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Vaccination to reduce severe COVID-19 and mortality in COVID-19 patients: a systematic review and meta-analysis

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Abstract. – OBJECTIVE: The outbreak of coronavirus disease (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has resulted in the death of up to 5 million people worldwide, with a mortality rate of approximately 2%. Wearing masks, maintaining social distance, tracking, and isolating close contacts are not sufficient to control the epidemic. The effectiveness of vaccines is affected by the willingness of people to be vaccinated. Therefore, in this review, we aimed to examine the efficacy of different types of vaccines in reducing hospitalization rates, disease severity, and mortality.

MATERIALS AND METHODS: We searched five databases (Embase, PubMed, Cochrane, EBSCO, and CEPS) for related research on September 3, 2021. We used a random-effects model for analysis.

RESULTS: Seven studies were identified, involving 1,366,700 participants (689,967 participants in the vaccinated group and 676,733 participants in the non-vaccinated group). There were 292 significant incidents (56 in the vaccinated group and 236 in the non-vaccinated group) with a risk ratio of 0.12 and a 95% confidence interval of 0.040-0.363. Compared with no vaccine, all types of vaccines can effectively prevent the rate of severe illness.

CONCLUSIONS: We evaluated whether different brands of vaccines or types of COVID-19 vaccines could prevent the risk of severe illness after diagnosis. The analysis showed that all types of vaccines can effectively prevent severe disease. Implementing epidemic prevention guidelines and obtaining vaccines in different countries can improve vaccine protection and reduce COVID-19-related deaths worldwide.

Key Words:
Vaccine, Novel coronavirus, Severe COVID-19.

Introduction

In 2021, the coronavirus disease (COVID-19) pandemic caused by the severe acute respiratory syndrome coronavirus (SARS-CoV-2) caused the death of at least 5 million people worldwide, with a mortality rate of approximately 2%[1,2]. In some countries, control measures such as using masks, maintaining social distance, screening of symptomatic people, tracing contacts, and quarantine have yielded promising results. However, these measures are subject to cooperation between the state and the public[3].

The above measures are not sufficient to completely control the spread of the pandemic, and the development of vaccines cannot be delayed. As of June 2021, various vaccines have been developed by multiple countries. After a series of efficacy and safety assessments, vaccinations have been carried out in several countries. Based on the published results of some large clinical trials, Moderna and Pfizer vaccines have the highest effective rates, with a protection rate reaching 90%[4].

The majority of people believe that the higher the effectiveness of the vaccine, the better it is; however, the purpose of the vaccine itself is to reduce hospitalization, severe illness, and mortality. The time and location of vaccine-related clinical trials will indirectly affect the effectiveness of vaccines, but this does not represent the quality of the vaccine itself.

Therefore, we aimed to examine the clinical benefits of vaccines in reducing severe illness and mortality through a literature search and comprehensive analysis.

Materials and Methods

Design and Search Strategy

By September 3, 2021, we conducted a systematic review and meta-analysis of random-

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ized controlled trials and observational studies available on EBSCO, PubMed, Embase, The Cochrane Library, and CEPS. The Medical Subject Headings (MeSH) terms were COVID-19, vaccine, severe COVID-19, and mortality. Studies had to provide data on the incidence of proven severe COVID-19 infections (such as nucleic acid testing by polymerase chain reaction). We manually searched articles from the reference lists. This systematic review was performed following the methodological approach described in the Cochrane Handbook Version 6.2 for the systematic review of interventions[5]. This method is explained according to the PRISMA-P statement (recommended report items for systematic review and meta-analysis protocols)[6] (**Supplementary File 1**). This systematic review protocol was registered at the International Prospective Register of Systematic Reviews database (CRD42021269803).

Literature Selection

Two independent researchers reviewed studies and evaluated their eligibility. If the study was a clinical trial using the same vaccine (e.g., Phase 1, Phase 2, and Phase 3), the final phase study was selected for analysis. Articles reporting incomplete data on severe COVID-19 or mortality were excluded.

Data Extraction and Study Quality

Two independent reviewers extracted the data in duplicate. The country, study design, age, sex, vaccine type, and dose were included in the extracted information. The original number of cases, severity of COVID-19, and deaths were recorded accurately.

Two independent reviewers independently assessed the quality of the study methodologies. For randomized controlled trials, we followed the revised means for determining the risk of bias in randomized trials (RoB 2)[7]. The cohort study followed the Newcastle-Ottawa Quality Rating Scale (NOS)[8]. If the results were inconsistent, we discussed the two reports and made a joint decision.

Statistical Analysis

A meta-analysis of ratios (95% confidence interval [CI]) was performed for mortality in patients with severe COVID-19 or SARS-CoV-2 infection. The risk ratio (RR) was calculated to identify the difference in severe COVID-19 or mortality with and without the vaccine. The pooled results are displayed in a forest plot (Figure 1). Heterogeneity was characterized using the appropriate *p*-values and I^2 statistics: 0-49%, 50-74%, and 75-100% represent mild, moderate, and severe heterogeneity, respectively. No potential publication bias was used because the number of articles was less than 10. Statistical analysis was performed using meta-analysis software (Comprehensive Meta-Analysis V3, Biostat, NJ, USA).

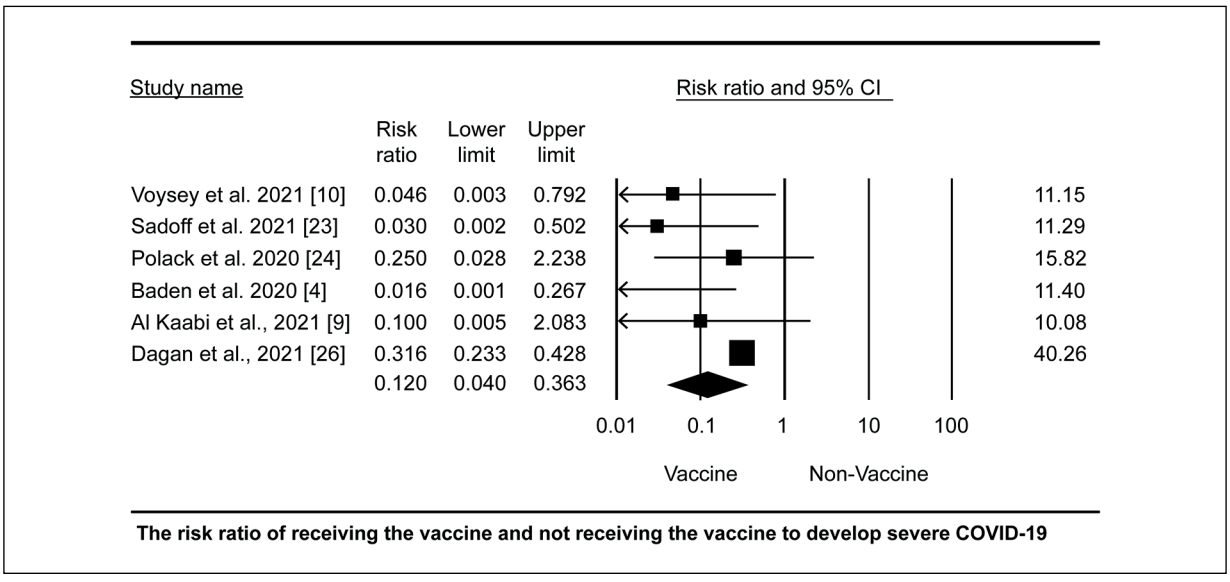

Figure 1. The risk ratio of receiving the vaccine and not receiving the vaccine of developing severe COVID-19.

Results

For the initial assessment, we identified 157 records in the PubMed (n = 68), Embase (n = 56), Cochrane Library (n = 0), EBSCO (n = 31), and CEPS (n = 2) databases, with only seven articles included in the full-text review (Figure 2). Seven studies involving 1,366,700 participants were included in this systematic review and meta-analysis, of which 689,967 were vaccinated and 676,733 were not. There were 292 confirmed COVID-19 severe cases, 56 of which were from the vaccinated group and 236 from the non-vaccinated group. Of the patients, 65.3% were men, and the average age was 47.6 years. Table I describes the characteristics of each article's research design, and Table II describes the characteristics of the included studies. The quality of the randomized clinical trial articles was evaluated using RoB 2 and that of cohort studies was evaluated using the NOS (Figure 3; Table III). Most of the seven studies included young and middle-aged patients, with an average age range of 31-52 years, with males accounting for approximately 38%-55% (in one of the studies, males accounted for 84%[9]).

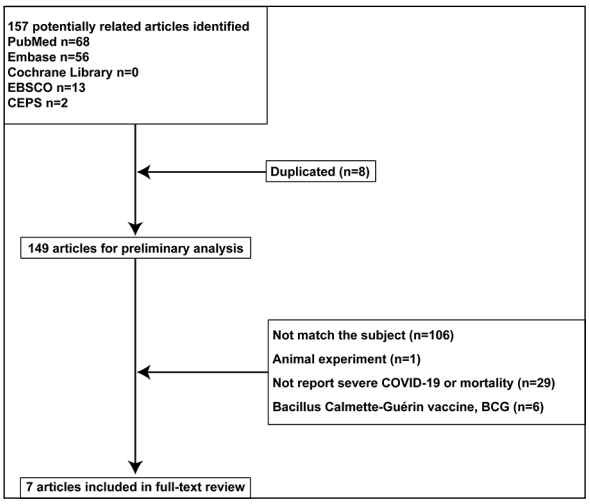

Figure 2. Study selection based on PRISMA diagram.

Table I. Characteristics of each study design.

Authors	Year	Study design	Period	Nation	Vaccine	Vaccine dose	Confirmatory test	Ref.
Voysey et al	2021	RCT	2020/4/23-2020/11/4	The United Kingdom, Brazil, South Africa.	ChAdOx1	2	RT-PCR	[10]
Sadoff et al	2021	RCT	2020/9/21-2021/1/22	Argentina, Brazil, Mexico, Peru, South Africa, and the United States.	Ad26.COV2.s	1	RT-PCR	[23]
Polack et al	2020	RCT	2020/7/27-1/14	152 sites (130 United States, 1 Argentina, 2 Brazil, 4 South Africa, 6 Germany, and 9 Turkey)	BNT162b2	2	RT-PCR	[24]
Madhi et al	2021	RCT	2020/6/24-2020/11/9	South Africa	ChAdOx1	2	RT-PCR	[25]
Baden et al	2021	RCT	2020/7/27-2020/10/23	United States	mRNA1273	2	RT-PCR	[4]
Al Kaabi et al	2021	RCT	2020/7/16-2020/12/31	The United Arab Emirates and Bahrain	WIV04 and HB02	2	RT-PCR	[9]
Dagan et al	2021	Cohort Study	2020/12/20-2021/2/1	Israel	BNT162b2	2	RT-PCR	[26]

Abbreviations: RCT, randomized controlled trial; RT-PCR, reverse transcriptase-polymerase chain reaction.

Table II. Characteristics of the included studies.

First Authors	Nation	Vaccine and Placebo	Dose	Age	Male, %	Ethnicity (White, %)	BMI ≥ 30.0, %	Severe COVID-19, n	Total case, n
Voysey[10]	The United. Kingdom, Brazil, South Africa	ChAdOx1	2	NA	38.7	82.8	NA	0	12021
		MenACWY or Saline		NA	38.8	83.9	NA	10	11724
Sadoff[23]	Argentina, Brazil, Mexico, Peru, South Africa, and the United States	Ad26.COV2.s	1	52	55.1	58.7	28.6	0	19306
		Saline		52	54.7	58.7	28.4	16	19178
Polack[24]	152 sites (130 United States, 1 Argentina, 2 Brazil, 4 South Africa, 6 Germany, and 9 Turkey)	BNT162b2	2	52	51.1	82.9	34.8	1	21669
		Saline		52	50.1	82.9	35.3	4	21686
Madhi[25]	South Africa	ChAdOx1	2	31	58.8	15.0	16.5	0	750
		Saline		31	55.4	16.7	19.5	0	717
Baden[4]	United States	mRNA1273	2	51.4	52.2	79.2	NA	0	14134
		Saline		51.3	53.1	79.1	NA	30	14073
Al Kaabil[9]	The United Arab Emirates and Bahrain	WIV04	2	36.2	84	NA	27 (mean)	0	12743
		HB02		36.1	84.5	NA	27 (mean)	0	12726
		Alum-only		36.2	84.8	NA	27 (mean)	2	12737
Dagan[26]	Israel	BNT162b2	2	45	50	NA	19.2	50	596618
		Non-Vaccine		45	50	NA	18.6	174	596618

Abbreviations: BMI, body mass index. Age is expressed as mean. Al Kaabi et al. did not provide the proportion of body mass index greater than 30% and only provided the average body mass index[9]. Madhi et al[25] did not perform meta-analysis analysis because neither group had patients with severe COVID-19.

We found seven studies reporting the severe COVID-19 event rate, ranging from 0% to 0.01% in a total of 689,967 vaccinated patients, and from 0.02% to 0.21% in a total of 676,733 non-vaccinated patients. One study was not included in the meta-analysis because neither the vaccinated nor the non-vaccinated groups had a serious COVID-19 event[10]. Meta-analysis of these studies

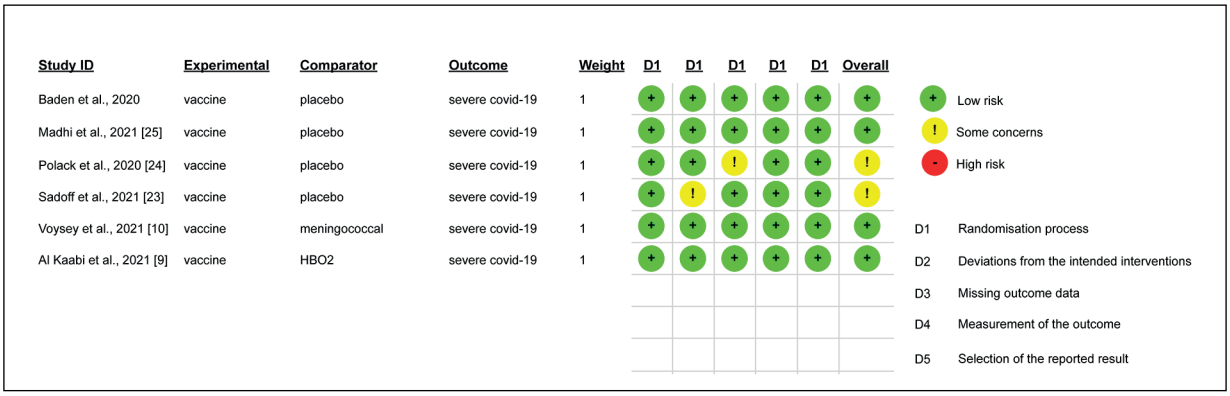

Figure 3. Bias tool risk, quality assessment of included randomized controlled trials using RoB 2.0.

Table III. Newcastle-Ottawa scale was used to reassess the quality of the cohort studies.

	Selection				Comparability		Outcome		Total points	Study quality
First author	1)	2)	3)	4)	1)	2)	1)	2)	3)		
Dagan	1	1	1	0	1	1	1	1	1	8	Good

showed that the risk ratio of the vaccinated group *vs.* the non-vaccinated was 0.12 (95% CI: 0.040-0.363; $p = 0.0003 < 0.05$; Figure 1), with significant differences ($I^2 = 44.2\%$).

Discussion

The results of this comprehensive analysis showed that irrespective of what vaccine or brand of vaccine is administered, there are significant differences in the number of severely ill hospitalized patients between the vaccinated and non-vaccinated groups. Allergic reactions to most vaccines are due to excipients and are treatable and manageable[11]. The safety of commercially available COVID-19 vaccines has been demonstrated in two meta-analyses[12,13]. As the epidemic continues, the number of people vaccinated globally continues to increase. Some large-scale observational studies have also shown that vaccinations, regardless of the type of vaccine, can reduce the chance of infection, minimize the number of severely ill hospitalized patients after illness, and reduce the medical burden[14-16].

A previous study showed that for every 10% increase in vaccine coverage, the mortality rate could be reduced by 7.6%[17]. According to the open database, as of November 30, 2021, the cumulative number of confirmed diagnoses worldwide has reached 261,978,819, with a death toll of 5,205,121, and case fatality rate of approximately 2%[18]. In most countries, COVID-19 vaccination is a public service, and the efficiency of government plays a vital role. Moreover, countries with more developed transportation have a higher rate of disease transmission than those with less developed transportation[17]. In addition to increasing vaccine coverage as quickly as possible to achieve herd immunity[19], the implementation of pandemic prevention policies and people's compliance with measures, such as wearing masks, maintaining social distance, screening for symptomatic people, and returning contact measures such as tracking and quarantine, also play an essential role in lowering the number of cases[3,20,21].

This study had some limitations. First, most of the studies included were on the original strain of the virus early in the COVID-19 pandemic. Mutant virus strains such as Delta and Omicron that have been subsequently discovered by the World Health Organization may require further research to confirm whether vaccines have the same effect in preventing severe disease[22]. Second, each country has different public health policies, epidemic prevention policies, and transportation development levels, which may indirectly affect the speed of virus transmission. Third, the studies did not mention the number of patients who recovered and the extent of subsequent complications. Finally, there is no research on the use of mixed vaccines to prevent severe illness.

Conclusions

In this study, we evaluated whether different brands or types of COVID-19 vaccines could prevent the risk of severe illness after diagnosis. Analysis showed that all types of vaccines can effectively prevent the occurrence of severe diseases. Implementing pandemic prevention policies in various countries and procuring vaccines will help improve vaccine coverage to reduce the number of deaths from COVID-19 worldwide.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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Authors' Contribution
Two authors (YZH and CCK) jointly designed the research and wrote the paper. YZH extracted and analyzed the data. Both authors approved the final version of the manuscript.

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References

1) Hodgson SH, Mansatta K, Mallett G, Harris V, Emary KR, Pollard AJ. What defines an efficacious COVID-19 vaccine? A review of the challenges assessing the clinical efficacy of vaccines against SARS-CoV-2. Lancet Infect Dis 2021; 21: e26-e35.
2) World Health Organization. WHO coronavirus disease (COVID-19) Dashboard. 2021. https://covid19.who.int. (Accessed on 1 September 2021)
3) Lai S, Ruktanonchai NW, Zhou L, Prosper O, Luo W, Floyd JR, Wesolowski A, Santillana M, Zhang C, Du X, Yu H, Tatem AJ. Effect of non-pharmaceutical interventions to contain COVID-19 in China. Nature 2020; 585: 410-413.
4) Baden LR, El Sahly HM, Essink B, Kotloff K, Frey S, Novak R, Diemert D, Spector SA, Rouphael N, Creech CB, McGettigan J, Khetan S, Segall N, Solis J, Brosz A, Fierro C, Schwartz H, Neuzil K, Corey L, Gilbert P, Janes H, Follmann D, Marovich M, Mascola J, Polakowski L, Ledgerwood J, Graham B, Bennett H, Pajon R, Knightly C, Leav B, Deng W, Zhou H, Han S, Miller J, Zaks, T. Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine. New Engl J Med 2020; 384: 403-416.
5) Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA. Cochrane Handbook for Systematic Reviews of Interventions. John Wiley & Sons, 2019.
6) Page MJ, McKenzie, JE, Bossuyt PM, Boutron I, Hoffmann, TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, Chou R, Glanville J, Grimshaw JM, Hróbjartsson A, Lalu MM, Li T, Loder EW, Mayo-Wilson E, McDonald S, McGuinness LA, Stewart LA, Thomas J, Tricco AC, Welch VA, Whiting P, Moher D. PRISMA 2020 statement: An updated guideline for reporting systematic reviews. Int J Surg 2021; 88: 105906.
7) Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, Cates CJ, Cheng HY, Corbett MS, Eldridge SM, Emberson JR, Hernan MA, Hopewell S, Hrobjartsson A, Junqueira DR, Juni P, Kirkham JJ, Lasserson T, Li T, McAleenan A, Reeves BC, Shepperd S, Shrier I, Stewart L, Tilling K, White IR, Whiting PF, Higgins JPT. RoB 2: a revised tool for assessing risk of bias in randomized trials. BMJ 2019; 366: l4898.
8) Zeng X, Zhang Y, Kwong JS, Zhang C, Li S, Sun F, Du L. The methodological quality assessment tools for preclinical and clinical studies, systematic review and meta-analysis, and clinical practice guideline: a systematic review. J Evid Based Med 2015; 8: 2-10.
9) Al Kaabi N, Zhang Y, Xia S, Yang Y, Al Qahtani MM, Abdulrazzaq N, Al Nusair M, Hassany M, Jawad JS, Abdalla J, Hussein SE, Al Mazrouei SK, Al Karam M, Li X, Yang X, Wang W, Lai B, Chen W, Huang S, Wang Q, Yang T, Liu Y, Ma R, Hussain ZM, Khan T, Saifuddin Fasihuddin M, You W, Xie Z, Zhao Y, Jiang Z, Zhao G, Zhang Y, Mahmoud S, ElTantawy I, Xiao P, Koshy A, Zaher WA, Wang H, Duan K, Pan A, Yang X. Effect of 2 inactivated SARS-CoV-2 vaccines on symptomatic COVID-19 infection in adults: a randomized clinical trial. JAMA 2021; 326: 35-45.
10) Voysey M, Clemens SAC, Madhi SA, Weckx LY, Folegatti PM, Aley PK, Angus B, Baillie VL, Barnabas SL, Bhorat QE, Bibi S, Briner C, Cicconi P, Collins AM, Colin-Jones R, Cutland CL, Darton TC, Dheda K, Duncan CJA, Emary KRW, Ewer KJ, Fairlie L, Faust SN, Feng S, Ferreira DM, Finn A, Goodman AL, Green CM, Green CA, Heath PT, Hill C, Hill H, Hirsch I, Hodgson SHC, Izu A, Jackson S, Jenkin D, Joe CCD, Kerridge S, Koen A, Kwatra G, Lazarus R, Lawrie AM, Lelliott A, Libri V, Lillie PJ, Mallory R, Mendes AVA, Milan EP, Minassian AM, McGregor A, Morrison H, Mujadidi YF, Nana A, O'Reilly PJ, Padayachee SD, Pittella A, Plested E, Pollock KM, Ramasamy MN, Rhead S, Schwarzbold AV, Singh N, Smith A, Song R, Snape MD, Sprinz E, Sutherland RK, Tarrant R, Thomson EC, Torok ME, Toshner M, Turner DPJ, Vekemans J, Villafana TL, Watson MEE, Williams CJ, Douglas AD, Hill AVS, Lambe T, Gilbert SC, Pollard AJ. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. Lancet 2021; 397: 99-111.
11) Castells MC, Phillips EJ. Maintaining safety with SARS-CoV-2 vaccines. New Engl J Med 2021; 384: 643-649.
12) Sharif N, Alzahrani KJ, Ahmed SN, Dey SK. Efficacy, immunogenicity and safety of COVID-19 vaccines: A systematic review and meta-analysis. Frontiers Immunol, 2021; 12: 714170.
13) Liu Q, Qin C, Liu M, Liu J. Effectiveness and safety of SARS-CoV-2 vaccine in real-world studies: a systematic review and meta-analysis. Infect Dis Poverty 2021; 10: 132.
14) Pritchard E, Matthews PC, Stoesser N, Eyre DW, Gethings, O, Vihta KD, Jones J, House T, VanSteenHouse H, Bell I, Bell JI, Newton J, Farrar J, Diamond I, Rourke E, Studley R, Crook D, Peto TEA, Walker S, Pouwels KB. Impact of vaccination on new SARS-CoV-2 infections in the United Kingdom. Nat Med 2021; 27: 1370-1378.
15) Lopez BJ, Andrews N, Gower C, Robertson C, Stowe J, Tessier E, Simmons R, Cottrell S, Rob-

erts R, O'Doherty M, Brown K, Cameron C, Stockton D, McMenamin J, Ramsay M. Effectiveness of Pfizer-BioNTech and Oxford-AstraZeneca vaccines on COVID-19 related symptoms, hospital admissions, and mortality in older adults in England: a negative case-control study. BMJ 2021; 373: n1088.

16) Menni C, Klaser K, May A, Polidori L, Capdevila J, Louca P, Sudre C, Nguyen L, Drew D, Merino J, Hu C, Meng SS, Antonelli M, Murray B, Canas L, Molteni E, Graham M, Modat M, Joshi AD, Mangino M, Hammers A, Goodman AL, Chan AT, Wolf J, Steves CJ, Vlades AM, Ourselin S, Spector TD. Vaccine side-effects and SARS-CoV-2 infection after vaccination in users of the COVID Symptom Study app in the UK: a prospective observational study. Lancet Infect Dis 2021; 21: 939-949.

17) Liang LL, Kuo HS, Ho HJ, Wu CY. COVID-19 vaccinations are associated with reduced fatality rates: Evidence from cross-county quasi-experiments. J Glob Health 2021; 11: 05019.

18) Dong E, Du H, Gardner L. An interactive web-based dashboard to track COVID-19 in real time. Lancet Infect Dis 2020; 20: 533-534.

19) Kwok KO, Lai F, Wei WI, Wong SYS, Tang JW. Herd immunity–estimating the level required to halt the COVID-19 epidemics in affected countries. J Infection 2020; 80: e32-e33.

20) Jernigan DB, COVID C, Team R. Update: public health response to the coronavirus disease 2019 outbreak—United States, February 24, 2020. MMWR-Morbid Mortal W 2020; 69: 216.

21) Talic S, Shah S, Wild H, Gasevic D, Maharaj A, Ademi Z, Li X, Xu W, Mesa-Eguiagaray I, Rostron J, Theodoratou E, Zhang X, Motee A, Liew D, Ilic D. Effectiveness of public health measures in reducing the incidence of COVID-19, SARS-CoV-2 transmission, and COVID-19 mortality: A systematic review and meta-analysis. BMJ 2021; 375: e068302.

22) World Health Organization. Tracking SARS-CoV-2 variants. 2021. https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/. (Accessed on 27 November 2021)

23) Sadoff J, Gray G, Vandebosch A, Cárdenas V, Shukarev G, Grinsztejn B, Goepfert PA, Truyers C, Fennema H, Spiessens B, Offergeld K, Scheper G, Taylor KL, Robb ML, Treanor J, Barouch DH, Stoddard J, Ryser MF, Marovich MA, Neuzil KM. ENSEMBLE Study Group. Safety and Efficacy of Single-Dose Ad26.COV2.S Vaccine against Covid-19. N Engl J Med 2021; 384, 2187-2201.

24) Polack FP, Thomas SJ, Kitchin N, Absalo J, Gurtman A, Lockhart S, Perez JL, Marc GP, Moreira ED, Zerbini Z, Bailey R, Swanson KA, Roychoudhury S, Koury K, Li P, Kalina WV, Cooper D, Frenck RW, Hammitt LL, Tureci O, Nell H, Schaefer A, Unal S, Tresnan DB, Mather S, Dormitzer PR, Sahin U, Jansen KU, Gruber WC. Safety and efficacy of the BNT162b2 mRNA COVID-19 vaccine. New Engl J Med 2020; 383: 2603-2615.

25) Madhi SA, Baillie V, Cutland CL, Voysey M, Koen AL, Fairlie L, Padayachee SD, Dheda K, Barnabas SL, Bhorat QE, Briner C, Kwatra G, Ahmed K, Aley P, Bhikha S, Bhiman JN, Bhorat AE, du Plessis J, Esmail A, Groenewald M, Horne E, Hwa SH, Jose A, Lambe T, Laubscher M, Malahleha M, Masenya M, Masilela M, McKenzie S, Molapo K, Moultrie A, Oelofse S, Patel F, Pillay S, Rhead S, Rodel H, Rossouw L, Taoushanis C, Tegally H, Thombrayil A, van Eck S, Wibmer CK, Durham NM, Kelly EJ, Villafana TL, Gilbert S, Pollard AJ, de Oliveira T, Moore PL, Sigal A, Izu A. Efficacy of the ChAdOx1 nCoV-19 Covid-19 Vaccine against the B.1.351 Variant. N Engl J Med 2021; 384: 1885-1898.

26) Dagan N, Barda N, Kepten E, Miron O, Perchik S, Katz MA, Hernán MA, Lipsitch M, Reis B, Balicer RD. BNT162b2 mRNA Covid-19 Vaccine in a Nationwide Mass Vaccination Setting. N Engl J Med 2021; 384, 1412-1423.