486 cases of suspected side effects with Spikevax were spontaneously reported to EudraVigilance from EU/EEA countries; 495 of these reported a fatal outcome[4,5]. By the same

[4] These figures have been calculated excluding cases reported from Northern Ireland (EU reporting requirements for suspected adverse reactions to EudraVigilance apply to Northern Ireland in accordance with the Protocol on Ireland/Northern Ireland).
[5] Source: EudraVigilance. These figures cannot be extracted directly from the public database of suspected adverse reactions, which groups information per type of side effects. As more than one suspected side effect may have been included in a single case report, the total number of side effects will never match the number of individual cases. Similarly, this public database does not provide the total number of cases reported with a fatal outcome.

date, more than 59.8 million doses of Spikevax had been given to people in the EU/EEA[6].

These reports describe suspected side effects in individuals, i.e. medical events observed following the use of a vaccine. The fact that someone has had a medical issue or died after vaccination does not necessarily mean that this was caused by the vaccine. This may have been caused, for example, by health problems not related to the vaccination.

The EU regulatory network continuously monitors EudraVigilance to detect any new safety issues. EudraVigilance relies on individual healthcare professionals and patients to report their own experience. The monitoring detects unusual or unexpected patterns in the reports received for further investigation and risk assessment. EMA's detailed assessments take into account all available data from all sources to draw a robust conclusion on the safety of the vaccine. These data include clinical trial results, reports of suspected side effects in EudraVigilance, epidemiological studies monitoring the safety of the vaccine, toxicological investigations and any other relevant information.

Planned and ongoing studies

The company that markets Spikevax will continue to provide results from the main clinical trial, which is ongoing for up to two years. It will also conduct additional studies to monitor the safety and effectiveness of the vaccine as it is used in vaccination campaigns and other clinical practice. For the list of planned and ongoing safety studies for Spikevax, see the risk management plan.

A paediatric investigation plan (PIP) for Spikevax is in place. This describes how the company collects data on the vaccine's efficacy and safety for its use in children.

In addition, EMA is coordinating observational studies in EU Member States looking at real-world data from clinical practice to monitor the safety and effectiveness of COVID-19 vaccines, including in pregnant women.

3. Other information for Spikevax

Spikevax (previously known as COVID-19 Vaccine Moderna) is a vaccine that was authorised in the EU on 6 January 2021 to prevent COVID-19 when infected with the coronavirus SARS-CoV-2. COVID-19 is a potentially severe disease that may result in death. The initial marketing

[6] The European Centre for Disease Prevention and Control (ECDC) collects these exposure data from EU Member States as well as from the additional countries of the European Economic Area (EEA) Norway, Iceland and Liechtenstein.

authorisation was for use in people aged 18 years and older; on 23 July 2021, the marketing authorisation was extended to use in individuals aged 12 years and older.

Spikevax contains a molecule called mRNA, which the body uses to temporarily produce the SARS-CoV-2 spike protein. The mRNA is broken down shortly after vaccination. The spike protein does not cause COVID-19.

Before Spikevax was granted an EU marketing authorisation, the efficacy and safety of the vaccine were assessed through pre-clinical studies and large clinical trials. More than 14,000 participants had been given the vaccine in clinical trials.

Like all medicines, this vaccine can cause side effects, although not everybody will experience them. The most common side effects known for Spikevax are usually mild or moderate and get better within a few days after vaccination.

More information on how Spikevax works and its use is available in all EU/EEA languages in the medicine overview. This includes information on use in pregnant and breastfeeding women and immunocompromised individuals.

The full product information with the summary of product characteristics and the package leaflet is also available in all EU/EEA languages.

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An agency of the European Union

6 October 2021

COVID-19 vaccine safety update

COVID-19 VACCINE JANSSEN

Janssen-Cilag International NV

The safety of COVID-19 Vaccine Janssen is continuously monitored and safety updates are regularly provided to the public. This document outlines the outcomes from the assessment of emerging worldwide safety data carried out by EMA's Pharmacovigilance Risk Assessment Committee (PRAC) (see section 1). It also contains high-level information from the reporting of suspected adverse reactions, which PRAC takes into account in its assessments (see section 2).

This safety update follows the update of 8 September 2021.

Main outcomes from PRAC's latest safety assessment

Venous thromboembolism (VTE, blood clotting in the veins) and immune thrombocytopenia (ITP, an autoimmune condition with low blood platelet levels) will be added to the product information as side effects of COVID-19 Vaccine Janssen, together with warnings and advice.

Transverse myelitis (inflammation in parts of the spinal cord) was recommended by PRAC to be added to the product information as a side effect of COVID-19 Vaccine Janssen.

The safety updates are published regularly at COVID-19 vaccines: authorised. All published safety updates for COVID-19 Vaccine Janssen are available at COVID-19 Vaccine Janssen: safety updates.

Since its marketing authorisation in the European Union (EU) on 11 March 2021 until 30 September 2021, more than 14.3 million doses of COVID-19 Vaccine Janssen have been administered in the EU/EEA[1].

More than 14.3 million
doses administered in EEA

1. Updates on safety assessments for COVID-19 Vaccine Janssen

During its meeting held 27 to 30 September 2021, PRAC assessed new safety data (see section 2 'How safety is monitored').

Venous thromboembolism (VTE)

Update to the COVID-19 Vaccine Janssen product information

Venous thromboembolism (VTE) has been kept under close monitoring by PRAC due to a higher proportion of cases of VTE observed in the vaccinated group compared with the placebo group in the large clinical trial used to authorise COVID-19 Vaccine Janssen (see section 3).

VTE is a condition in which a blood clot forms in a deep vein, usually in a leg, arm or groin, and may travel to the lungs causing a blockage of the blood supply, with possibly life-threatening consequences (this safety issue is distinct from thrombosis with thrombocytopenia syndrome [TTS], see below).

At its meeting held 27 to 30 September 2021, PRAC reviewed new data from the clinical trial used to authorise COVID-19 Vaccine Janssen (COV3001), as well as data from another large clinical study (COV3009).

During the double-blind period (median follow-up time of 123 days) of the first, still ongoing, phase 3 study (COV3001), venous thromboembolic events were observed in 26 out of 21,894 (0.1%) individuals who received COVID-19 Vaccine Janssen and in 9 out of 21,882 (0.04%) individuals who received placebo. Of these, venous thromboembolic events were observed within 28 days in 8 individuals who received COVID-19 Vaccine Janssen and in 4 individuals who received placebo. Most of the observed

[1] The European Centre for Disease Prevention and Control (ECDC) collects these exposure data from EU Member States as well as from the additional countries of the European Economic Area (EEA) Norway, Iceland and Liechtenstein.

events involved deep vein thrombosis and pulmonary embolism (21 individuals who received COVID-19 Vaccine Janssen and 8 individuals who received placebo during the entire double-blind phase). The majority of events were reported in individuals with at least one predisposing risk factor for VTE.

In the other ongoing phase 3 study (COV3009, 15,708 individuals receiving the vaccine and 15,592 receiving placebo), there was no increase in venous thromboembolic events among individuals who received COVID-19 Vaccine Janssen (median follow-up time of 70 days).

When taking all evidence into account, PRAC concluded that there is a reasonable possibility that VTE is linked to vaccination with COVID-19 Vaccine Janssen. PRAC therefore recommended adding VTE to the product information of COVID-19 Vaccine Janssen as a rare side effect (i.e. occurring in less than 1 in 1,000 individuals), together with warnings for healthcare professionals and people taking the vaccine, especially those who may have an increased risk of VTE.

PRAC also agreed on a direct healthcare professional communication (DHPC) to raise awareness among healthcare professionals. Following agreement of the Committee for Medicinal Products for Human Use (CHMP) on the product information update and the DHPC, the DHPC will be disseminated to healthcare professionals by the marketing authorisation holder according to an agreed communication plan. The DHPC will be available on a dedicated page on the EMA website and in the national DHPC registers of EU Member States[2].

Healthcare professionals should be aware that:

- VTE has been observed rarely following vaccination with COVID-19 Vaccine Janssen; and
- the risk of VTE should be considered for individuals with increased risk factors for thromboembolism (blood clots).

Reminder: Individuals diagnosed with thrombocytopenia within three weeks after vaccination with COVID-19 Vaccine Janssen should be actively investigated for signs of thrombosis. Similarly, individuals who present with thrombosis within three weeks of vaccination should be evaluated for thrombocytopenia. This is important to assess a potential diagnosis of thrombosis with thrombocytopenia syndrome (TTS), which requires specialised clinical management.

Vaccinated individuals should seek immediate medical attention if they:

- develop shortness of breath, chest pain, leg swelling, leg pain or persistent abdominal pain following vaccination; or
- experience severe or persistent headaches, blurred vision, mental status changes or seizures (fits) a few days following vaccination.

[2] See Meeting Highlights from the Pharmacovigilance Risk Assessment Committee (PRAC) 27 - 30 September 2021

Immune thrombocytopenia (ITP)

Update to the COVID-19 Vaccine Janssen product information

In August 2021, PRAC recommended updating the product information of COVID-19 Vaccine Janssen to include immune thrombocytopenia (ITP) as a side effect, together with a warning to alert healthcare professionals and people taking the vaccine[3].

ITP is a condition in which the immune system mistakenly targets blood cells called platelets that are needed for normal blood clotting. Very low levels of blood platelets can be associated with bleeding and serious health problems.

At its meeting held 27 to 30 September 2021, PRAC finalised the update of the product information, allocating ITP to the 'unknown frequency' category, because it is generally difficult to robustly estimate side effect frequencies from cases of suspected side effects that have been reported spontaneously by healthcare professionals or patients. Spontaneously reported cases concern suspected side effects, i.e. medical events that have been observed after vaccination, but which are not necessarily related to or caused by the vaccine.

PRAC also agreed on a direct healthcare professional communication (DHPC) to raise awareness among healthcare professionals. Following agreement of the Committee for Medicinal Products for Human Use (CHMP) on the product information update and the DHPC, the DHPC will be disseminated to healthcare professionals by the marketing authorisation holder according to an agreed communication plan. The DHPC will be available on a dedicated page on the EMA website and in the national DHPC registers of EU Member States[4].

Healthcare professionals should be aware that:

- cases of ITP, some with very low platelet levels (<20,000 per µL), have been reported very rarely, usually within the first four weeks after receiving COVID-19 Vaccine Janssen; this included cases with bleeding and cases with a fatal outcome; some of these occurred in individuals with a history of ITP;
- if an individual has a history of ITP, the risk of developing low platelet levels should be considered before vaccination, and platelet monitoring is recommended after vaccination.

Reminder: Individuals diagnosed with thrombocytopenia within three weeks after vaccination with COVID-19 Vaccine Janssen should be actively investigated for signs of thrombosis. Similarly, individuals who present with thrombosis within three weeks of vaccination should be evaluated for thrombocytopenia. This is important to assess a potential diagnosis of thrombosis with thrombocytopenia syndrome (TTS), which requires specialised clinical management.

[3] See safety update for COVID-19 Vaccine Janssen of 11 August 2021

[4] See Meeting Highlights from the Pharmacovigilance Risk Assessment Committee (PRAC) 27 - 30 September 2021

Vaccinated individuals should:

- seek immediate medical attention if they experience unexplained bleeding or skin bruising or pinpoint round spots beyond the site of vaccination, appearing a few days after vaccination.

Thrombosis with thrombocytopenia syndrome (TTS)

Update to the COVID-19 Vaccine Janssen product information

In May 2021, the product information of COVID-19 Vaccine Janssen was updated with regard to the very rare risk of thrombosis (formation of blood clots in the blood vessels) with thrombocytopenia (low blood platelets) syndrome (TTS)[5].

Data on TTS are kept under close monitoring for further characterisation of risk factors, and PRAC now concluded that the product information should be further updated by removing the current statement that reported TSS cases occurred mostly in women, since the previously observed sex imbalance between cases could no longer be observed.

Of the cases reported spontaneously as TTS worldwide by the end of August 2021, 73% of cases were reported in subjects below 60 years of age. In most cases sex was known, and around 44% were in women below the age of 60 years. Spontaneously reported cases concern suspected side effects, i.e. medical events that have been observed after vaccination, but which are not necessarily related to or caused by the vaccine.

Reminder: People should seek immediate medical attention if they experience severe or persistent headache, blurred vision, confusion, seizures, shortness of breath, chest pain, leg swelling, leg pain, persistent abdominal pain, unusual bleeding or skin bruising or pinpoint round spots beyond the site of vaccination within three weeks of vaccination, as these could be signs of TTS.

Transverse myelitis

Update to the COVID-19 Vaccine Janssen product information

PRAC recommended that transverse myelitis (inflammation in parts of the spinal cord) should be added to the product information as a side effect of COVID-19 Vaccine Janssen.

This conclusion is based on worldwide transverse myelitis cases spontaneously reported by 31 August 2021, of which 10 have been assessed to have at least a possible causal relationship with the vaccine, and 1 a probable causal relationship (more than 33 million doses of COVID-19 Vaccine Janssen were estimated to have been administered worldwide by 31 August 2021). Spontaneously reported cases concern

[5] See safety update for COVID-19 Vaccine Janssen of 11 May 2021

suspected side effects, i.e. medical events that have been observed after vaccination, but which are not necessarily related to or caused by the vaccine.

The frequency category is proposed to be 'unknown frequency', because it is generally difficult to robustly estimate side effect frequencies from cases of suspected side effects that have been reported spontaneously by healthcare professionals or patients.

Dizziness

Update to the COVID-19 Vaccine Janssen product information

In August 2021, PRAC recommended adding dizziness to the product information as a side effect of COVID-19 Vaccine Janssen[6].

PRAC has now finalised the product information and allocated this side effect to the frequency category 'uncommon' (i.e. occurring in less than 1 in 100 individuals), based on clinical trial data.

2. How safety is monitored

As for all COVID-19 vaccines, relevant new information emerging on COVID-19 Vaccine Janssen is collected and promptly reviewed. This is in line with the pharmacovigilance plan for COVID-19 vaccines of the EU regulatory network (comprising the regulatory bodies of the EU Member States, EMA and the European Commission).

Summary safety reports

The pharmacovigilance plan for COVID-19 vaccines includes Monthly Summary Safety Reports (MSSRs) which are compiled by the marketing authorisation holders to support timely and continuous benefit-risk evaluations for COVID-19 vaccines used during the pandemic. MSSRs are intended to be compiled for at least the first six months of marketing (afterwards, pandemic summary safety reports may cover time periods longer than a month). These reports complement the submission of Periodic Safety Update Reports (PSURs).

Case reports of suspected side effects

Collecting reports of medical events and problems that occur following the use of a medicine, and therefore might be side effects, is one of the pillars of the EU safety monitoring system. Healthcare professionals and vaccinated individuals are encouraged to report to their national competent authorities all suspected side effects individuals may have

[6] See safety update for COVID-19 Vaccine Janssen of 11 August 2021

experienced after receiving a vaccine even if it is unclear whether the vaccine was the cause. For more information on how to report, including the importance of detailing the vaccine product name and the batch, see Reporting suspected side effects.

These spontaneous reports are collected in EudraVigilance, the EU database used for monitoring and analysing suspected side effects. Publicly available information can be accessed via EudraVigilance – European database of suspected drug reaction reports in all EU/EEA languages. Search for "COVID-19 VACCINE JANSSEN (AD26.COV2.S)" to see all suspected side effect cases reported for COVID-19 Vaccine Janssen.

As of 30 September 2021, a total of 23,455 cases of suspected side effects with COVID-19 Vaccine Janssen were spontaneously reported to EudraVigilance from EU/EEA countries; 171 of these reported a fatal outcome[7,8]. By the same date, more than 14.3 million doses of COVID-19 Vaccine Janssen had been given to people in the EU/EEA[9].

These reports describe suspected side effects in individuals, i.e. medical events observed following the use of a vaccine. The fact that someone has had a medical issue or died after vaccination does not necessarily mean that this was caused by the vaccine. This may have been caused, for example, by health problems not related to the vaccination.

The EU regulatory network continuously monitors EudraVigilance to detect any new safety issues. EudraVigilance relies on individual healthcare professionals and patients to report their own experience. The monitoring detects unusual or unexpected patterns in the reports received for further investigation and risk assessment. EMA's detailed assessments take into account all available data from all sources to draw a robust conclusion on the safety of the vaccine. These data include clinical trial results, reports of suspected side effects in EudraVigilance, epidemiological studies monitoring the safety of the vaccine, toxicological investigations and any other relevant information.

Planned and ongoing studies

The company that markets COVID-19 Vaccine Janssen will continue to provide results from ongoing clinical trials. It will also conduct additional

[7] These figures have been calculated excluding cases reported from Northern Ireland (EU reporting requirements for suspected adverse reactions to EudraVigilance apply to Northern Ireland in accordance with the Protocol on Ireland/Northern Ireland).
[8] Source: EudraVigilance. These figures cannot be extracted directly from the public database of suspected adverse reactions, which groups information per type of side effects. As more than one suspected side effect may have been included in a single case report, the total number of side effects will never match the number of individual cases. Similarly, this public database does not provide the total number of cases reported with a fatal outcome.
[9] The European Centre for Disease Prevention and Control (ECDC) collects these exposure data from EU Member States as well as from the additional countries of the European Economic Area (EEA) Norway, Iceland and Liechtenstein.

studies to monitor the safety and effectiveness of the vaccine as it is used in vaccination campaigns and other clinical practice. For the list of planned and ongoing safety studies for COVID-19 Vaccine Janssen, see the risk management plan.

A paediatric investigation plan (PIP) for COVID-19 Vaccine Janssen is in place. This describes how the company will collect data on the vaccine's efficacy and safety for its potential use in children.

In addition, EMA is coordinating observational studies in EU Member States looking at real-world data from clinical practice to monitor the safety and effectiveness of COVID-19 vaccines, including in pregnant women.

3. Other information for COVID-19 Vaccine Janssen

COVID-19 Vaccine Janssen is a vaccine that was authorised in the EU on 11 March 2021 for use in people aged 18 years and older to prevent COVID-19 when infected with the coronavirus SARS-CoV-2. COVID-19 is a potentially severe disease that may result in death.

COVID-19 Vaccine Janssen contains an adenovirus that has been modified to carry molecules of DNA, which the body uses to temporarily produce the SARS-CoV-2 spike protein. The spike protein does not cause COVID-19. The adenovirus cannot reproduce and does not cause viral disease.

Before COVID-19 Vaccine Janssen was granted an EU marketing authorisation, the efficacy and safety of the vaccine were assessed through pre-clinical studies and large clinical trials. More than 27,000 participants had been given the vaccine in clinical trials.

Like all medicines, this vaccine can cause side effects, although not everybody will experience them. The most common side effects known for COVID-19 Vaccine Janssen are usually mild or moderate and get better within a few days after vaccination.

More information on how COVID-19 Vaccine Janssen works and its use is available in all EU/EEA languages in the medicine overview. This includes information on use in pregnant and breastfeeding women and immunocompromised individuals.

The full product information with the summary of product characteristics and the package leaflet is also available in all EU/EEA languages.

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11 November 2021

COVID-19 vaccine safety update

VAXZEVRIA

AstraZeneca AB

The safety of Vaxzevria is continuously monitored and safety updates are regularly provided to the public. This document outlines the outcomes from the assessment of emerging worldwide safety data carried out by EMA's Pharmacovigilance Risk Assessment Committee (PRAC) (see section 1). It also contains high-level information from the reporting of suspected adverse reactions, which PRAC takes into account in its assessments (see section 2).

This safety update follows the update of 6 October 2021.

Main outcomes from PRAC's latest safety assessment

Cerebrovascular venous and sinus thrombosis (CVST; blood clots in the brain) without thrombocytopenia (low blood platelet levels) has been observed very rarely following vaccination with Vaxzevria.

CVST will be added to the product information as a side effect of Vaxzevria.

The safety updates are published regularly at COVID-19 vaccines: authorised. All published safety updates for Vaxzevria are available at Vaxzevria: safety updates.

Since its marketing authorisation in the European Union (EU) on 29 January 2021 until 29 October 2021, almost 68.8 million doses of Vaxzevria have been administered in the EU/EEA[1].

1. Updates on safety assessments for Vaxzevria

During its meetings held 25 to 28 October 2021 and 04 November 2021, PRAC assessed new safety data for Vaxzevria (see section 2 'How safety is monitored').

Cerebrovascular venous and sinus thrombosis (CVST)

PRAC finalised its assessment of cases reporting CVST (blood clots in the brain) without thrombocytopenia (low blood platelets) after vaccination with Vaxzevria. Thrombosis (formation of blood clots in blood vessels) with thrombocytopenia syndrome (TTS) is already a known very rare side effect of Vaxzevria[2].

CVST is a rare type of stroke which occurs when a blood clot forms in the brain's venous sinuses, preventing blood from draining out of the brain. As a result, blood vessels may break and leak blood into the brain tissues, forming a haemorrhage.

PRAC assessed all available data and recommended updating the product information to include CVST as a side effect of Vaxzevria.

Cumulatively, up to 30 September 2021, 458 cases of CVST without thrombocytopenia have been reported globally following vaccination with Vaxzevria (293 medically confirmed) and 33 of these cases occurred after the second dose. The assigned frequency category will be 'unknown frequency', because it is generally difficult to robustly estimate side effect frequencies from cases of suspected side effects that have been reported spontaneously by healthcare professionals or patients. Spontaneously reported cases concern suspected side effects, i.e. medical events that

[1] The European Centre for Disease Prevention and Control (ECDC) collects these exposure data from EU Member States as well as from the additional countries of the European Economic Area (EEA) Norway, Iceland and Liechtenstein.
[2] See Vaxzevria, COVID-19 Vaccine (ChAdOx1-S [recombinant]) (europa.eu)

have been observed after vaccination, but which are not necessarily related to or caused by the vaccine.

In addition, the following warning statements for healthcare professionals and vaccinated individuals are recommended for inclusion in the product information:

Healthcare professionals should be aware that:

- Events of cerebrovascular venous and sinus thrombosis (CVST) without thrombocytopenia have been observed very rarely following vaccination with Vaxzevria. Some cases had a fatal outcome;
- The majority of these cases occurred within the first four weeks of vaccination;
- This information should be considered for individuals at increased risk for CVST;
- These events may require different treatment approaches than thrombosis with thrombocytopenia syndrome (TTS) and healthcare professionals should consult applicable guidances.

Vaccinated individuals should be aware that:

- blood clots in the brain, not associated with low levels of platelets, have been observed very rarely following vaccination with Vaxzevria;
- The majority of these cases occurred within the first four weeks of vaccination. Some cases had a fatal outcome.

Multisystem inflammatory syndrome (MIS)

PRAC has concluded that there is currently insufficient evidence of a possible link between Vaxzevria and very rare cases of multisystem inflammatory syndrome (MIS).

MIS is a rare serious inflammatory condition affecting many parts of the body, and symptoms can include tiredness, persistent severe fever, diarrhoea, vomiting, stomach pain, headache, chest pain and difficulty breathing. MIS has previously been reported following COVID-19 disease.

The committee's assessment is based on available spontaneously reported adverse events and currently does not warrant an update of the product information. Only a small number of case reports were identified as meeting the case definition of MIS. However, these cases lacked sufficient information, preventing an adequate assessment of causality.

2. How safety is monitored

As for all COVID-19 vaccines, relevant new information emerging on Vaxzevria is collected and promptly reviewed. This is in line with the pharmacovigilance plan for COVID-19 vaccines of the EU regulatory network (comprising the regulatory bodies of the EU Member States, EMA and the European Commission).

Summary safety reports

The pharmacovigilance plan for COVID-19 vaccines includes Monthly Summary Safety Reports (MSSRs) which are compiled by the marketing authorisation holders to support timely and continuous benefit-risk evaluations for COVID-19 vaccines used during the pandemic. MSSRs are intended to be compiled for at least the first six months of marketing (afterwards, pandemic summary safety reports may cover time periods longer than a month). These reports complement the submission of Periodic Safety Update Reports (PSURs).

Case reports of suspected side effects

Collecting reports of medical events and problems that occur following the use of a medicine, and therefore might be side effects, is one of the pillars of the EU safety monitoring system. Healthcare professionals and vaccinated individuals are encouraged to report to their national competent authorities all suspected side effects individuals may have experienced after receiving a vaccine even if it is unclear whether the vaccine was the cause. For more information on how to report, including the importance of detailing the vaccine product name and the batch, see Reporting suspected side effects.

These spontaneous reports are collected in EudraVigilance, the EU database used for monitoring and analysing suspected side effects. Publicly available information can be accessed via EudraVigilance – European database of suspected drug reaction reports in all EU/EEA languages. Search for "COVID-19 VACCINE ASTRAZENECA (CHADOX1 NCOV-19)" to see all suspected side effect cases reported for Vaxzevria.

As of 28 October 2021, a total of 214,528 cases of suspected side effects with Vaxzevria were spontaneously reported to EudraVigilance from EU/EEA countries; 1,259 of these reported a fatal outcome[3,4]. By the same date, almost 68.8 million doses of Vaxzevria had been given to people in the EU/EEA[5].

These reports describe suspected side effects in individuals, i.e. medical events observed following the use of a vaccine. The fact that someone has had a medical issue or died after vaccination

[3] These figures have been calculated excluding cases reported from Northern Ireland (EU reporting requirements for suspected adverse reactions to EudraVigilance apply to Northern Ireland in accordance with the Protocol on Ireland/Northern Ireland).
[4] Source: EudraVigilance. These figures cannot be extracted directly from the public database of suspected adverse reactions, which groups information per type of side effects. As more than one suspected side effect may have been included in a single case report, the total number of side effects will never match the number of individual cases. Similarly, this public database does not provide the total number of cases reported with a fatal outcome.
[5] The European Centre for Disease Prevention and Control (ECDC) collects these exposure data from EU Member States as well as from the additional countries of the European Economic Area (EEA) Norway, Iceland and Liechtenstein.

does not necessarily mean that this was caused by the vaccine. This may have been caused, for example, by health problems not related to the vaccination.

The EU regulatory network continuously monitors EudraVigilance to detect any new safety issues. EudraVigilance relies on individual healthcare professionals and patients to report their own experience. The monitoring detects unusual or unexpected patterns in the reports received for further investigation and risk assessment. EMA's detailed assessments take into account all available data from all sources to draw a robust conclusion on the safety of the vaccine. These data include clinical trial results, reports of suspected side effects in EudraVigilance, epidemiological studies monitoring the safety of the vaccine, toxicological investigations and any other relevant information.

Planned and ongoing studies

The company that markets Vaxzevria will continue to provide results from the main clinical trials, which are ongoing. It will also conduct additional studies to monitor the safety and effectiveness of the vaccine as it is used in vaccination campaigns and other clinical practice. For the list of planned and ongoing safety studies for Vaxzevria, see the risk management plan.

A paediatric investigation plan (PIP) for Vaxzevria is in place. This describes how the company will collect data on the vaccine's efficacy and safety for its potential use in children.

In addition, EMA is coordinating observational studies in EU Member States looking at real-world data from clinical practice to monitor the safety and effectiveness of COVID-19 vaccines, including in pregnant women.

3. Other information for Vaxzevria

Vaxzevria (previously COVID-19 Vaccine AstraZeneca) is a vaccine that was authorised in the EU on 29 January 2021 for use in people aged 18 years and older to prevent COVID-19 when infected with the coronavirus SARS-CoV-2. COVID-19 is a potentially severe disease that may result in death.

Vaxzevria contains an adenovirus that has been modified to carry molecules of DNA, which the body uses to temporarily produce the SARS-CoV-2 spike protein. The spike protein does not cause COVID-19. The adenovirus cannot reproduce and does not cause viral disease.

Before Vaxzevria was granted an EU marketing authorisation, the efficacy and safety of the vaccine were assessed through pre-clinical studies and large clinical trials. More than 12,000 participants had been given the vaccine in clinical trials.

Like all medicines, this vaccine can cause side effects, although not everybody will experience them. The most common side effects known for

Vaxzevria are usually mild or moderate and get better within a few days after vaccination.

More information on how Vaxzevria works and its use is available in all EU/EEA languages in the medicine overview. This includes information on use in pregnant and breastfeeding women and immunocompromised individuals.

The full product information with the summary of product characteristics and the package leaflet is also available in all EU/EEA languages.

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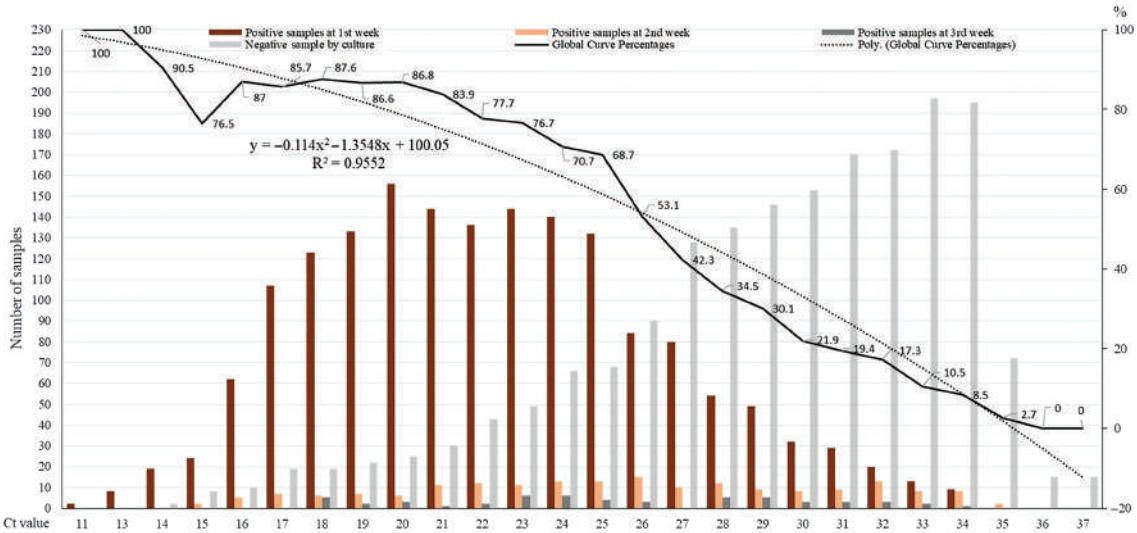
Correlation Between 3790 Quantitative Polymerase Chain Reaction–Positives Samples and Positive Cell Cultures, Including 1941 Severe Acute Respiratory Syndrome Coronavirus 2 Isolates

To the Editor—The outbreak of the coronavirus disease 2019 (COVID-19) pandemic due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was declared a pandemic on 12 March 2020 by the World Health Organization [1]. A major issue related to the outbreak has been to correlate viral RNA load obtained after reverse-transcription polymerase chain reaction (RT-PCR) and expressed as the cycle threshold (Ct) with contagiousness and therefore duration of eviction from contacts and discharge from specialized infectious disease wards. Several recent publications, based on more than 100 studies, have attempted to propose a cutoff Ct value and duration of eviction, with a consensus at approximately Ct >30 and at least 10 days, respectively [2–5]. However, in an article published in *Clinical Infectious Diseases*, Bullard et al reported that patients could not be contagious with Ct >25 as the virus is not detected in culture above this value [6]. This limit was then evoked in the French media during an interview with a member of the French Scientific Council Covid-19 as a possible value above which patients are no longer contagious [7].

At the beginning of the outbreak, we correlated Ct values obtained using our PCR technique based on amplification of the E gene and the results of the culture [8]. Since the beginning of the pandemic, we have performed 250 566 SARS-CoV-2 RT-PCR for 179 151 patients, of whom 13 161 (7.3%) tested positive. Up to the end of May, 3790 of these samples, reported as positive on nasopharyngeal samples, were inoculated and managed for culture as previously described [8]. Of these 3790 inoculated samples, 1941 SARS-CoV-2 isolates could be obtained after the first inoculation or up to 2 blind subcultures. The correlation between the scanner values and the positivity of the culture allows us to observe that the image obtained with 10 times more isolates than in our preliminary work (1941 vs 129) does not change significantly (Figure 1). It can be observed that at Ct = 25, up to 70% of patients remain positive in culture and that at Ct = 30 this value drops to 20%. At Ct = 35, the value we used to report a positive result for PCR, <3% of cultures are positive. Our Ct value of 35, initially based on the results



Ct value	11	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37
Number of samples (N = 3790)	2	8	21	34	77	133	153	164	190	186	193	210	225	217	192	218	206	209	196	211	208	220	213	74	15	15
Total positive (n = 1941)	2	8	19	26	67	114	134	142	165	156	150	161	159	149	102	90	71	63	43	41	36	23	18	2	0	0
Week 1: number of positives (n = 1700)	2	8	19	24	62	107	123	133	156	144	136	144	140	132	84	80	54	49	32	29	20	13	9	0	0	0
(% by total positive)	(100)	(100)	(100)	(92.3)	(92.5)	(93.9)	(91.8)	(93.7)	(94.5)	(92.3)	(90.7)	(89.4)	(88.1)	(88.6)	(82.4)	(88.9)	(76.1)	(77.8)	(74.4)	(70.7)	(55.6)	(56.5)	(50.0)	(0)	(-)	(-)
Week 2: number of positives (n = 187)	0	0	0	2	5	7	6	7	6	11	12	11	13	13	15	10	12	9	8	9	13	8	8	2	0	0
(% by total positive)	(0)	(0)	(0)	(7.7)	(7.5)	(6.1)	(4.5)	(4.9)	(3.6)	(7.1)	(8.0)	(6.8)	(8.2)	(8.7)	(14.7)	(11.1)	(16.9)	(14.3)	(18.6)	(22.0)	(36.1)	(34.8)	(44.0)	(100)	(-)	(-)
Week 3: number of positives (n = 54)	0	0	0	0	0	0	5	2	3	1	2	6	6	4	3	0	5	5	3	3	3	2	1	0	0	0
(% by total positive)	(0)	(0)	(0)	(0)	(0)	(0)	(3.7)	(1.4)	(1.8)	(0.6)	(1.3)	(3.7)	(3.8)	(2.7)	(2.9)	(0)	(7.0)	(7.9)	(7.0)	(7.3)	(8.3)	(8.7)	(5.6)	(0)	(-)	(-)
Negative cultured (n = 1849)	0	0	2	8	10	19	19	22	25	30	43	49	66	68	90	128	135	146	153	170	172	197	195	72	15	15

Figure 1. Percentage of positive viral cultures of severe acute respiratory syndrome coronavirus 2 polymerase chain reaction–positive nasopharyngeal samples from coronavirus disease 2019 patients, according to Ct value (plain line). The dashed curve indicates the polynomial regression curve. Abbreviations: Ct, cycle threshold; Poly., polynomial.

obtained by RT-PCR on control negative samples in our laboratory and initial results of cultures [8], is validated by the results herein presented and is in correlation with what was proposed in Korea [9] and Taiwan [10]. We could observe that subcultures, especially the first one, allow an increasing percentage of viral isolation in samples with Ct values, confirming that these high Ct values are mostly correlated with low viral loads. From our cohort, we now need to try to understand and define the duration and frequency of live virus shedding in patients on a case-by-case basis in the rare cases when the PCR is positive beyond 10 days, often at a Ct >30. In any cases, these rare cases should not impact public health decisions.

Notes

Ethical approval. The protocol was approved by the University Hospital Institute Méditerranée Infection Ethical Committee. All patients provided informed consent in accordance with the Declaration of Helsinki.

Financial support. This research was funded by the French Government under the Investissements d'avenir (Investments for the Future) program managed by the Agence Nationale de la Recherche (French National Agency for Research; reference: Méditerranée Infection 10-IAHU-03) and by Région Provence-Alpes-Côte d'Azur and European funding Fond Europen de Recheche et de developpement (FEDER) PRIMI.

Potential conflicts of interest. D. R. reports grants from the Hitachi High-Tech Corporation outside the submitted work. All other authors report no potential conflicts. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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Clinical Infectious Diseases® 2021;72(11):e932–3

DOI: 10.1093/cid/ciaa1491

The Vaccine Adverse Event Reporting System (VAERS) Results

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This dataset has been updated since this request was saved, which could lead to differences in results.

Vaccine Type	Vaccine Manufacturer	Events Reported	Percent (of 1,315,380)
ADENOVIRUS TYPE 4 &7 VACCINE, LIVE ORAL (ADEN_4_7)	TEVA PHARMACEUTICALS	159	0.01%
ADENOVIRUS TYPE 4 &7 VACCINE, LIVE ORAL (ADEN_4_7)	Total	159	0.01%
ADENOVIRUS VACCINE LIVE ORAL TYPE 7 (ADEN)	PFIZER\WYETH	8	0.00%
ADENOVIRUS VACCINE LIVE ORAL TYPE 7 (ADEN)	UNKNOWN MANUFACTURER	3	0.00%
ADENOVIRUS VACCINE LIVE ORAL TYPE 7 (ADEN)	Total	11	0.00%
ANTHRAX VACCINE (ANTH)	EMERGENT BIOSOLUTIONS	6,277	0.48%
ANTHRAX VACCINE (ANTH)	MICHIGAN DEPT PUB HLTH	1,981	0.15%
ANTHRAX VACCINE (ANTH)	UNKNOWN MANUFACTURER	913	0.07%
ANTHRAX VACCINE (ANTH)	Total	9,171	0.70%
BACILLUS CALMETTE-GUERIN VACCINE (BCG)	ORGANON-TEKNIKA	65	0.00%
BACILLUS CALMETTE-GUERIN VACCINE (BCG)	SANOFI PASTEUR	37	0.00%
BACILLUS CALMETTE-GUERIN VACCINE (BCG)	UNKNOWN MANUFACTURER	94	0.01%
BACILLUS CALMETTE-GUERIN VACCINE (BCG)	Total	196	0.01%
CENTRAL EUROPEAN ENCEPHALITIS (CEE)	UNKNOWN MANUFACTURER	1	0.00%
CENTRAL EUROPEAN ENCEPHALITIS (CEE)	Total	1	0.00%
CHOLERA VACCINE (CHOL)	LEDERLE LABORATORIES	6	0.00%
CHOLERA VACCINE (CHOL)	PAXVAX	81	0.01%
CHOLERA VACCINE (CHOL)	PFIZER\WYETH	71	0.01%
CHOLERA VACCINE (CHOL)	UNKNOWN MANUFACTURER	34	0.00%
CHOLERA VACCINE (CHOL)	Total	192	0.01%
COMVAX (HBHEPB)	MERCK & CO. INC.	5,400	0.41%
COMVAX (HBHEPB)	UNKNOWN MANUFACTURER	14	0.00%
COMVAX (HBHEPB)	Total	5,414	0.41%
COVID19 VACCINE (COVID19)	JANSSEN	54,366	4.13%
COVID19 VACCINE (COVID19)	MODERNA	290,910	22.12%
COVID19 VACCINE (COVID19)	PFIZER\BIONTECH	269,114	20.46%
COVID19 VACCINE (COVID19)	UNKNOWN MANUFACTURER	1,313	0.10%
COVID19 VACCINE (COVID19)	Total	615,703	46.81%
DENGUE TETRAVALENT VACCINE (DENGVAXIA) (DF)	SANOFI PASTEUR	16	0.00%
DENGUE TETRAVALENT VACCINE (DENGVAXIA) (DF)	Total	16	0.00%
DIPHTHERIA AND TETANUS TOXOIDS ACELLULAR PERTUSSIS POLIOVIRUS INACTIVATED HAEMOPHILUS INFLUENZA B AND HEPATITIS B VACCINE (HEXAVAX) (6VAX-F)	GLAXOSMITHKLINE BIOLOGICALS	38	0.00%
DIPHTHERIA AND TETANUS TOXOIDS ACELLULAR PERTUSSIS POLIOVIRUS INACTIVATED HAEMOPHILUS INFLUENZA B AND HEPATITIS B VACCINE (HEXAVAX) (6VAX-F)	SANOFI PASTEUR	28	0.00%
DIPHTHERIA AND TETANUS TOXOIDS ACELLULAR PERTUSSIS POLIOVIRUS INACTIVATED HAEMOPHILUS INFLUENZA B AND HEPATITIS B VACCINE (HEXAVAX) (6VAX-F)	UNKNOWN MANUFACTURER	128	0.01%
DIPHTHERIA AND TETANUS TOXOIDS ACELLULAR PERTUSSIS POLIOVIRUS INACTIVATED HAEMOPHILUS INFLUENZA B AND HEPATITIS B VACCINE (HEXAVAX) (6VAX-F)	Total	194	0.01%

Vaccine Type	Vaccine Manufacturer	Events Reported	Percent (of 1,315,380)
DIPHTHERIA AND TETANUS TOXOIDS AND ACELLULAR PERTUSSIS VACCINE (DTAP)	BAXTER HEALTHCARE CORP.	43	0.00%
DIPHTHERIA AND TETANUS TOXOIDS AND ACELLULAR PERTUSSIS VACCINE (DTAP)	CONNAUGHT LABORATORIES	6,344	0.48%
DIPHTHERIA AND TETANUS TOXOIDS AND ACELLULAR PERTUSSIS VACCINE (DTAP)	GLAXOSMITHKLINE BIOLOGICALS	11,910	0.91%
DIPHTHERIA AND TETANUS TOXOIDS AND ACELLULAR PERTUSSIS VACCINE (DTAP)	NORTH AMERICAN VACCINES	60	0.00%
DIPHTHERIA AND TETANUS TOXOIDS AND ACELLULAR PERTUSSIS VACCINE (DTAP)	PFIZER\WYETH	3,345	0.25%
DIPHTHERIA AND TETANUS TOXOIDS AND ACELLULAR PERTUSSIS VACCINE (DTAP)	SANOFI PASTEUR	23,023	1.75%
DIPHTHERIA AND TETANUS TOXOIDS AND ACELLULAR PERTUSSIS VACCINE (DTAP)	SMITHKLINE BEECHAM	7,026	0.53%
DIPHTHERIA AND TETANUS TOXOIDS AND ACELLULAR PERTUSSIS VACCINE (DTAP)	UNKNOWN MANUFACTURER	4,629	0.35%
DIPHTHERIA AND TETANUS TOXOIDS AND ACELLULAR PERTUSSIS VACCINE (DTAP)	**Total**	**56,380**	**4.29%**
DIPHTHERIA AND TETANUS TOXOIDS AND ACELLULAR PERTUSSIS VACCINE + INACTIVATED POLIOVIRUS VACCINE (DTAPIPV)	GLAXOSMITHKLINE BIOLOGICALS	7,648	0.58%
DIPHTHERIA AND TETANUS TOXOIDS AND ACELLULAR PERTUSSIS VACCINE + INACTIVATED POLIOVIRUS VACCINE (DTAPIPV)	SANOFI PASTEUR	973	0.07%
DIPHTHERIA AND TETANUS TOXOIDS AND ACELLULAR PERTUSSIS VACCINE + INACTIVATED POLIOVIRUS VACCINE (DTAPIPV)	UNKNOWN MANUFACTURER	148	0.01%
DIPHTHERIA AND TETANUS TOXOIDS AND ACELLULAR PERTUSSIS VACCINE + INACTIVATED POLIOVIRUS VACCINE (DTAPIPV)	**Total**	**8,769**	**0.67%**
DIPHTHERIA AND TETANUS TOXOIDS AND ACELLULAR PERTUSSIS VACCINE + HEPATITIS B + INACTIVATED POLIOVIRUS VACCINE (DTAPHEPBIP)	GLAXOSMITHKLINE BIOLOGICALS	11,088	0.84%
DIPHTHERIA AND TETANUS TOXOIDS AND ACELLULAR PERTUSSIS VACCINE + HEPATITIS B + INACTIVATED POLIOVIRUS VACCINE (DTAPHEPBIP)	UNKNOWN MANUFACTURER	163	0.01%
DIPHTHERIA AND TETANUS TOXOIDS AND ACELLULAR PERTUSSIS VACCINE + HEPATITIS B + INACTIVATED POLIOVIRUS VACCINE (DTAPHEPBIP)	**Total**	**11,251**	**0.86%**
DIPHTHERIA AND TETANUS TOXOIDS AND ACELLULAR PERTUSSIS VACCINE + INACTIVATED POLIOVIRUS VACCINE + HAEMOPHILUS B CONJUGATE VACCINE (DTAPIPVHIB)	GLAXOSMITHKLINE BIOLOGICALS	32	0.00%
DIPHTHERIA AND TETANUS TOXOIDS AND ACELLULAR PERTUSSIS VACCINE + INACTIVATED POLIOVIRUS VACCINE + HAEMOPHILUS B CONJUGATE VACCINE (DTAPIPVHIB)	SANOFI PASTEUR	8,451	0.64%
DIPHTHERIA AND TETANUS TOXOIDS AND ACELLULAR PERTUSSIS VACCINE + INACTIVATED POLIOVIRUS VACCINE + HAEMOPHILUS B CONJUGATE VACCINE (DTAPIPVHIB)	UNKNOWN MANUFACTURER	87	0.01%
DIPHTHERIA AND TETANUS TOXOIDS AND ACELLULAR PERTUSSIS VACCINE + INACTIVATED POLIOVIRUS VACCINE + HAEMOPHILUS B CONJUGATE VACCINE (DTAPIPVHIB)	**Total**	**8,570**	**0.65%**
DIPHTHERIA AND TETANUS TOXOIDS AND PERTUSSIS VACCINE (DTP)	CONNAUGHT LABORATORIES	9,422	0.72%
DIPHTHERIA AND TETANUS TOXOIDS AND PERTUSSIS VACCINE (DTP)	EMERGENT BIOSOLUTIONS	2	0.00%
DIPHTHERIA AND TETANUS TOXOIDS AND PERTUSSIS VACCINE (DTP)	LEDERLE LABORATORIES	8,132	0.62%
DIPHTHERIA AND TETANUS TOXOIDS AND PERTUSSIS VACCINE (DTP)	MASS. PUB HLTH BIOL LAB	465	0.04%
DIPHTHERIA AND TETANUS TOXOIDS AND PERTUSSIS VACCINE (DTP)	MICHIGAN DEPT PUB HLTH	721	0.05%
DIPHTHERIA AND TETANUS TOXOIDS AND PERTUSSIS VACCINE (DTP)	PFIZER\WYETH	22	0.00%
DIPHTHERIA AND TETANUS TOXOIDS AND PERTUSSIS VACCINE (DTP)	SANOFI PASTEUR	250	0.02%
DIPHTHERIA AND TETANUS TOXOIDS AND PERTUSSIS VACCINE (DTP)	UNKNOWN MANUFACTURER	1,771	0.13%
DIPHTHERIA AND TETANUS TOXOIDS AND PERTUSSIS VACCINE (DTP)	**Total**	**20,785**	**1.58%**
DIPHTHERIA AND TETANUS TOXOIDS AND PERTUSSIS VACCINE + INACTIVATED POLIOVIRUS VACCINE + HAEMOPHILUS B CONJUGATE VACCINE (TETANUS TOXOID CONJUGATE) (DTPPHIB)	UNKNOWN MANUFACTURER	51	0.00%
DIPHTHERIA AND TETANUS TOXOIDS AND PERTUSSIS VACCINE + INACTIVATED POLIOVIRUS VACCINE + HAEMOPHILUS B CONJUGATE VACCINE (TETANUS TOXOID CONJUGATE) (DTPPHIB)	**Total**	**51**	**0.00%**
DIPHTHERIA AND TETANUS TOXOIDS PERTUSSIS AND HAEMOPHILUS INFLUENZA B VACCINE (HEXAVAX) (DTPHIB)	PFIZER\WYETH	5,926	0.45%
DIPHTHERIA AND TETANUS TOXOIDS PERTUSSIS AND HAEMOPHILUS INFLUENZA B VACCINE (HEXAVAX) (DTPHIB)	SANOFI PASTEUR	47	0.00%

Vaccine Type	Vaccine Manufacturer	Events Reported	Percent (of 1,315,380)
DIPHTHERIA AND TETANUS TOXOIDS PERTUSSIS AND HAEMOPHILUS INFLUENZA B VACCINE (HEXAVAX) (DTPHIB)	UNKNOWN MANUFACTURER	104	0.01%
DIPHTHERIA AND TETANUS TOXOIDS PERTUSSIS AND HAEMOPHILUS INFLUENZA B VACCINE (HEXAVAX) (DTPHIB)	**Total**	**6,077**	**0.46%**
DIPHTHERIA AND TETANUS TOXOIDS, PEDIATRIC (DT)	BSI	68	0.01%
DIPHTHERIA AND TETANUS TOXOIDS, PEDIATRIC (DT)	CONNAUGHT LABORATORIES	615	0.05%
DIPHTHERIA AND TETANUS TOXOIDS, PEDIATRIC (DT)	CONNAUGHT LTD.	45	0.00%
DIPHTHERIA AND TETANUS TOXOIDS, PEDIATRIC (DT)	EMERGENT BIOSOLUTIONS	2	0.00%
DIPHTHERIA AND TETANUS TOXOIDS, PEDIATRIC (DT)	GLAXOSMITHKLINE BIOLOGICALS	79	0.01%
DIPHTHERIA AND TETANUS TOXOIDS, PEDIATRIC (DT)	LEDERLE LABORATORIES	373	0.03%
DIPHTHERIA AND TETANUS TOXOIDS, PEDIATRIC (DT)	MASS. PUB HLTH BIOL LAB	68	0.01%
DIPHTHERIA AND TETANUS TOXOIDS, PEDIATRIC (DT)	MICHIGAN DEPT PUB HLTH	39	0.00%
DIPHTHERIA AND TETANUS TOXOIDS, PEDIATRIC (DT)	PFIZER\WYETH	186	0.01%
DIPHTHERIA AND TETANUS TOXOIDS, PEDIATRIC (DT)	SANOFI PASTEUR	557	0.04%
DIPHTHERIA AND TETANUS TOXOIDS, PEDIATRIC (DT)	SCLAVO	66	0.01%
DIPHTHERIA AND TETANUS TOXOIDS, PEDIATRIC (DT)	UNKNOWN MANUFACTURER	292	0.02%
DIPHTHERIA AND TETANUS TOXOIDS, PEDIATRIC (DT)	**Total**	**2,390**	**0.18%**
DIPHTHERIA TOXOID (DTOX)	UNKNOWN MANUFACTURER	76	0.01%
DIPHTHERIA TOXOID (DTOX)	**Total**	**76**	**0.01%**
DIPHTHERIA/PERTUSSIS/POLIO (ORAL [LIVE] OR INACTIVATED NOT NOTED) (DPP)	NOVARTIS VACCINES AND DIAGNOSTICS	23	0.00%
DIPHTHERIA/PERTUSSIS/POLIO (ORAL [LIVE] OR INACTIVATED NOT NOTED) (DPP)	UNKNOWN MANUFACTURER	174	0.01%
DIPHTHERIA/PERTUSSIS/POLIO (ORAL [LIVE] OR INACTIVATED NOT NOTED) (DPP)	**Total**	**197**	**0.01%**
DIPHTHERIA/TETANUS/PERTUSSIS/HEPATITIS B (DTPHEP)	GLAXOSMITHKLINE BIOLOGICALS	16	0.00%
DIPHTHERIA/TETANUS/PERTUSSIS/HEPATITIS B (DTPHEP)	UNKNOWN MANUFACTURER	25	0.00%
DIPHTHERIA/TETANUS/PERTUSSIS/HEPATITIS B (DTPHEP)	**Total**	**41**	**0.00%**
DIPHTHERIA/TETANUS/WHOLE PERTUSSIS-INACTIVATED POLIO VIRUS-HAEMOPHILUS INFLUENZA B (PENTACOQR) (DTPIHI)	UNKNOWN MANUFACTURER	57	0.00%
DIPHTHERIA/TETANUS/WHOLE PERTUSSIS-INACTIVATED POLIO VIRUS-HAEMOPHILUS INFLUENZA B (PENTACOQR) (DTPIHI)	**Total**	**57**	**0.00%**
DT-IPV COMBINED DT AND IPV VACCINE (DTIPV)	UNKNOWN MANUFACTURER	28	0.00%
DT-IPV COMBINED DT AND IPV VACCINE (DTIPV)	**Total**	**28**	**0.00%**
DTP-IPV COMBINED DTP AND IPV VACCINE (DTPIPV)	BERNA BIOTECH, LTD.	2	0.00%
DTP-IPV COMBINED DTP AND IPV VACCINE (DTPIPV)	SANOFI PASTEUR	43	0.00%
DTP-IPV COMBINED DTP AND IPV VACCINE (DTPIPV)	UNKNOWN MANUFACTURER	41	0.00%
DTP-IPV COMBINED DTP AND IPV VACCINE (DTPIPV)	**Total**	**86**	**0.01%**
DTPPVHBHPB (DTPPVHBHPB)	MSP VACCINE COMPANY	1	0.00%
DTPPVHBHPB (DTPPVHBHPB)	**Total**	**1**	**0.00%**
EBOLA ZAIRE VACCINE (EBZR)	MERCK & CO. INC.	21	0.00%
EBOLA ZAIRE VACCINE (EBZR)	**Total**	**21**	**0.00%**
HAEMOPHILUS B CONJUGATE VACCINE (HIBV)	CONNAUGHT LABORATORIES	5,122	0.39%
HAEMOPHILUS B CONJUGATE VACCINE (HIBV)	GLAXOSMITHKLINE BIOLOGICALS	624	0.05%
HAEMOPHILUS B CONJUGATE VACCINE (HIBV)	LEDERLE PRAXSIS	11	0.00%
HAEMOPHILUS B CONJUGATE VACCINE (HIBV)	MERCK & CO. INC.	12,477	0.95%
HAEMOPHILUS B CONJUGATE VACCINE (HIBV)	PFIZER\WYETH	14,368	1.09%
HAEMOPHILUS B CONJUGATE VACCINE (HIBV)	SANOFI PASTEUR	13,093	1.00%
HAEMOPHILUS B CONJUGATE VACCINE (HIBV)	UNKNOWN MANUFACTURER	2,970	0.23%
HAEMOPHILUS B CONJUGATE VACCINE (HIBV)	**Total**	**48,665**	**3.70%**
HAEMOPHILUS B POLYSACCHARIDE VACCINE (HBPV)	PFIZER\WYETH	237	0.02%
HAEMOPHILUS B POLYSACCHARIDE VACCINE (HBPV)	UNKNOWN	21	0.00%

Vaccine Type	Vaccine Manufacturer	Events Reported	Percent (of 1,315,380)
HAEMOPHILUS B POLYSACCHARIDE VACCINE (HBPV)	Total	258	0.02%
HEPATITIS A (HEPA)	GLAXOSMITHKLINE BIOLOGICALS	17,483	1.33%
HEPATITIS A (HEPA)	MERCK & CO. INC.	14,816	1.13%
HEPATITIS A (HEPA)	SMITHKLINE BEECHAM	2,099	0.16%
HEPATITIS A (HEPA)	UNKNOWN MANUFACTURER	2,400	0.18%
HEPATITIS A (HEPA)	Total	36,798	2.80%
HEPATITIS A AND HEPATITIS B VACCINE (HEPAB)	GLAXOSMITHKLINE BIOLOGICALS	2,855	0.22%
HEPATITIS A AND HEPATITIS B VACCINE (HEPAB)	SMITHKLINE BEECHAM	80	0.01%
HEPATITIS A AND HEPATITIS B VACCINE (HEPAB)	UNKNOWN MANUFACTURER	115	0.01%
HEPATITIS A AND HEPATITIS B VACCINE (HEPAB)	Total	3,050	0.23%
HEPATITIS A AND TYPHOID VACCINES (HEPATYP)	GLAXOSMITHKLINE BIOLOGICALS	5	0.00%
HEPATITIS A AND TYPHOID VACCINES (HEPATYP)	Total	5	0.00%
HEPATITIS B VACCINE (HEP)	DYNAVAX TECHNOLOGIES CORPORATION	340	0.03%
HEPATITIS B VACCINE (HEP)	GLAXOSMITHKLINE BIOLOGICALS	11,029	0.84%
HEPATITIS B VACCINE (HEP)	MERCK & CO. INC.	27,573	2.10%
HEPATITIS B VACCINE (HEP)	SANOFI PASTEUR	55	0.00%
HEPATITIS B VACCINE (HEP)	SMITHKLINE BEECHAM	15,934	1.21%
HEPATITIS B VACCINE (HEP)	UNKNOWN MANUFACTURER	3,755	0.29%
HEPATITIS B VACCINE (HEP)	Total	58,686	4.46%
HUMAN PAPILLOMAVIRUS (TYPES 6, 11, 16, 18) RECOMBINANT VACCINE (HPV4)	MERCK & CO. INC.	36,962	2.81%
HUMAN PAPILLOMAVIRUS (TYPES 6, 11, 16, 18) RECOMBINANT VACCINE (HPV4)	Total	36,962	2.81%
HUMAN PAPILLOMAVIRUS (TYPES 6, 11,16, 18, 31, 33, 45, 52, 58) RECOMBINANT VACCINE (HPV9)	MERCK & CO. INC.	14,400	1.09%
HUMAN PAPILLOMAVIRUS (TYPES 6, 11,16, 18, 31, 33, 45, 52, 58) RECOMBINANT VACCINE (HPV9)	Total	14,400	1.09%
HUMAN PAPILLOMAVIRUS VACCINE (HPVX)	UNKNOWN MANUFACTURER	1,050	0.08%
HUMAN PAPILLOMAVIRUS VACCINE (HPVX)	Total	1,050	0.08%
HUMAN PAPILLOVAVIRUS BIVALENT (HPV2)	GLAXOSMITHKLINE BIOLOGICALS	261	0.02%
HUMAN PAPILLOVAVIRUS BIVALENT (HPV2)	Total	261	0.02%
INFLUENZA (H1N1) MONOVALENT (INJECTED) (FLU(H1N1))	CSL LIMITED	275	0.02%
INFLUENZA (H1N1) MONOVALENT (INJECTED) (FLU(H1N1))	GLAXOSMITHKLINE BIOLOGICALS	56	0.00%
INFLUENZA (H1N1) MONOVALENT (INJECTED) (FLU(H1N1))	NOVARTIS VACCINES AND DIAGNOSTICS	3,417	0.26%
INFLUENZA (H1N1) MONOVALENT (INJECTED) (FLU(H1N1))	SANOFI PASTEUR	4,743	0.36%
INFLUENZA (H1N1) MONOVALENT (INJECTED) (FLU(H1N1))	Total	8,491	0.65%
INFLUENZA (H1N1) MONOVALENT, (INTRANASAL SPRAY) (FLUN(H1N1))	MEDIMMUNE VACCINES, INC.	2,889	0.22%
INFLUENZA (H1N1) MONOVALENT, (INTRANASAL SPRAY) (FLUN(H1N1))	Total	2,889	0.22%
INFLUENZA VIRUS VACCINE, NO BRAND NAME (FLUX(SEASONAL))	CSL LIMITED	5	0.00%
INFLUENZA VIRUS VACCINE, NO BRAND NAME (FLUX(SEASONAL))	NOVARTIS VACCINES AND DIAGNOSTICS	6	0.00%
INFLUENZA VIRUS VACCINE, NO BRAND NAME (FLUX(SEASONAL))	PFIZER\WYETH	1,811	0.14%
INFLUENZA VIRUS VACCINE, NO BRAND NAME (FLUX(SEASONAL))	SANOFI PASTEUR	449	0.03%
INFLUENZA VIRUS VACCINE, NO BRAND NAME (FLUX(SEASONAL))	UNKNOWN MANUFACTURER	18,293	1.39%
INFLUENZA VIRUS VACCINE, NO BRAND NAME (FLUX(SEASONAL))	Total	20,564	1.56%
INFLUENZA VIRUS VACCINE, QUADRIVALENT (INJECTED) (FLU4(SEASONAL))	GLAXOSMITHKLINE BIOLOGICALS	12,191	0.93%
INFLUENZA VIRUS VACCINE, QUADRIVALENT (INJECTED) (FLU4(SEASONAL))	SANOFI PASTEUR	15,116	1.15%

Vaccine Type	Vaccine Manufacturer	Events Reported	Percent (of 1,315,380)
INFLUENZA VIRUS VACCINE, QUADRIVALENT (INJECTED) (FLU4(SEASONAL))	SEQIRUS, INC.	3,528	0.27%
INFLUENZA VIRUS VACCINE, QUADRIVALENT (INJECTED) (FLU4(SEASONAL))	**Total**	**30,835**	**2.34%**
INFLUENZA VIRUS VACCINE, QUADRIVALENT (INTRANASAL SPRAY) (FLUN4(SEASONAL))	MEDIMMUNE VACCINES, INC.	3,005	0.23%
INFLUENZA VIRUS VACCINE, QUADRIVALENT (INTRANASAL SPRAY) (FLUN4(SEASONAL))	**Total**	**3,005**	**0.23%**
INFLUENZA VIRUS VACCINE, QUADRIVALENT, ADJUVANT (INJECTED) (FLUA4(SEASONAL))	SEQIRUS, INC.	824	0.06%
INFLUENZA VIRUS VACCINE, QUADRIVALENT, ADJUVANT (INJECTED) (FLUA4(SEASONAL))	**Total**	**824**	**0.06%**
INFLUENZA VIRUS VACCINE, QUADRIVALENT, CELL-CULTURE-DERIVED (INJECTED) (FLUC4(SEASONAL))	SEQIRUS, INC.	4,617	0.35%
INFLUENZA VIRUS VACCINE, QUADRIVALENT, CELL-CULTURE-DERIVED (INJECTED) (FLUC4(SEASONAL))	**Total**	**4,617**	**0.35%**
INFLUENZA VIRUS VACCINE, QUADRIVALENT, RECOMBINANT (INJECTED) (FLUR4(SEASONAL))	PROTEIN SCIENCES CORPORATION	1,876	0.14%
INFLUENZA VIRUS VACCINE, QUADRIVALENT, RECOMBINANT (INJECTED) (FLUR4(SEASONAL))	**Total**	**1,876**	**0.14%**
INFLUENZA VIRUS VACCINE, TRIVALENT (INJECTED) (FLU3(SEASONAL))	AVENTIS PASTEUR	617	0.05%
INFLUENZA VIRUS VACCINE, TRIVALENT (INJECTED) (FLU3(SEASONAL))	CONNAUGHT LABORATORIES	4,233	0.32%
INFLUENZA VIRUS VACCINE, TRIVALENT (INJECTED) (FLU3(SEASONAL))	CSL LIMITED	7,162	0.54%
INFLUENZA VIRUS VACCINE, TRIVALENT (INJECTED) (FLU3(SEASONAL))	EVANS VACCINES	2,149	0.16%
INFLUENZA VIRUS VACCINE, TRIVALENT (INJECTED) (FLU3(SEASONAL))	GLAXOSMITHKLINE BIOLOGICALS	7,912	0.60%
INFLUENZA VIRUS VACCINE, TRIVALENT (INJECTED) (FLU3(SEASONAL))	LEDERLE LABORATORIES	111	0.01%
INFLUENZA VIRUS VACCINE, TRIVALENT (INJECTED) (FLU3(SEASONAL))	MEDEVA PHARMA, LTD.	843	0.06%
INFLUENZA VIRUS VACCINE, TRIVALENT (INJECTED) (FLU3(SEASONAL))	NOVARTIS VACCINES AND DIAGNOSTICS	15,179	1.15%
INFLUENZA VIRUS VACCINE, TRIVALENT (INJECTED) (FLU3(SEASONAL))	PARKDALE PHARMACEUTICALS	470	0.04%
INFLUENZA VIRUS VACCINE, TRIVALENT (INJECTED) (FLU3(SEASONAL))	PARKE-DAVIS	1,340	0.10%
INFLUENZA VIRUS VACCINE, TRIVALENT (INJECTED) (FLU3(SEASONAL))	PFIZER\WYETH	4,426	0.34%
INFLUENZA VIRUS VACCINE, TRIVALENT (INJECTED) (FLU3(SEASONAL))	SANOFI PASTEUR	48,796	3.71%
INFLUENZA VIRUS VACCINE, TRIVALENT (INJECTED) (FLU3(SEASONAL))	**Total**	**93,238**	**7.09%**
INFLUENZA VIRUS VACCINE, TRIVALENT (INTRANASAL SPRAY) (FLUN3(SEASONAL))	MEDIMMUNE VACCINES, INC.	5,813	0.44%
INFLUENZA VIRUS VACCINE, TRIVALENT (INTRANASAL SPRAY) (FLUN3(SEASONAL))	**Total**	**5,813**	**0.44%**
INFLUENZA VIRUS VACCINE, TRIVALENT, ADJUVANT (INJECTED) (FLUA3(SEASONAL))	NOVARTIS VACCINES AND DIAGNOSTICS	2,426	0.18%
INFLUENZA VIRUS VACCINE, TRIVALENT, ADJUVANT (INJECTED) (FLUA3(SEASONAL))	**Total**	**2,426**	**0.18%**
INFLUENZA VIRUS VACCINE, TRIVALENT, CELL-CULTURE-DERIVED (INJECTED) (FLUC3(SEASONAL))	NOVARTIS VACCINES AND DIAGNOSTICS	1,024	0.08%
INFLUENZA VIRUS VACCINE, TRIVALENT, CELL-CULTURE-DERIVED (INJECTED) (FLUC3(SEASONAL))	**Total**	**1,024**	**0.08%**
INFLUENZA VIRUS VACCINE, TRIVALENT, RECOMBINANT (INJECTED) (FLUR3(SEASONAL))	PROTEIN SCIENCES CORPORATION	200	0.02%
INFLUENZA VIRUS VACCINE, TRIVALENT, RECOMBINANT (INJECTED) (FLUR3(SEASONAL))	**Total**	**200**	**0.02%**
INFLUENZA(H1N1) MONOVALENT, UNKNOWN MANUFACTURER (FLUX(H1N1))	UNKNOWN MANUFACTURER	2,015	0.15%
INFLUENZA(H1N1) MONOVALENT, UNKNOWN MANUFACTURER (FLUX(H1N1))	**Total**	**2,015**	**0.15%**
JAPANESE ENCEPHALITIS VIRUS VACCINE (JEV)	CONNAUGHT LABORATORIES	189	0.01%
JAPANESE ENCEPHALITIS VIRUS VACCINE (JEV)	SANOFI PASTEUR	297	0.02%
JAPANESE ENCEPHALITIS VIRUS VACCINE (JEV)	**Total**	**486**	**0.04%**

Vaccine Type	Vaccine Manufacturer	Events Reported	Percent (of 1,315,380)
JAPANESE ENCEPHALITIS VIRUS VACCINE (NO BRAND NAME) (JEVX)	UNKNOWN MANUFACTURER	39	0.00%
JAPANESE ENCEPHALITIS VIRUS VACCINE (NO BRAND NAME) (JEVX)	**Total**	**39**	**0.00%**
JAPANESE ENCEPHALITIS VIRUS VACCINE, INACTIVATED, ADSORBED (JEV1)	INTERCELL AG	373	0.03%
JAPANESE ENCEPHALITIS VIRUS VACCINE, INACTIVATED, ADSORBED (JEV1)	**Total**	**373**	**0.03%**
LYME VACCINE (LYMERIX) (LYME)	GLAXOSMITHKLINE BIOLOGICALS	637	0.05%
LYME VACCINE (LYMERIX) (LYME)	SMITHKLINE BEECHAM	1,585	0.12%
LYME VACCINE (LYMERIX) (LYME)	**Total**	**2,222**	**0.17%**
MEASLES AND MUMPS VIRUS VACCINE, LIVE (MM)	MERCK & CO. INC.	54	0.00%
MEASLES AND MUMPS VIRUS VACCINE, LIVE (MM)	UNKNOWN MANUFACTURER	12	0.00%
MEASLES AND MUMPS VIRUS VACCINE, LIVE (MM)	**Total**	**66**	**0.01%**
MEASLES AND RUBELLA VACCINE (MER)	MERCK & CO. INC.	156	0.01%
MEASLES AND RUBELLA VACCINE (MER)	UNKNOWN MANUFACTURER	5	0.00%
MEASLES AND RUBELLA VACCINE (MER)	**Total**	**161**	**0.01%**
MEASLES VACCINE (MEA)	MERCK & CO. INC.	594	0.05%
MEASLES VACCINE (MEA)	UNKNOWN MANUFACTURER	46	0.00%
MEASLES VACCINE (MEA)	**Total**	**640**	**0.05%**
MEASLES, MUMPS AND RUBELLA VIRUS VACCINE, LIVE (MMR)	GLAXOSMITHKLINE BIOLOGICALS	98	0.01%
MEASLES, MUMPS AND RUBELLA VIRUS VACCINE, LIVE (MMR)	MERCK & CO. INC.	72,594	5.52%
MEASLES, MUMPS AND RUBELLA VIRUS VACCINE, LIVE (MMR)	UNKNOWN MANUFACTURER	3,804	0.29%
MEASLES, MUMPS AND RUBELLA VIRUS VACCINE, LIVE (MMR)	**Total**	**76,496**	**5.82%**
MEASLES, MUMPS, RUBELLA, AND VARICELLA VACCINE (PROQUAD) (MMRV)	MERCK & CO. INC.	15,810	1.20%
MEASLES, MUMPS, RUBELLA, AND VARICELLA VACCINE (PROQUAD) (MMRV)	UNKNOWN MANUFACTURER	340	0.03%
MEASLES, MUMPS, RUBELLA, AND VARICELLA VACCINE (PROQUAD) (MMRV)	**Total**	**16,150**	**1.23%**
MENINGICOCCAL GROUP C & Y + HIB (MNQHIB)	GLAXOSMITHKLINE BIOLOGICALS	22	0.00%
MENINGICOCCAL GROUP C & Y + HIB (MNQHIB)	**Total**	**22**	**0.00%**
MENINGOCOCCAL B VACCINE (MENB)	NOVARTIS VACCINES AND DIAGNOSTICS	3,256	0.25%
MENINGOCOCCAL B VACCINE (MENB)	PFIZER\WYETH	2,943	0.22%
MENINGOCOCCAL B VACCINE (MENB)	**Total**	**6,199**	**0.47%**
MENINGOCOCCAL CONJUGATE VACCINE (MNC)	PFIZER\WYETH	1	0.00%
MENINGOCOCCAL CONJUGATE VACCINE (MNC)	**Total**	**1**	**0.00%**
MENINGOCOCCAL GROUPS C AND Y + HAEMOPHILUS B TETANUS TOXOID CONJUGATE VACCINE (MENHIB)	GLAXOSMITHKLINE BIOLOGICALS	8	0.00%
MENINGOCOCCAL GROUPS C AND Y + HAEMOPHILUS B TETANUS TOXOID CONJUGATE VACCINE (MENHIB)	UNKNOWN MANUFACTURER	11	0.00%
MENINGOCOCCAL GROUPS C AND Y + HAEMOPHILUS B TETANUS TOXOID CONJUGATE VACCINE (MENHIB)	**Total**	**19**	**0.00%**
MENINGOCOCCAL POLYSACCHARIDE VACCINE (MEN)	CONNAUGHT LABORATORIES	382	0.03%
MENINGOCOCCAL POLYSACCHARIDE VACCINE (MEN)	CONNAUGHT LTD.	69	0.01%
MENINGOCOCCAL POLYSACCHARIDE VACCINE (MEN)	SANOFI PASTEUR	1,039	0.08%
MENINGOCOCCAL POLYSACCHARIDE VACCINE (MEN)	UNKNOWN MANUFACTURER	1,232	0.09%
MENINGOCOCCAL POLYSACCHARIDE VACCINE (MEN)	**Total**	**2,722**	**0.21%**
MENINGOCOCCAL VACCINE (MENACTRA) (MNQ)	NOVARTIS VACCINES AND DIAGNOSTICS	5,864	0.45%
MENINGOCOCCAL VACCINE (MENACTRA) (MNQ)	SANOFI PASTEUR	17,648	1.34%
MENINGOCOCCAL VACCINE (MENACTRA) (MNQ)	UNKNOWN MANUFACTURER	78	0.01%
MENINGOCOCCAL VACCINE (MENACTRA) (MNQ)	**Total**	**23,590**	**1.79%**
MUMPS AND RUBELLA VIRUS VACCINE, LIVE (MUR)	MERCK & CO. INC.	26	0.00%
MUMPS AND RUBELLA VIRUS VACCINE, LIVE (MUR)	UNKNOWN MANUFACTURER	2	0.00%

MUMPS AND RUBELLA VIRUS VACCINE, LIVE (MUR)	Total	28	0.00%
Vaccine Type	Vaccine Manufacturer	Events Reported	Percent (of 1,315,380)
MUMPS VIRUS VACCINE, LIVE (MU)	MERCK & CO. INC.	138	0.01%
MUMPS VIRUS VACCINE, LIVE (MU)	UNKNOWN MANUFACTURER	17	0.00%
MUMPS VIRUS VACCINE, LIVE (MU)	Total	155	0.01%
PANDEMIC FLU VACCINE (H5N1)	SANOFI PASTEUR	4	0.00%
PANDEMIC FLU VACCINE (H5N1)	Total	4	0.00%
PERTUSSIS, ADSORBED VACCINE (PER)	EMERGENT BIOSOLUTIONS	100	0.01%
PERTUSSIS, ADSORBED VACCINE (PER)	UNKNOWN MANUFACTURER	41	0.00%
PERTUSSIS, ADSORBED VACCINE (PER)	Total	141	0.01%
PLAGUE VACCINE (PLAGUE)	GREER LABORATORIES, INC.	11	0.00%
PLAGUE VACCINE (PLAGUE)	MILES LABORATORIES	13	0.00%
PLAGUE VACCINE (PLAGUE)	UNKNOWN MANUFACTURER	4	0.00%
PLAGUE VACCINE (PLAGUE)	Total	28	0.00%
PNEUMOCOCCAL VACCINE, POLYVALENT (PPV)	MERCK & CO. INC.	52,455	3.99%
PNEUMOCOCCAL VACCINE, POLYVALENT (PPV)	PFIZER\WYETH	2,938	0.22%
PNEUMOCOCCAL VACCINE, POLYVALENT (PPV)	UNKNOWN MANUFACTURER	4,459	0.34%
PNEUMOCOCCAL VACCINE, POLYVALENT (PPV)	Total	59,852	4.55%
PNEUMOCOCCAL, 10-VALENT VACCINE (SYNFLORIX) (PNC10)	GLAXOSMITHKLINE BIOLOGICALS	37	0.00%
PNEUMOCOCCAL, 10-VALENT VACCINE (SYNFLORIX) (PNC10)	Total	37	0.00%
PNEUMOCOCCAL, 13-VALENT VACCINE (PREVNAR) (PNC13)	PFIZER\WYETH	27,363	2.08%
PNEUMOCOCCAL, 13-VALENT VACCINE (PREVNAR) (PNC13)	Total	27,363	2.08%
PNEUMOCOCCAL, 7-VALENT VACCINE (PREVNAR) (PNC)	PFIZER\WYETH	23,352	1.78%
PNEUMOCOCCAL, 7-VALENT VACCINE (PREVNAR) (PNC)	Total	23,352	1.78%
POLIOVIRUS VACCINE INACTIVATED (IPV)	CONNAUGHT LTD.	5,505	0.42%
POLIOVIRUS VACCINE INACTIVATED (IPV)	PASTEUR MERIEUX CONNAUGHT	104	0.01%
POLIOVIRUS VACCINE INACTIVATED (IPV)	PASTEUR MERIEUX INST.	1,357	0.10%
POLIOVIRUS VACCINE INACTIVATED (IPV)	PFIZER\WYETH	134	0.01%
POLIOVIRUS VACCINE INACTIVATED (IPV)	SANOFI PASTEUR	26,635	2.02%
POLIOVIRUS VACCINE INACTIVATED (IPV)	UNKNOWN MANUFACTURER	2,769	0.21%
POLIOVIRUS VACCINE INACTIVATED (IPV)	Total	36,504	2.78%
POLIOVIRUS VACCINE TRIVALENT, LIVE, ORAL (OPV)	PFIZER\WYETH	22,504	1.71%
POLIOVIRUS VACCINE TRIVALENT, LIVE, ORAL (OPV)	UNKNOWN MANUFACTURER	1,195	0.09%
POLIOVIRUS VACCINE TRIVALENT, LIVE, ORAL (OPV)	Total	23,699	1.80%
RABIES VIRUS VACCINE (RAB)	CONNAUGHT LTD.	53	0.00%
RABIES VIRUS VACCINE (RAB)	EMERGENT BIOSOLUTIONS	4	0.00%
RABIES VIRUS VACCINE (RAB)	MICHIGAN DEPT PUB HLTH	92	0.01%
RABIES VIRUS VACCINE (RAB)	NOVARTIS VACCINES AND DIAGNOSTICS	1,494	0.11%
RABIES VIRUS VACCINE (RAB)	PASTEUR MERIEUX INST.	1,161	0.09%
RABIES VIRUS VACCINE (RAB)	SANOFI PASTEUR	1,102	0.08%
RABIES VIRUS VACCINE (RAB)	UNKNOWN MANUFACTURER	257	0.02%
RABIES VIRUS VACCINE (RAB)	Total	4,163	0.32%
ROTAVIRUS (NO BRAND NAME) (RVX)	UNKNOWN MANUFACTURER	880	0.07%
ROTAVIRUS (NO BRAND NAME) (RVX)	Total	880	0.07%
ROTAVIRUS VACCINE (ROTASHIELD) (RV)	PFIZER\WYETH	698	0.05%
ROTAVIRUS VACCINE (ROTASHIELD) (RV)	Total	698	0.05%
ROTAVIRUS VACCINE, LIVE, ORAL (RV1)	GLAXOSMITHKLINE BIOLOGICALS	2,460	0.19%
ROTAVIRUS VACCINE, LIVE, ORAL (RV1)	Total	2,460	0.19%
ROTAVIRUS VACCINE, LIVE, ORAL, PENTAVALENT (RV5)	MERCK & CO. INC.	19,039	1.45%
ROTAVIRUS VACCINE, LIVE, ORAL, PENTAVALENT (RV5)	Total	19,039	1.45%

Vaccine Type	Vaccine Manufacturer	Events Reported	Percent (of 1,315,380)
RUBELLA VACCINE (RUB)	BURROUGHS WELLCOME	3	0.00%
RUBELLA VACCINE (RUB)	MERCK & CO. INC.	810	0.06%
RUBELLA VACCINE (RUB)	SANOFI PASTEUR	4	0.00%
RUBELLA VACCINE (RUB)	UNKNOWN MANUFACTURER	67	0.01%
RUBELLA VACCINE (RUB)	**Total**	**884**	**0.07%**
SMALLPOX VACCINE (SMALL)	PFIZER\WYETH	3,361	0.26%
SMALLPOX VACCINE (SMALL)	SANOFI PASTEUR	1,849	0.14%
SMALLPOX VACCINE (SMALL)	UNKNOWN MANUFACTURER	501	0.04%
SMALLPOX VACCINE (SMALL)	**Total**	**5,711**	**0.43%**
SUMMER/SPRING ENCEPHALITIS VACCINE (SSE) (SSEV)	UNKNOWN MANUFACTURER	3	0.00%
SUMMER/SPRING ENCEPHALITIS VACCINE (SSE) (SSEV)	**Total**	**3**	**0.00%**
TETANUS AND DIPHTHERIA TOXOIDS AND ACELLULAR PERTUSSIS VACCINE (BOOSTRIX/ADACEL) (TDAP)	GLAXOSMITHKLINE BIOLOGICALS	13,018	0.99%
TETANUS AND DIPHTHERIA TOXOIDS AND ACELLULAR PERTUSSIS VACCINE (BOOSTRIX/ADACEL) (TDAP)	SANOFI PASTEUR	22,486	1.71%
TETANUS AND DIPHTHERIA TOXOIDS AND ACELLULAR PERTUSSIS VACCINE (BOOSTRIX/ADACEL) (TDAP)	UNKNOWN MANUFACTURER	2,559	0.19%
TETANUS AND DIPHTHERIA TOXOIDS AND ACELLULAR PERTUSSIS VACCINE (BOOSTRIX/ADACEL) (TDAP)	**Total**	**38,063**	**2.89%**
TETANUS AND DIPHTHERIA TOXOIDS, ADULT (TD)	AVENTIS PASTEUR	1,568	0.12%
TETANUS AND DIPHTHERIA TOXOIDS, ADULT (TD)	CONNAUGHT LABORATORIES	5,398	0.41%
TETANUS AND DIPHTHERIA TOXOIDS, ADULT (TD)	GLAXOSMITHKLINE BIOLOGICALS	51	0.00%
TETANUS AND DIPHTHERIA TOXOIDS, ADULT (TD)	LEDERLE LABORATORIES	2,178	0.17%
TETANUS AND DIPHTHERIA TOXOIDS, ADULT (TD)	MASS. PUB HLTH BIOL LAB	1,105	0.08%
TETANUS AND DIPHTHERIA TOXOIDS, ADULT (TD)	MICHIGAN DEPT PUB HLTH	96	0.01%
TETANUS AND DIPHTHERIA TOXOIDS, ADULT (TD)	PFIZER\WYETH	1,340	0.10%
TETANUS AND DIPHTHERIA TOXOIDS, ADULT (TD)	SANOFI PASTEUR	4,071	0.31%
TETANUS AND DIPHTHERIA TOXOIDS, ADULT (TD)	SCLAVO	143	0.01%
TETANUS AND DIPHTHERIA TOXOIDS, ADULT (TD)	UNKNOWN MANUFACTURER	1,624	0.12%
TETANUS AND DIPHTHERIA TOXOIDS, ADULT (TD)	**Total**	**17,574**	**1.34%**
TETANUS TOXOID (TTOX)	BERNA BIOTECH, LTD.	37	0.00%
TETANUS TOXOID (TTOX)	CONNAUGHT LABORATORIES	281	0.02%
TETANUS TOXOID (TTOX)	EMERGENT BIOSOLUTIONS	6	0.00%
TETANUS TOXOID (TTOX)	GLAXOSMITHKLINE BIOLOGICALS	31	0.00%
TETANUS TOXOID (TTOX)	LEDERLE LABORATORIES	260	0.02%
TETANUS TOXOID (TTOX)	MASS. PUB HLTH BIOL LAB	66	0.01%
TETANUS TOXOID (TTOX)	MEDEVA PHARMA, LTD.	6	0.00%
TETANUS TOXOID (TTOX)	MICHIGAN DEPT PUB HLTH	2	0.00%
TETANUS TOXOID (TTOX)	PFIZER\WYETH	311	0.02%
TETANUS TOXOID (TTOX)	SANOFI PASTEUR	958	0.07%
TETANUS TOXOID (TTOX)	SCLAVO	36	0.00%
TETANUS TOXOID (TTOX)	UNKNOWN MANUFACTURER	1,231	0.09%
TETANUS TOXOID (TTOX)	**Total**	**3,225**	**0.25%**
TETANUS, DIPHTHERIA AND ACELLULAR PERTUSSIS, AND INACTIVATED POLIO VIRUS (TDAPIPV)	GLAXOSMITHKLINE BIOLOGICALS	8	0.00%
TETANUS, DIPHTHERIA AND ACELLULAR PERTUSSIS, AND INACTIVATED POLIO VIRUS (TDAPIPV)	UNKNOWN MANUFACTURER	1	0.00%
TETANUS, DIPHTHERIA AND ACELLULAR PERTUSSIS, AND INACTIVATED POLIO VIRUS (TDAPIPV)	**Total**	**9**	**0.00%**
TETRAMUNE (DTAPH)	SANOFI PASTEUR	550	0.04%
TETRAMUNE (DTAPH)	UNKNOWN MANUFACTURER	153	0.01%

Vaccine Type	Vaccine Manufacturer	Events Reported	Percent (of 1,315,380)
TETRAMUNE (DTAPH)	Total	703	0.05%
TICK-BORNE ENCEPHALITIS VACCINE (TBE) (TBE)	UNKNOWN MANUFACTURER	3	0.00%
TICK-BORNE ENCEPHALITIS VACCINE (TBE) (TBE)	Total	3	0.00%
TYPHOID VACCINE (TYP)	BERNA BIOTECH, LTD.	2,418	0.18%
TYPHOID VACCINE (TYP)	CONNAUGHT LABORATORIES	310	0.02%
TYPHOID VACCINE (TYP)	PFIZER\WYETH	730	0.06%
TYPHOID VACCINE (TYP)	SANOFI PASTEUR	3,513	0.27%
TYPHOID VACCINE (TYP)	UNKNOWN MANUFACTURER	907	0.07%
TYPHOID VACCINE (TYP)	Total	7,878	0.60%
VARIVAX-VARICELLA VIRUS LIVE (VARCEL)	GLAXOSMITHKLINE BIOLOGICALS	174	0.01%
VARIVAX-VARICELLA VIRUS LIVE (VARCEL)	MERCK & CO. INC.	76,211	5.79%
VARIVAX-VARICELLA VIRUS LIVE (VARCEL)	UNKNOWN MANUFACTURER	2,494	0.19%
VARIVAX-VARICELLA VIRUS LIVE (VARCEL)	Total	78,879	6.00%
YELLOW FEVER VACCINE (YF)	CONNAUGHT LABORATORIES	549	0.04%
YELLOW FEVER VACCINE (YF)	SANOFI PASTEUR	2,619	0.20%
YELLOW FEVER VACCINE (YF)	UNKNOWN MANUFACTURER	271	0.02%
YELLOW FEVER VACCINE (YF)	Total	3,439	0.26%
ZOSTER VACCINE (VARZOS)	GLAXOSMITHKLINE BIOLOGICALS	46,600	3.54%
ZOSTER VACCINE (VARZOS)	MERCK & CO. INC.	40,659	3.09%
ZOSTER VACCINE (VARZOS)	UNKNOWN MANUFACTURER	2,141	0.16%
ZOSTER VACCINE (VARZOS)	Total	89,400	6.80%
UNKNOWN VACCINES (UNK)	CONNAUGHT LABORATORIES	8	0.00%
UNKNOWN VACCINES (UNK)	MASS. PUB HLTH BIOL LAB	1	0.00%
UNKNOWN VACCINES (UNK)	MERCK & CO. INC.	30	0.00%
UNKNOWN VACCINES (UNK)	UNKNOWN MANUFACTURER	11,359	0.86%
UNKNOWN VACCINES (UNK)	Total	11,398	0.87%
Total		1,708,547	129.89%

Note: Submitting a report to VAERS does not mean that healthcare personnel or the vaccine caused or contributed to the adverse event (possible side effect).

Notes:

Caveats: VAERS accepts reports of adverse events and reactions that occur following vaccination. Healthcare providers, vaccine manufacturers, and the public can submit reports to VAERS. While very important in monitoring vaccine safety, VAERS reports alone cannot be used to determine if a vaccine caused or contributed to an adverse event or illness. The reports may contain information that is incomplete, inaccurate, coincidental, or unverifiable. Most reports to VAERS are voluntary, which means they are subject to biases. This creates specific limitations on how the data can be used scientifically. Data from VAERS reports should always be interpreted with these limitations in mind.

The strengths of VAERS are that it is national in scope and can quickly provide an early warning of a safety problem with a vaccine. As part of CDC and FDA's multi-system approach to post-licensure vaccine safety monitoring, VAERS is designed to rapidly detect unusual or unexpected patterns of adverse events, also known as "safety signals." If a safety signal is found in VAERS, further studies can be done in safety systems such as the CDC's Vaccine Safety Datalink (VSD) or the Clinical Immunization Safety Assessment (CISA) project. These systems do not have the same limitations as VAERS, and can better assess health risks and possible connections between adverse events and a vaccine.

Key considerations and limitations of VAERS data:

- Vaccine providers are encouraged to report any clinically significant health problem following vaccination to VAERS, whether or not they believe the vaccine was the cause.
- Reports may include incomplete, inaccurate, coincidental and unverified information.
- The number of reports alone cannot be interpreted or used to reach conclusions about the existence, severity, frequency, or rates of problems associated with vaccines.
- VAERS data are limited to vaccine adverse event reports received between 1990 and the most recent date for which data are available.
- VAERS data do not represent all known safety information for a vaccine and should be interpreted in the context of other scientific information.

Some items may have more than 1 occurrence in any single event report, such as Symptoms, Vaccine Products, Manufacturers, and Event Categories. If data are grouped by any of these items, then the number in the Events Reported column may exceed the total number of unique events. If percentages are shown, then the associated percentage of total unique event reports will exceed 100% in such cases. For example, the number of Symptoms mentioned is likely to exceed the number of events reported, because many reports include more than 1 Symptom. When more than 1 Symptom occurs in a single report, then the percentage of Symptoms to unique events is more than 100%. More information. (/wonder/help/vaers.html#Suppress)

Data contains VAERS reports processed as of 10/01/2021. The VAERS data in WONDER are updated weekly, yet the VAERS system receives continuous updates including revisions and new reports for preceding time periods. Duplicate event reports and/or reports determined to be false are removed from VAERS. More information. (/wonder/help/vaers.html#Reporting)

About COVID19 vaccines:

- For more information on how many persons have been vaccinated in the US for COVID19 to date, see https://covid.cdc.gov/covid-data-tracker/#vaccinations/ (https://covid.cdc.gov/covid-data-tracker/#vaccinations/).
- One report may state that the patient received more than one brand of COVID-19 vaccine on the same visit. This is a reporting error, but explains why the total number of reports may not equal the total number of COVID-19 vaccine doses.

Help: See The Vaccine Adverse Event Reporting System (VAERS) Documentation (/wonder/help/vaers.html) for more information.

Query Date: Oct 14, 2021 6:25:46 AM

Suggested Citation:

United States Department of Health and Human Services (DHHS), Public Health Service (PHS), Centers for Disease Control (CDC) / Food and Drug Administration (FDA), Vaccine Adverse Event Reporting System (VAERS) 1990 - 10/01/2021, CDC WONDER On-line Database. Accessed at http://wonder.cdc.gov/vaers.html on Oct 14, 2021 6:25:46 AM

Query Criteria:

State / Territory: The United States/Territories/Unknown
Group By: Vaccine Type; Vaccine Manufacturer
Show Totals: True
Show Zero Values: False

Selected Adverse Events Reported after COVID-19 Vaccination

Updated Nov. 10, 2021
Languages
Print
NOTICE: CDC now recommends that children between the ages of 5 and 11 years receive the Pfizer-BioNTech pediatric COVID-19 Vaccine. Learn more about vaccines for children and teens.
Safety of COVID-19 Vaccines
Some people have no side effects. Many people have reported side effects that are generally mild to moderate and should go away within a few days.
Are the Vaccines Safe?

What You Need to Know

- COVID-19 vaccines are **safe and effective**.
- Millions of people in the United States have received COVID-19 vaccines under the most intense safety monitoring in U.S. history.
- CDC recommends everyone ages 5 years and older get vaccinated as soon as possible to help protect against COVID-19 and the related, potentially severe complications that can occur.
- CDC, the U.S. Food and Drug Administration (FDA), and other federal agencies are monitoring the safety of COVID-19 vaccines.
- Adverse events described on this page have been reported to the Vaccine Adverse Event Reporting System (VAERS)external icon.
- VAERS accepts reports of any adverse event following any vaccination.
- Reports of adverse events to VAERS following vaccination, including deaths, do not necessarily mean that a vaccine caused a health problem**.**

Serious adverse events after COVID-19 vaccination are rare but may occur. For public awareness and in the interest of transparency, CDC is providing timely updates on the following serious adverse events of interest:

- **Anaphylaxis, a severe type of allergic reaction, following administration of COVID-19 vaccination is rare** and has occurred in approximately 2 to 5 people per million vaccinated in the United States**.** Anaphylaxis can occur after any kind of vaccination. If it happens, healthcare providers can effectively and immediately treat the reaction. Learn more about COVID-19 vaccines and allergic reactions, including anaphylaxis.

- **Thrombosis with thrombocytopenia syndrome (TTS) occurring after Johnson & Johnson's Janssen (J&J/Janssen) COVID-19 vaccination is rare.** As of November 4, 2021, more than 15.7 million doses of the J&J/Janssen COVID-19 vaccine have been given in the United States. CDC and FDA have identified 50 confirmed reports of people who got the J&J/Janssen COVID-19 vaccine and later developed TTS, including 5 confirmed reports of death. Women ages 18-49, especially, should be aware of the rare but increased risk of this adverse event. There are other COVID-19 vaccine options available for which this risk has not been seen. Learn more about J&J/Janssen COVID-19 vaccine and TTS.
    - To date, two confirmed cases of TTS following mRNA COVID-19 vaccination (Moderna) have been reported to VAERS after more than 409 million doses of mRNA COVID-19 vaccines administered in the United States. Based on available data, there is not an increased risk for TTS after mRNA COVID-19 vaccination.
- CDC and FDA are monitoring reports of Guillain-Barré Syndrome (GBS) in people who have received the J&J/Janssen COVID-19 vaccine. GBS is a rare disorder where the body's immune system damages nerve cells, causing muscle weakness and sometimes paralysis. Most people fully recover from GBS, but some have permanent nerve damage. After more than 15.7 million J&J/Janssen COVID-19 vaccine doses administered, there have been around 250 preliminary reports of GBS identified in VAERS as of November 4, 2021. These cases have largely been reported about 2 weeks after vaccination and mostly in men, many ages 50 years and older. CDC will continue to monitor for and evaluate reports of GBS occurring after COVID-19 vaccination and will share more information as it becomes available.
- **Myocarditis and pericarditis occurring after COVID-19 vaccination are rare.** As of November 4, 2021, VAERS has received 1,783 reports of myocarditis or pericarditis among people ages 12–29 years who received COVID-19 vaccines. Most cases have been reported after mRNA COVID-19 vaccination (Pfizer-BioNTech or Moderna), particularly in male adolescents and young adults after the second dose. Through follow-up, including medical record reviews, CDC and FDA have confirmed 1,031 reports of myocarditis or pericarditis. Learn more about myocarditis and pericarditis after mRNA COVID-19 vaccination.

- **Reports of death after COVID-19 vaccination are rare**. More than 432 million doses of COVID-19 vaccines were administered in the United States from December 14, 2020, through November 8, 2021. During this time, VAERS received 9,549 reports of death (0.0022%) among people who received a COVID-19 vaccine. FDA requires healthcare providers to report any death after COVID-19 vaccination to VAERS, even if it's unclear whether the vaccine was the cause. **Reports of adverse events to VAERS following vaccination, including deaths, do not necessarily mean that a vaccine caused a health problem.** A review of available clinical information, including death certificates, autopsy, and medical records has not established a causal link to COVID-19 vaccines. However, recent reports indicate a plausible causal relationship between the J&J/Janssen COVID-19 vaccine and TTS, a rare and serious adverse event that causes blood clots with low platelets, which has caused 5 deaths pdf icon[1,438 KB, 33 pages].