RNA based vaccines

BNT162b2-Pfizer/BioNTech/ Fosun Pharma

Comparison: BNT162b2 vs Placebo (Developer:)

Walsh 2020

Trial: NCT04368728, Walsh E, N Engl J Med, 2020 (published in peer reviewed journal), first published as preprint Walsh E medRxiv 2020

Methods	RCT
	Phase 1
	Blinding: triple blinding
	Date of study: 05/04/2020 to 06/22/2020
	Location: Multicenter / United States
	Follow-up duration (months): 1.68
	Vaccine group: **18–55y:** 10 µg BNT162b1 (n = 12); 20 µg BNT162b1 (n = 12); 30 µg BNT162b1 (n = 12); 100 µg BNT162b1 (n = 12); Placebo 1 (n = 12); 10 µg BNT162b2 (n = 12); 20 µg BNT162b2 (n = 12); 30 µg BNT162b2 (n = 12); Placebo 2 (n = 9) **65–85y:** 10 µg BNT162b1 (n = 12); 20 µg BNT162b1 (n = 12); 30 µg BNT162b1 (n = 12); Placebo 3 (n = 9); 10 µg BNT162b2 (n = 12); 20 µg BNT162b2 (n = 12); 30 µg BNT162b2 (n = 12); Placebo 4 (n = 9)
Participants	**Population randomized:** 195 participants (n1=24 / n2=24 / n3=24 / n4=12 / n5=21 / n6=24 / n7=24 / n8=24 / n9=18)
	Characteristics of participants Type of participants: Healthy volunteers N=195 Children: 0 Pregnant women: 0 Immunocompromised patients: 0 Age mean: NR Age range: 24-82 Men: 83
	Description of participants Healthy SARS-CoV-2 serology/DNA negative adults in four centers in USA
	Inclusion criteria • Male or female participants between the ages of 18 and 55 years, inclusive, 65 and 85 years, inclusive, or ≥12 years, inclusive, at randomization (dependent upon study phase). (Note that participants <18 years of age cannot be enrolled in the EU) • Participants who are willing and able to comply with all scheduled visits, vaccination plan, laboratory tests, lifestyle considerations, and other study procedures • Healthy participants who are determined by medical history, physical examination, and clinical judgment of the investigator to be eligible for inclusion in the study • Participants who, in the judgment of the investigator, are at risk for acquiring COVID-19 • Capable of giving personal signed informed consent
	Exclusion criteria • Key exclusion criteria were known infection with human immunodeficiency virus, hepatitis C virus, or hepatitis B virus

	• An immunocompromised condition • A history of autoimmune disease • A previous clinical or microbiologic diagnosis of Covid-19 • The receipt of medications intended to prevent Covid-19 • Any previous coronavirus vaccination • Positive test for SARS-CoV-2 IgM or IgG at the screening visit • Positive nasal-swab results on a SARS-CoV-2 nucleic acid amplification test within 24 hours before the receipt of trial vaccine or placebo
	Withdrawals: 0 withdrawal due to adverse events
Interventions	**Intervention** • BNT162b1 - 2 IM doses of 10-µg BNT162b1 per dose (D0/21) • BNT162b1 - 2 IM doses of 20-µg BNT162b1 per dose (D0/21) • BNT162b1 - 2 IM doses of 30-µg BNT162b1 per dose (D0/21) • BNT162b1 - 2 IM doses of 100-µg BNT162b1 per dose (D0/21) • BNT162b2 - 2 IM doses of 10-µg BNT162b2 per dose (D0/21) • BNT162b2 - 2 IM doses of 20-µg BNT162b2 per dose (D0/21) • BNT162b2 - 2 IM doses of 30-µg BNT162b2 per dose (D0/21)
	Control • Normal saline placebo (0.9% sodium chloride) x 2 doses (D0/21) • Normal saline placebo (0.9% sodium chloride) x 2 doses (D0/21)
Outcomes	**Primary outcome of the trial:** **In the report:** • Solicited local reactions (i.e., specific local reactions as prompted by and recorded in an electronic diary), systemic events, and use of antipyretic or pain medication within 7 days after the receipt of vaccine or placebo, as prompted by and recorded in an electronic diary (Phase 1) • Unsolicited adverse events and serious adverse events (i.e., those reported by the participants, without electronic diary prompts), assessed from the receipt of the first dose through 1 month and 6 months, respectively, after the receipt of the second dose; clinical laboratory abnormalities, assessed 1 day and 7 days after the receipt of vaccine or placebo; and grading shifts in laboratory assessments between baseline and 1 day and 7 days after the first dose and between 2 days and 7 days after the second dose (Phase 1) **In the register:** • Percentage of participants in Phase 1 with local reactions, systemic events [Time Frame: For 7 days after dose 1 and dose 2] • Adverse events [Time Frame: From dose 1 through 1 month after the last dose] • Serious adverse events [Time Frame: From dose 1 through 6 months after the last dose] • Abnormal hematology and chemistry laboratory values [Time Frame: 1 day and 7 days after dose 1 and 7 days after dose 2] • Grading shifts in hematology and chemistry laboratory assessments [Time Frame: Between baseline and 1 day and day 7 after dose 1, 7 days after dose 2]
Notes	**Funding**: Private (BioNTech, Pfizer)
	Conflict of interest: Yes. Quote: "Dr. Walsh reports grants from Pfizer, during the conduct of the study; grants from Merck, grants from Janssen, grants from Pfizer, outside the submitted work; Dr. Raabe reports other from Pfizer, during the conduct of the study; grants from NIAID , outside the submitted work; Dr. Falsey reports grants from Pfizer, during the conduct of the study; grants from Janssen, grants from Merck, Sharpe and Dohme, personal fees from Novavax, outside the submitted work; Dr. Mulligan reports grants from Pfizer, during the conduct of the study; grants from Lilly,

	personal fees from Meissa Vaccines, Inc., grants from Sanofi, outside the submitted work; Drs. Gruber, Kitchin, Absalon, Bailey, Cooper, Dormitzer, Gurtman, Neuzil, Jansen, Kalina, Koury, Li, Lockhart, Swanson and Tompkins report personal fees and other from Pfizer Inc, outside the submitted work; Dr. Shi has a patent Reverse genetic system of SARS-CoV-2 licensed."
	Protocol: English
	Statistical plan: Yes
	Data-sharing stated: Yes

Frenck 2021

Trial: NCT04368728, Frenck R, N Engl J Med, 2021 (published in peer reviewed journal)

Methods	RCT
	Phase 3
	Blinding: triple blinding
	Date of study: 10/15/2020 to 12/01/2021
	Location: Multicenter / USA
	Follow-up duration (months): 4.7
	Vaccine group: 30 mcg BNT162b2 (n = 1134); Placebo (n = 1130)
Participants	**Population randomized:** 2264 participants (n1=1134 / n2=1130)
	Characteristics of participants Type of participants: Adolescents N=2264 Pregnant women: 0 Age mean: NR Age range: 12-15 Men: 1152
	Description of participants Adolescents aged 12 to 15 years with no previous Covid-19 diagnosis or SARS-CoV-2 infection in 29 centers in the USA
	Inclusion criteria • Adolescents 12 to 15 years of age • Healthy or stable preexisting disease (including hepatitis B, hepatitis C, or human immunodeficiency virus infection)
	Exclusion criteria • Previous clinical or virologic Covid-19 diagnosis or SARS-CoV-2 infection • Previous coronavirus vaccination • Diagnosis of an immunocompromising or immunodeficiency disorder, or treatment with immunosuppressive therapy (including cytotoxic agents and systemic glucocorticoids)
	Withdrawals: 2 withdrawal due to adverse events
Interventions	**Intervention:** BNT162b2 - 2 IM doses of 3mcg (D0/21)
	Control: Placebo

Outcomes	**Primary outcome of the trial:** **In the report:** NR **In the register:** • Confirmed COVID-19 in Phase 2/3 participants without evidence of infection before vaccination [Time Frame: From 7 days after the second dose of study intervention to the end of the study, up to 2 years] • Confirmed COVID-19 in Phase 2/3 participants with and without evidence of infection before vaccination [Time Frame: From 7 days after the second dose of study intervention to the end of the study, up to 2 years] • Percentage of participants 12-15 years of age in Phase 3 reporting adverse events [Time Frame: From dose 1 through 1 month after the last dose], [Time Frame: From dose 1 through 6 months after the last dose • In participants 12-15 years of age randomized in Phase 3, percentage of participants reporting local reactions [Time Frame: For 7 days after dose 1 and dose 2]; In participants 12-15 years of age randomized in Phase 3, percentage of participants reporting systemic events [Time Frame: For 7 days after dose 1 and dose 2]
Notes	**Funding**: Private (BioNTech and Pfizer)
	Conflict of interest: Yes. Quote: "William C. Gruber, Nicholas Kitchin, Stephen Lockhart, Ruth Bailey, Alejandra Gurtman, Judith Absalon, Kena A. Swanson, Kenneth Koury, Warren V. Kalina, David Cooper, Philip R. Dormitzer, Kathrin U. Jansen, John L. Perez, Hua Ma, Xia Xu, Susan Mather and Dina B. Tresnan are employees of Pfizer. Özlem Türeci and Uğur Şahin are employees of BioNTech."
	Protocol: English
	Statistical plan: Yes
	Data-sharing stated: Yes

Thomas 2021

Trial: NCT04368728, Thomas S, N Engl J Med, 2021 (published in peer reviewed journal) first published as preprint Thomas S, medRxiv, 2021

Previous publications: FDA breifing document BNT162b2, 2020, Polack F P, N Engl J Med, 2020

Methods	RCT
	Phase 2-3
	Blinding: double blinding
	Date of study: 07/27/2020 to 01/11/2021
	Location: Multicenter / Multinational
	Follow-up duration (months): 6
	Vaccine group: BNT162b2 (n = 22085); Placebo (n=22080)
Participants	**Population randomized:** 44165 participants (n1=22085 / n2=22080)
	Characteristics of participants Type of participants: Children, adolescent, adults N=44165 Children: 0 Pregnant women: 0 Immunocompromised patients: 0 Age mean: NR Age range: 16-91 Men: 22420
	Description of participants Children (>=12Y yo), adolescents and adults, with no history or SARS-CoV 2 infection at 152 sites in Argentina, Brazil, Germany, South Africa, Turkey and USA
	Inclusion criteria • Participants 12 years or older • Participants who were healthy or had stable chronic medical conditions
	Exclusion criteria • An active immunocompromising condition or recent immunosuppressive therapy • Participants with a COVID-19 medical history
	Withdrawals: 68 withdrawal due to adverse events
Interventions	**Intervention:** BNT162b2- 2 IM doses of 30 mcg (D0/21)
	Control: Placebo

Outcomes	**Primary outcome of the trial:** **In the report:** • Safety end points included solicited, prespecified local reactions, systemic events, and antipyretic or pain medication use during the first 7 days after receipt of each vaccine or placebo dose, which were recorded in an electronic diary; unsolicited adverse events after receipt of the first dose through 1 month after the second dose; and serious adverse events after receipt of the first dose through 1 and 6 months after the second dose was received • BNT162b2 efficacy against laboratory-confirmed Covid-19 with an onset of 7 days or more after the second dose was assessed and summarized descriptively in participants without serologic or virologic evidence of SARS-CoV-2 infection within 7 days after the second dose and in participants with or without evidence of previous infection. Efficacy against severe Covid-19 was also assessed. Lineages of SARS-CoV-2 detected in midturbinate specimens are reported here for Covid-19 cases that occurred 7 days or more after the second dose in South African participants without evidence of previous infection **In the register:** • In the first 360 participants randomized into Phase 2/3, percentage of participants reporting local reactions [Time Frame: For 7 days after dose 1 and dose 2] Pain at the injection site, redness, and swelling as self-reported on electronic diaries • In the first 360 participants randomized into Phase 2/3, percentage of participants reporting systemic events [Time Frame: For 7 days after dose 1 and dose 2] Fever, fatigue, headache, chills, vomiting, diarrhea, new or worsened muscle pain, and new or worsened joint pain as self-reported on electronic diaries • In the first 360 participants randomized into Phase 2/3, percentage of participants reporting adverse events [Time Frame: From dose 1 through 1 month after the last dose] As elicited by investigational site staff • In the first 360 participants randomized into Phase 2/3, percentage of participants reporting serious adverse events [Time Frame: From dose 1 through 6 months after the last dose] As elicited by investigational site staff • In a subset of at least 6000 participants randomized in Phase 2/3, percentage of participants reporting local reactions [Time Frame: For 7 days after dose 1 and dose 2] • Pain at the injection site, redness, and swelling as self-reported on electronic diaries • In a subset of at least 6000 participants randomized in Phase 2/3, percentage of participants reporting systemic events [Time Frame: For 7 days after dose 1 and dose 2] Fever, fatigue, headache, chills, vomiting, diarrhea, new or worsened muscle pain, and new or worsened joint pain as self-reported on electronic diaries • Percentage of participants in Phase 2/3 reporting adverse events [Time Frame: From dose 1 through 1 month after the last dose] As elicited by investigational site staff • Percentage of participants in Phase 2/3 reporting serious adverse events [Time Frame: From dose 1 through 6 months after the last dose] As elicited by investigational site staff • Confirmed COVID-19 in Phase 2/3 participants without evidence of infection before vaccination [Time Frame: From 7 days after the second dose of study intervention to the end of the study, up to 2 years] Per 1000 person-years of follow-up • Confirmed COVID-19 in Phase 2/3 participants with and without evidence of infection before vaccination [Time Frame: From 7 days after the second dose of study intervention to the end of the study, up to 2 years] Per 1000 person-years of follow-up • Percentage of participants 12-15 years of age in Phase 3 reporting adverse events [Time Frame: From dose 1 through 1 month after the last dose] As elicited by investigational site staff • Percentage of participants 12-15 years of age in Phase 3 reporting adverse events [Time Frame: From dose 1 through 6 months after the last dose] As elicited by investigational site staff • In participants 12-15 years of age randomized in Phase 3, percentage of participants reporting local reactions [Time Frame: For 7 days after dose 1 and dose 2] Pain at the injection site, redness, and swelling as self-reported on electronic diaries

	• In participants 12-15 years of age randomized in Phase 3, percentage of participants reporting systemic events [Time Frame: For 7 days after dose 1 and dose 2] Fever, fatigue, headache, chills, vomiting, diarrhea, new or worsened muscle pain, and new or worsened joint pain as self-reported on electronic diaries • In participants who receive BNT162b2SA given as 1 or 2 doses, percentage of participants reporting adverse events [Time Frame: From dose 1 through 1 month after the last dose] As elicited by investigational site staff • In participants who receive BNT162b2SA given as 1 or 2 doses, percentage of participants reporting serious adverse events [Time Frame: From dose 1 through 5 or 6 months after the last dose] As elicited by investigational site staff • In participants, who receive BNT162b2SA given as 1 or 2 doses, percentage of participants reporting local reactions [Time Frame: For 7 days after dose 1 (and dose 2)] Pain at the injection site, redness, and swelling as self-reported on electronic diaries • In participants who receive BNT162b2SA given as 1 or 2 doses, percentage of participants reporting systemic events [Time Frame: For 7 days after dose 1 (and dose 2)] Fever, fatigue, headache, chills, vomiting, diarrhea, new or worsened muscle pain, and new or worsened joint pain as self-reported on electronic diaries • In participants who receive a third dose of BNT162b2, percentage of participants reporting adverse events [Time Frame: From the third dose through 1 month after the third dose] As elicited by investigational site staff • In participants who receive a third dose of BNT162b2, percentage of participants reporting serious adverse events [Time Frame: From the third dose through 6 months after the third dose] As elicited by investigational site staff • In participants who receive a third dose of BNT162b2, percentage of participants reporting local reactions [Time Frame: For 7 days after the third dose] Pain at the injection site, redness, and swelling as self-reported on electronic diaries • In participants who receive a third dose of BNT162b2, percentage of participants reporting systemic events [Time Frame: For 7 days after the third dose] Fever, fatigue, headache, chills, vomiting, diarrhea, new or worsened muscle pain, and new or worsened joint pain as self-reported on electronic diaries • Noninferiority of the SARS-CoV-2 reference strain neutralizing titers after a third dose of BNT162b2 at 30 μg compared to after 2 doses of BNT162b2, in the same individuals [Time Frame: 1 month after the third dose] As measured at the central laboratory • Noninferiority of the SARS-CoV-2 SA strain neutralizing titers after one dose of BNT162b2SA compared to the SARS-CoV-2 reference strain neutralizing titers after 2 doses of BNT162b2, in the same individuals [Time Frame: 1 month after the third dose] As measured at the central laboratory • Noninferiority of the SARS-CoV-2 SA strain neutralizing titers after 2 doses of BNT162b2SA compared to the SARS-CoV-2 reference strain neutralizing titers after 2 doses of BNT162b2 [Time Frame: 1 month after the second dose] As measured at the central laboratory

Notes	**Funding**: Private (BioNTech/Pfizer)
	Conflict of interest: Yes. Quote: "The corresponding author and 20 other authors are Pfizer employees. From earlier trial report (Polack 2020): Dr. Thomas reports other from Pfizer, during the conduct of the study; personal fees from Merck, personal fees from Sanofi, personal fees from Takeda, personal fees from Themisbio, personal fees from Janssen, outside the submitted work."
	Protocol: English
	Statistical plan: Yes
	Data-sharing stated: Yes

mRNA-1273- ModernaTX

Comparison: mRNA-1273 vs placebo

Ali 2021

Trial: NCT04649151, Ali K, N Engl J Med, 2021 (published in peer reviewed journal)

Methods	RCT
	Phase 2-3
	Blinding: double blinding
	Date of study: 12/09/2020 to 02/28/2021
	Location: Multicenter / USA
	Follow-up duration (months): *
	Vaccine group: 100 mcg mRNA-1273 (n=2489); Placebo (n=1243)
Participants	**Population randomized:** 3732 participants (n1=2489 / n2=1243)
	Characteristics of participants Type of participants: Adolescents N=3732 Children: 3726 Pregnant women: 0 Age mean: 14.3 years Age range: 12-17 Men: 1915
	Description of participants Healthy adolescents in 26 centers in the USA
	Inclusion criteria • Male and female adolescents between the ages of 12 and 17 years considered to be in good general health by the investigators
	Exclusion criteria • Travel outside of the United States in the 28 days before screening • Pregnancy or breast-feeding • Acute illness or fever 24 hours before or at screening • Previous administration of an investigational vaccine against SARS-CoV-2 • Current treatment with investigational agents for prophylaxis against Covid-19
	Withdrawals: 2 withdrawal due to adverse events
Interventions	**Intervention:** mRNA-1273 - 2 IM doses of 100 mcg (D0/D28)
	Control: Placebo

Outcomes	**Primary outcome of the trial** **In the report:** • Safety • Reactogenicity • Geometric mean titer ratio of pseudovirus neutralizing antibody titers • Serologic response **In the register:** • Number of Participants with Solicited Local and Systemic Adverse Reactions (ARs) [Time Frame: Up to Day 36 (7 days after each dose)] • Number of Participants with Unsolicited Adverse Events (AEs) [Time Frame: Up to Day 57 (28 days after each dose)] • Number of Participants with Serious Adverse Events (SAEs), Medically Attended AEs (MAAEs), or Adverse Events of Special Interest (AESI) of Multisystem Inflammatory Syndrome in Children (MIS-C) [Time Frame: Up to Day 394 (1 year after second dose)] • Number of Participants with Serum Antibody (Ab) Levels that Meet or Exceed the Threshold of Protection From COVID-19 [Time Frame: Day 57 (28 days after second dose)]; • Geometric Mean (GM) of the Serum Ab Level [Time Frame: Day 57 (28 days after second dose)] • Seroresponse Rate of Vaccine Recipients [Time Frame: Day 57 (28 days after second dose)]
Notes	**Funding**: Mixed (Moderna; Office of the Assistant Secretary for Preparedness and Response, Biomedical Advanced Research and Development Authority (BARDA))
	Conflict of interest: Yes. Quote: "The corresponding author Roderick McPhee is an employee of the developer Moderna. Jacqueline Miller: Employment - Head of development activities for vaccines and monoclonal antibodies at Moderna; Stock; Stock options."
	Protocol: English
	Statistical plan: Yes
	Data-sharing stated: No

El Sahly 2021

Trial: NCT04470427, El Sahly HM, N Engl J Med, 2021 (published in peer reviewed journal)

First published as FDA briefing document Moderna COVID-19 Vaccine and later as Baden LR, N Engl J Med 2020.

Methods	RCT
	Phase 3
	Blinding: triple blinding
	Date of study: 07/27/2020 to 10/23/2020
	Location: Multicenter / United States
	Follow-up duration (months): 5.3
	Vaccine group: 100 mcg mRNA-1273 (n=15209); Placebo (n = 15206)
Participants	**Population randomized:** 30415 participants (n1=15209 / n2=15206)
	Characteristics of participants Type of participants: Healthy volunteers N=30415 Children: 0 Pregnant women: 0

	Age mean: 51.4 Age range: 18-95 Men: 15974
	Description of participants Healthy adults with no known history of SARS-CoV-2 infection in 99 centers in the US
	Inclusion criteria • Adults, ≥ 18 years of age at time of consent, who are at high risk of SARS-CoV-2 infection, defined as adults whose locations or circumstances put them at appreciable risk of exposure to SARS-CoV-2 and COVID-19 • Informed consent • Able to comply with study procedures based on the assessment of the Investigator • Female participants of nonchildbearing potential may be enrolled in the study • Female participants of childbearing potential may be enrolled in the study if the participant fulfills all the following criteria - negative pregnancy test at Screening and on the day of the first dose (Day 1) • Practiced adequate contraception or has abstained from all activities that could result in pregnancy for at least 28 days prior to the first dose (Day 1) • Agreed to continue adequate contraception through 3 months following the second dose (Day 29) • Not currently breastfeeding • Healthy adults or adults with pre-existing medical conditions who are in stable condition. A stable medical condition is defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 3 months before enrollment
	Exclusion criteria • Acutely ill or febrile 72 hours prior to or at screening • Pregnant or breastfeeding • Known history of SARS-CoV-2 infection • Prior administration of an investigational coronavirus (SARS-CoV, MERS-CoV) vaccine or current/planned simultaneous participation in another interventional study to prevent or treat COVID-19 • Demonstrated inability to comply with the study procedures. • Immediate family member or household member of this study's personnel. • Known or suspected allergy or history of anaphylaxis, urticaria, or other significant adverse reaction to the vaccine or its excipients • Bleeding disorder considered a contraindication to intramuscular injection or phlebotomy • Has received or plans to receive a non-study vaccine within 28 days prior to or after any dose of IP (except for seasonal influenza vaccine). • Has participated in an interventional clinical study within 28 days prior to the day of enrollment • Immunosuppressive or immunodeficient state, asplenia, recurrent severe infections (HIV-positive participants with CD4 count ≥350 cells/mm3 and an undetectable HIV viral load within the past year [low level variations from 50-500 viral copies which do not lead to changes in antiretroviral therapy [ART] are permitted]) • Has received systemic immunosuppressants or immune-modifying drugs for >14 days in total within 6 months prior to Screening (for corticosteroids ≥ 20 mg/day of prednisone equivalent) • Has received systemic immunoglobulins or blood products within 3 months prior to the day of screening • Has donated ≥ 450 mL of blood products within 28 days prior to Screening
	Withdrawals: 15 withdrawal due to adverse events
Interventions	**Intervention:** mRNA-1273 - 2 IM doses of 100-mcg mRNA-1273 (D1/28)

	Control: Placebo
Outcomes	**Primary outcome of the trial** **In the report**: • Vaccine efficacy in preventing a first occurrence of Covid-19 with onset at least 14 days after the second injection **In the register:** • Number of Participants with a First Occurrence of COVID-19 Starting 14 Days after Second Dose of mRNA-1273 [Time Frame: Day 29 (second dose) up to Day 759 (2 years after second dose)] • Number of Participants with Adverse Events (AEs) or Medically Attended AEs (MAAEs) Leading to Withdrawal [Time Frame: Up to Day 759 (2 years after second dose)] • Number of Participants with Solicited Local and Systemic Adverse Reactions (ARs) [Time Frame: Up to Day 8 (7 days after first dose) and up to Day 36 (7 days after second dose)] • Number of Participants with Unsolicited AEs [Time Frame: Up to Day 57 (28 days after each dose)]
Notes	**Funding**: Mixed (Moderna; Office of the Assistant Secretary for Preparedness and Response, Biomedical Advanced Research and Development Authority (BARDA))
	Conflict of interest: Yes. Quote: "Dr. Baden is a Deputy Editor at the New England Journal of Medicine. Dr. Baden is involved in HIV and COVID vaccine clinical trials conducted in collaboration with the NIH, HIV Vaccine Trials Network (HVTN), COVID Vaccine Prevention Network (CoVPN), International AIDS Vaccine Initiative (IAVI), Crucell/Janssen, Moderna, Military HIV Research Program (MHRP), Gates Foundation, and the Ragon Institute; Dr. El Sahly reports grants from NIH, during the conduct of the study; Dr. Zaks reports personal fees and other from Moderna Inc., outside the submitted work."
	Protocol: English
	Statistical plan: Yes
	Data-sharing stated: Yes

CVnCoV - CureVac AG

Comparison: CVnCoV vs Placebo

Kremsner 2021

Trial: NCT04652102; EudraCT 2020-003998-22, Kremsner P, SSRN, 2021 (Preprint)

Methods	RCT
	Phase 2-3
	Blinding: triple blinding
	Date of study: 12/11/2020 to 04/12/2021
	Location: Multicenter / Belgium, Germany, The Netherlands, Spain, Argentina, Colombia, Dominican Republic, Mexico, Panama, Peru
	Follow-up duration (months): 6.23
	Vaccine group: 12 mcg CVnCoV (n=19783); Placebo (n=19746)
Participants	**Population randomized:** 39529 participants (n1=19783 / n2=19746)
	Characteristics of participants Type of participants: Adults N=39529 Children: 0 Pregnant women: 0 Immunocompromised patients: 0 Age mean: NR Age range: 18-98 Men: 21672
	Description of participants Adults with no history of COVID-19 in 47 centers in Belgium, Germany, The Netherlands, Spain, Argentina, Colombia, Dominican Republic, Mexico, Panama and Peru
	Inclusion criteria • Male or female participants 18 years of age or older • Willing and able to provide written informed consent prior to initiation of any trial procedures • Expected compliance with protocol procedures and availability for clinical follow-up through the last planned visit • Females of non-childbearing potential defined as follows: surgically sterile (history of bilateral tubal ligation/occlusion, bilateral oophorectomy or hysterectomy) or postmenopausal {defined as amenorrhea for ≥12 consecutive months prior to screening (Day 1) without an alternative medical cause}. A follicle-stimulating hormone (FSH) level may be measured at the discretion of the Investigator to confirm postmenopausal status • Females of childbearing potential: negative pregnancy test (human chorionic gonadotropin [hCG]) within 24 hours prior to each trial vaccination on Day 1 and Day 29 • Females of childbearing potential must use highly effective methods of birth control from 2 weeks before the first administration of the trial vaccine until 3 months following the last administration
	Exclusion criteria • History of virologically confirmed COVID-19 illness • For females: pregnancy or lactation • Use of any investigational or non-registered product (vaccine or drug) within 28 days preceding the administration of trial vaccine or planned use during the trial • Receipt of any licensed vaccines within 28 days (for live vaccines) or 14 days (for inactivated or any other vaccines) prior to administration of the first trial vaccine

	• Prior administration of any investigational SARS-CoV-2 vaccine or another coronavirus (SARS-CoV, Middle East Respiratory Syndrome-CoV) vaccine or planned used during the trial • Any treatment with immunosuppressants or other immune-modifying drugs (including but not limited to anabolic steroids, corticosteroids, biologicals and methotrexate) for > 14 days total within 6 months preceding the administration of trial vaccine or planned use during the trial. For corticosteroid use, this means prednisone or equivalent, 0.5 mg/kg/day for 14 days or more. The use of inhaled, topical, or localized injections of corticosteroids (e.g., for joint pain/inflammation) is permitted • Any medically diagnosed or suspected immunosuppressive or immunodeficient condition based on medical history and physical examination including known infection with human immunodeficiency virus (HIV), hepatitis B virus (HBV) or hepatitis C virus (HCV) • Current diagnosis of or treatment for cancer including leukemia, lymphoma, Hodgkin disease, multiple myeloma or generalized malignancy • Chronic renal failure or nephrotic syndrome • Receipt of an organ or bone marrow transplant • History of angioedema (hereditary or idiopathic) or history of any anaphylactic reaction • History of potential immune-mediated disease (pIMD) • History of allergy to any component of CVnCoV • Administration of immunoglobulins or any blood products within 3 months prior to the administration of trial vaccine or planned receipt during the trial • Participants with a significant acute or chronic medical or psychiatric illness that, in the opinion of the Investigator, precludes trial participation (e.g., may increase the risk of trial participation, render the participant unable to meet the requirements of the trial, or may interfere with the participant's trial evaluations) • Participants with impaired coagulation or any bleeding disorder in whom an intramuscular injection or a blood draw is contraindicated • Foreseeable non-compliance with the trial procedure as judged by the Investigator.
	Withdrawals: 41 withdrawal due to adverse events
Interventions	**Intervention:** CVnCoV - 2 IM doses of 12 mcg (D0/28)
	Control: Placebo

Outcomes	**Primary outcome of the trial:** **In the report:** • The occurrence of a first episode of virologically confirmed COVID-19 of any severity, caused by any strain, in all participants, from two weeks after the second dose onward **In the register:** • Number of participants who experience a first episode of virologically confirmed {reverse transcription polymerase chain reaction (RT-PCR) positive} case of COVID-19 of any severity [Time Frame: Day 1 to Day 393] • Number of participants who experience one or more medically attended adverse events (AEs) [Time Frame: Day 29 to Day 211] • Intensity grading of medically attended adverse events (AEs) per FDA toxicity grading scale [Time Frame: Day 29 to Day 211] • Number of participants who experience one or more treatment-related medically attended adverse events (AEs) [Time Frame: Day 29 to Day 211] • Number of participants who experience one or more serious adverse events (SAEs) [Time Frame: Day 29 to Day 393] • Intensity grading of serious adverse events (SAEs) per FDA toxicity grading scale [Time Frame: Day 29 to Day 393] • Number of participants who experience one or more treatment-related serious adverse events (SAEs) [Time Frame: Day 29 to Day 393] • Number of participants who experience one or more adverse events of special interest (AESI) [Time Frame: Day 29 to Day 393] • Intensity grading of adverse events of special interest (AESI) per FDA toxicity grading scale [Time Frame: Day 29 to Day 393] • Number of participants who experience one or more treatment-related adverse events of special interest (AESI) [Time Frame: Day 29 to Day 393] • Number of participants who experience a fatal serious adverse event (SAE) [Time Frame: Day 29 to Day 393]
Notes	**Funding**: Mixed (The German Federal Ministry of Education and Research (BMBF), CureVac AG)
	Conflict of interest: Yes. Quote: "PGK [first author & analysis] declares institutional funding from CureVac during the conduct of this study, and is a member of the scientific advisory board for the HERALD clinical trial. LO [last author & analysis] is employed by CureVac, and holds stock options, and is the holder of a pending patent. OSK [analysis] declares consultant fees from CureVac during the conduct of this study, and is a member of the DSMB for a CVnCoV phase 1 trial. TV [analysis] declares consultant fees from CureVac during the conduct of this study, and consultant fees from CureVac, AstraZeneca, Pfizer, Johnson&Johnson, and Moderna outside of the submitted work."
	Protocol: NR
	Statistical plan: NR
	Data-sharing stated: Yes

Non-replicating viral vector

ChAdOx1- Astra Zeneca + University of Oxford

Comparison: ChAdOx1/ SII-ChAdOx1 nCoV-19 vs Placebo/MenACWY

Asano 2021

Trial: NCT04568031, Asano M, Int J Infect Dis, 2021 (published in peer reviewed journal)

Methods	RCT
	Phase 1-2
	Blinding: double blinding
	Date of study: 08/01/2020 (end date not reported)
	Location: Multicenter / Japan
	Follow-up duration (months): 1.9
	Vaccine group: ChAdOx1-S (n=192); Placebo (n=64)
Participants	**Population randomized:** 256 participants (n1=192 / n2=64)
	Characteristics of participants Type of participants: Adults N=256 Children: 0 Pregnant women: 0 Immunocompromised patients: 0 Age mean: Age range: NR Men: 169
	Description of participants Adults with or without mild, well-controlled co-morbidities seronegative and PCR negative to SARS-CoV-2 at 5 centres in Japan
	Inclusion criteria • Adults aged ≥18 years • Seronegative to SARS-CoV-2 at screening • Negative reverse-transcriptase polymerase chain reaction test for SARS-CoV-2 • Mild/moderate, well-controlled comorbidities were allowed
	Exclusion criteria • History of laboratory-confirmed SARS-CoV-2 infection • Pregnant women • New onset of fever • Any confirmed or suspected immunodeficient state • Receipt of any vaccine within 30 days before and after each study dose • or prior or planned receipt of an investigational or licensed vaccine or product that may impact interpretation of trial data (e.g., adenovirus-vectored vaccines or coronavirus vaccines)

	• Severe and/or uncontrolled cardiovascular, respiratory, gastrointestinal, hepatic, or renal disease, endocrine disorder, or neurologic illness
	Withdrawals: 0 withdrawal due to adverse events
Interventions	**Intervention:** ChAdOx1 - 2 IM doses of 5 × 10^10 vp (D0/28)
	Control: Placebo
Outcomes	**Primary outcome of the trial:** **In the report:** • Immunogenicity, measured by anti-SARS-CoV-2 spike seroresponse (≥4-fold rise in titers from Day 1 baseline value) at Day 57; 2) • Safety, measured by occurrence of solicited local and systemic reactogenicity signs/symptoms in the 6 days after each dose; occurrence of unsolicited AEs, serious AEs (SAEs), and AEs of special interest (AESIs) for 28 days after each dose • Change from baseline in safety laboratory measures **In the register:** • Proportion of participants who have a post treatment seroresponse to the spike antigens of AZD1222 [Time Frame: Day 57] • The incidence of local and systemic solicited reactogenicity signs and symptoms for 7 days following throughout vaccination [Time Frame: Day 1 to 8] • The incidence of local and systemic solicited reactogenicity signs and symptoms for 7 days following throughout vaccination [Time Frame: Day 29 to 36] • The incidence of AEs, serious adverse events (SAEs) and adverse events of special interest (AESIs) [Time Frame: Day 1 through Day 57] • Biochemistry; change from baseline for blood chemistry measures [Time Frame: Day 8, Day 29, Day 36, and Day 57] • Haematology; change from baseline for hematology/hemostasis measures [Time Frame: Day 8, Day 29, Day 36, and Day 57]
Notes	**Funding**: Private (AstraZeneca)
	Conflict of interest: Yes. Quote: "JV was an employee and stockholder of AstraZeneca at the time of the study. All other authors are employees of, and hold or may hold stock in, AstraZeneca."
	Protocol: NR
	Statistical plan: NR
	Data-sharing stated: Yes

Clemens 2021 (results for this trial are also included in Voysey 2021)

Trial: ISRCTN89951424, Clemens S, Nat. Commun., 2021 (published in peer reviewed journal)

Methods	RCT
	Phase 3

	Blinding: double blinding
	Date of study: 2020/06/23 to 2020/12/01
	Location: Multicenter / Brazil
	Follow-up duration (months): 8.27
	Vaccine group: ChAdOx1-S (n=5207); Placebo (n=5209)
Participants	**Population randomized:** 10,416 participants (n1=5207 / n2=5209)
	Characteristics of participants Type of participants: Adults N=10,416 Children: 0 Pregnant women: 0 Immunocompromised patients: 0 Age mean: Age range: NR Men: 4,268
	Description of participants Adults that were SARS-CoV-2 seronegative and with no history of COVID-19 in six centers in Brazil.
	Inclusion criteria • Individuals aged 18 and over • Health professionals and/or adults at high risk of exposure to SARS-CoV-2 • Able and willing (in the Investigator's opinion) to comply with all study requirements • Willing to allow the investigators to discuss the volunteer's medical history with their General Practitioner/personal doctor and access all medical records when relevant to study procedures • For females of childbearing potential only, willingness to practice continuous effective contraception during the study and a negative pregnancy test on the day(s) of screening and vaccination • Agreement to refrain from blood donation during the course of the study • Provide written informed consent
	Exclusion criteria • Individuals aged 18 and over • Health professionals and/or adults at high risk of exposure to SARS-CoV-2 • Able and willing (in the Investigator's opinion) to comply with all study requirements • Willing to allow the investigators to discuss the volunteer's medical history with their General Practitioner/personal doctor and access all medical records when relevant to study procedures • For females of childbearing potential only, willingness to practice continuous effective contraception during the study and a negative pregnancy test on the day(s) of screening and vaccination • Agreement to refrain from blood donation during the course of the study • Provide written informed consent • • Exclusion criteria •

	• Participation in COVID-19 prophylactic drug trials for the duration of the study (Participation in COVID-19 treatment trials is allowed in the event of hospitalisation due to COVID-19. The study team should be informed as soon as possible) • Participation in SARS-CoV-2 serological surveys where participants are informed of their serostatus for the duration of the study • Planned receipt of any vaccine (licensed or investigational), other than the study intervention, within 30 days before and after study vaccination • Prior receipt of an investigational or licensed vaccine likely to impact on interpretation of the trial data (e.g. Adenovirus vectored vaccines, any coronavirus vaccines) • Administration of immunoglobulins and/or any blood products within the three months preceding the planned administration of the vaccine candidate • Any confirmed or suspected immunosuppressive or immunodeficient state, asplenia, recurrent severe infections and chronic use (more than 14 days) of immunosuppressant medication within the past 6 months except topical steroids or short-term oral steroids (course lasting ≤14 days) • History of allergic disease or reactions likely to be exacerbated by any component of ChAdOx1 nCoV-19 or MenACWY or paracetamol • Any history of angioedema • Any history of anaphylaxis • Pregnancy, lactation or willingness/intention to become pregnant during the study • Current diagnosis of or treatment for cancer (except basal cell carcinoma of the skin and cervical carcinoma in situ) • History of serious psychiatric condition likely to affect participation in the study • Bleeding disorder (e.g. factor deficiency, coagulopathy or platelet disorder), or prior history of significant bleeding or bruising following IM injections or venepuncture • Suspected or known current alcohol or drug dependency • Severe and/or uncontrolled cardiovascular disease, respiratory disease, gastrointestinal disease, liver disease, renal disease, endocrine disorder and neurological illness (mild/moderate well-controlled comorbidities are allowed) • History of laboratory-confirmed COVID-19 • Seropositive for SARS-CoV-2 antibodies before enrolment • New onset of fever or a cough or shortness of breath or anosmia/ageusia since February 2020, unless seronegative for SARS-CoV-2 antibodies at screening • Continuous use of anticoagulants, such as coumarins and related anticoagulants (i.e. warfarin) or novel oral anticoagulants (i.e. apixaban, rivaroxaban, dabigatran and edoxaban) • Any other significant disease, disorder or finding which may significantly increase the risk to the volunteer because of participation in the study, affect the ability of the volunteer to participate in the study or impair interpretation of the study data
	Withdrawals: NR
Interventions	**Intervention:** 2 IM doses of 3.5-6.5 x 10^10 vp, 4 to 12 weeks apart
	Control: 1 IM dose of Men ACWY control vaccine and 1 IM dose of normal saline placebo, 4 to 12 weeks apart

Outcomes	**Primary outcome of the trial:** **In the report:** • Virologically-confirmed, symptomatic COVID-19, defined as a NAAT-positive swab combined with at least one of: fever >37.8ºC, cough, shortness of breath, anosmia or ageusia **In the register:** • Virologically confirmed (PCV positive) symptomatic cases of COVID-19 over the course of 12 months
Notes	**Funding**: Mixed (UKRI, NIHR, Wellcome Trust, CEPI, Lemann Foundation, Rede D'Or, and Brava and Telles Foundation, NIHR Oxford Biomedical Research Centre, and AstraZeneca)
	Conflict of interest: Yes. Quote: " SCG is cofounder of Vaccitech (collaborators in the early development of this vaccine candidate) and named as an inventor on a patent covering use of ChAdOx1-vectored vaccines (PCT/GB2012/000467) and a patent application covering this SARS-CoV-2 vaccine. PMF is a consultant to Vaccitech. AJP is Chair of the UK Department of Health and Social Care's JCVI, but does not participate in policy advice on coronavirus vaccines, and is a member of the WHO Strategic Advisory Group of Experts (SAGE). AJP is a NIHR Senior Investigators."
	Protocol: Yes. In English
	Statistical plan: Yes
	Data-sharing stated: Yes

Emary 2021 (results for this trial are also included in Voysey 2021)

Trial: NCT04400838, Emary K, Lancet, 2021 (published in peer reviewed journal)

Methods	RCT
	Phase 2-3
	Blinding: single blinding
	Date of study: 05/31/2020 to 11/13/2020
	Location: Multicenter / UK
	Follow-up duration (months): 4.93
	Vaccine group: ChAdOx1 (n=5600); MenACWY (n = 5211)
Participants	**Population randomized** 10673 participants (n1=5489 / n2=5184)
	Characteristics of participants Type of participants: People in close contact with COVID-19 patients N=10673 Children: 0 Pregnant women: 0 Immunocompromised patients: 0

	Age mean: NR Age range: NR Men: 1992
	Description of participants Adults seronegative at baseline enrolled at 19 study sites in UK
	Inclusion criteria • Adults aged 18 years and older • Participants in occupations with potentially high SARS-CoV-2 exposure, such as those in health and social care settings • Able and willing (in the Investigator's opinion) to comply with all study requirements • Willing to allow the investigators to discuss the volunteer's medical history with their General Practitioner/personal doctor and access all medical records when relevant to study procedures • For females of childbearing potential only, willingness to practice continuous effective contraception during the study and a negative pregnancy test on the day(s) of screening and vaccination • Agreement to refrain from blood donation during the course of the study • Provide written informed consent.
	Exclusion criteria • Participation in COVID-19 prophylactic drug trials for the duration of the study • Participation in SARS-CoV-2 serological surveys where participants are informed of their serostatus for the duration of the study • Receipt of any vaccine (licensed or investigational) other than the study intervention within 30 days before and after each study vaccination, with the exception of the licensed seasonal influenza vaccination and the licensed pneumococcal vaccination. Participants will be encouraged to receive these vaccinations at least 7 days before or after their study vaccine • Prior or planned receipt of an investigational or licensed vaccine or product likely to impact on interpretation of the trial data (e.g., Adenovirus vectored vaccines, any coronavirus vaccines) • Administration of immunoglobulins and/or any blood products within the three months preceding the planned administration of the vaccine candidate • Any confirmed or suspected immunosuppressive or immunodeficient state, asplenia, recurrent severe infections and use of immunosuppressant medication within the past 6 months, except topical steroids or short-term oral steroids (course lasting ?14 days) • History of allergic disease or reactions likely to be exacerbated by any component of ChAdOx1 nCoV-19 or MenACWY • Any history of angioedema • Any history of anaphylaxis • Pregnancy, lactation or willingness/intention to become pregnant during the study • Current diagnosis of or treatment for cancer (except basal cell carcinoma of the skin and cervical carcinoma in situ) • History of serious psychiatric condition likely to affect participation in the study • Bleeding disorder (e.g., factor deficiency, coagulopathy or platelet disorder), or prior history of significant bleeding or bruising following IM injections or venepuncture • Continuous use of anticoagulants, such as coumarins and related anticoagulants (i.e. warfarin) or novel oral anticoagulants (i.e. apixaban, rivaroxaban, dabigatran and edoxaban) • Suspected or known current alcohol or drug dependency • Any other significant disease, disorder or finding which may significantly increase the risk to the volunteer because of participation in the study, affect the ability of the volunteer to participate in the study or impair interpretation of the study data

	• Severe and/or uncontrolled cardiovascular disease, respiratory disease, gastrointestinal disease, liver disease, renal disease, endocrine disorder and neurological illness (mild/moderate well controlled comorbidities are allowed)
	Withdrawals: 0 withdrawal due to adverse events
Interventions	**Intervention:** ChAdOx1 - 2 IM doses (5 x 10^10 vp) (D0/28)
	Control: MenACWY - 2 IM doses of MenACWY vaccine (D0/28)
Outcomes	**Primary outcome of the trial:** **In the report:** • Symptomatic COVID-19 disease, defined as a positive NAAT result on an upper airway swab in a participant with at least one symptom, including cough, fever of 37·8°C or higher, shortness of breath, anosmia, or ageusia **In the register** • Assess the efficacy of the candidate ChAdOx1 nCoV-19 against COVID-19 in adults aged 18 years and older. [Time Frame: Study duration (12 months from last vaccination)] Number of virologically confirmed (PCR or NAAT positive) symptomatic cases of COVID-19 • Assess the safety of the candidate vaccine ChAdOx1 nCoV-19 in adults [Time Frame: Study duration (12 months from last vaccination)] Occurrence of serious adverse events (SAEs) throughout the study duration
Notes	**Funding**: Mixed (UK Research and Innovation, Engineering and Physical Sciences Research Council, Coalition for Epidemic Preparedness Innovations, NIHR, Medical Research Council and Wellcome Trust Core Award.)
	Conflict of interest: Yes. Quote: "Oxford University has entered into a partnership with AstraZeneca for further development of ChAdOx1 nCoV-19. AstraZeneca reviewed the data from the study and the final manuscript before submission but the authors retained editorial control.AJP and SNF are NIHR senior investigators"
	Protocol: English
	Statistical plan: Yes
	Data-sharing stated: Yes

Falsey 2021

Trial: NCT04516746, Falsey A, N Engl J Med, 2021 (published in peer reviewed journal)

Methods	RCT
	Phase 3
	Blinding: double blinding
	Date of study: 08/28/2020 to 01/15/2021
	Location: Multicenter / Chile, Peru, USA
	Follow-up duration (months): 6.27
	Vaccine group: ChAdOx1 (n = 21,635); Placebo (n = 10,816)
Participants	**Population randomized:** 32451 participants (n1=21635 / n2=10816)
	Characteristics of participants Type of participants: Adults N=32451 Children: 0 Pregnant women: 0 Immunocompromised patients: 9 Age mean: NR Age range: 18-100 Men: 18015
	Description of participants Adults (22% over 65 years) at high risk for exposure to SARS-CoV-2 and populations at increased risk for Covid-19 complications at 88 sites in USA, Chile, and Peru
	Inclusion criteria • Adult, 18 years of age or older at the time of consent • Increased risk of SARS-CoV-2 infection • Medically stable such that, according to the judgment of the investigator, hospitalization within the trial period was not anticipated and the participant appeared likely to be able to remain in the trial through the end of protocol-specified follow-up • Contraceptive use by women should be consistent with local regulations regarding the methods of contraception for those participating in clinical studies • Women of childbearing potential were required to: Have a negative pregnancy test on the day of screening and on Day 1, and Use one highly effective form of birth control for at least 28 days prior to Day 1 and agree to continue using one highly effective form of birth control through 60 days following administration of the second dose of trial intervention • Women were considered of childbearing potential unless they met either of the following criteria: surgically sterilized (including bilateral tubal ligation, bilateral oophorectomy, or hysterectomy) or postmenopausal • Capable of giving signed informed consent (or legally authorized representative able to provide consent)
	Exclusion criteria

	• History of allergy to any component of the vaccine • History of Guillain-Barré syndrome or any other demyelinating condition • Significant infection or other acute illness, including fever over 100°F (over 37°C) on the day prior to or day of randomization • History of laboratory-confirmed SARS-CoV-2 infection • Any confirmed or suspected immunosuppressive or immunodeficient state, including asplenia • Recurrent severe infections and use of immunosuppressant medication within the past 6 months (20 mg/kg/day or more of prednisone or its equivalent, given daily or on alternate days for 15 days or more within 30 days prior to administration of trial intervention) • History of primary malignancy except for: malignancy with low potential risk for recurrence after curative treatment (for example, history of childhood leukemia) or metastasis (for example, indolent prostate cancer) in the opinion of the site investigator, adequately treated non-melanoma skin cancer or lentigo maligna without evidence of disease, adequately treated uterine cervical carcinoma in situ without evidence of disease, localized prostate cancer • Clinically significant bleeding disorder (for example, factor deficiency, coagulopathy, or platelet disorder), or prior history of significant bleeding or bruising following intramuscular injections or venipuncture • Severe and/or uncontrolled cardiovascular disease, respiratory disease, gastrointestinal disease, liver disease, renal disease, endocrine disorder, and neurological illness, as judged by the Investigator (mild/moderate well-controlled coexisting conditions are allowed) • Any other significant disease, disorder, or finding that may have significantly increased the risk to the participant because of participation in the trial, affect the ability of the participant to participate in the trial, or impair interpretation of the trial data • Receipt of, or planned receipt of investigational products indicated for the treatment or prevention of SARS-CoV-2 or Covid-19 • For participants who became hospitalized with Covid-19, receipt of licensed treatment options and/or participation in investigational treatment studies was permitted • Receipt of any vaccine (licensed or investigational) other than licensed influenza vaccines within 30 days prior to and after administration of trial intervention • Receipt of immunoglobulins and/or any blood products within 3 months prior to administration of trial intervention or expected receipt during the period of trial follow-up • Involvement in the planning and/or conduct of this trial (applied to both Sponsor staff and/or staff at the trial site) • For women only: pregnancy (confirmed with positive pregnancy test) or breastfeeding • Had donated 450 mL or more of blood products within 30 days prior to randomization or expected to donate within 90 days of administration of second dose of trial intervention
	Withdrawals: 8 withdrawal due to adverse events
Interventions	**Intervention:** ChAdOx1 - 2 IM doses of 5×10^10 vp (D0/28)
	Control: Placebo
Outcomes	**Primary outcome of the trial:** **In the report:** • The first occurrence of SARS-CoV-2 symptomatic illness, confirmed by positive results on RT-PCR testing, with onset 15 days or more after the second dose of vaccine or placebo among participants who were seronegative for Covid-19 at baseline **In the register:** • The efficacy of 2 IM doses of AZD1222 compared to saline placebo for the prevention of COVID-19 [Time Frame: 1 year]: SARS-CoV-2 RT-PCR-positive symptomatic illness ≥ 15 days post second dose of study intervention

	• The safety and tolerability of 2 IM doses of AZD1222 compared to saline placebo [Time Frame: a: 28 days post each dose of study Intervention. / b: from Day 1 post-treatment through Day 730.]: Incidence of adverse events. Incidence of serious adverse events, medically attended adverse events, and adverse events of special interest • The reactogenicity of 2 IM doses of AZD1222 compared to saline placebo (Substudy only) [Time Frame: 7 days post each dose of study intervention.]: Incidence of local and systemic solicited adverse events
Notes	**Funding**: Mixed (AstraZeneca; the Office of the Assistant Secretary for Preparedness and Response, Biomedical Advanced Research and Development Authority; the Infectious Diseases Clinical Research Consortium through the National Institute of Allergy and Infectious Diseases, part of the NIH)
	Conflict of interest: Yes. Quote: "Several authors, including corresponding author and last author, are affiliated or employed by the manufacturer"
	Protocol: English
	Statistical plan: Yes
	Data-sharing stated: Yes

Kulkarni 2021

Trial: CTRI/2020/08/027170, Kulkarni P, SSRN, 2021 (Preprint)

Methods	RCT
	Phase 2-3
	Blinding: triple blinding
	Date of study: 08/25/2020 to 10/31/2020
	Location: Multicenter / India
	Follow-up duration (months): 6
	Vaccine group: SII-ChAdOx1 (Covishield) (n = 900); Placebo (adjuvant) (n = 300)
Participants	**Population randomized:** 1200 participants (n1=900 / n2=300)
	Characteristics of participants Type of participants: Adults N=1200 Children: 0 Pregnant women: 0 Immunocompromised patients: 0 Age mean: NR Age range: 18-84 Men: 915
	Description of participants Adults (seronegative and seropositive) without a history of COVID and not immunocompromised at 14 centers in India
	Inclusion criteria • Adults aged 18 years and older • Individuals with controlled comorbid conditions, including diabetes and hypertension, and controlled cardiovascular, respiratory, hepatic, renal and neurological conditions were eligible • Female participants were required to have a negative pregnancy test prior to enrolment and were required to use adequate contraception from 28 days before the first dose through 28 days after the second dose of vaccine
	Exclusion criteria • Acute illness • Known prior SARS-CoV-2 infection • An immunosuppressive condition or receipt of immunosuppressive therapy
	Withdrawals: 0 withdrawal due to adverse events
Interventions	**Intervention:** SII-ChAdOx1 nCoV-19 - 2 IM doses of 5x10^10 vp (D0/28)
	Control: Placebo

Outcomes	**Primary outcome of the trial:** **In the report:** • Causally related SAEs (as assessed by both investigators and the sponsor) reported through the day 180 study visit **In the register:** • Occurrence of causally related SAEs throughout the study duration following vaccination
Notes	**Funding**: Mixed (Serum Institute of India Pvt Ltd, Indian Council of Medical Research, AstraZeneca)
	Conflict of interest: Yes. Quote: "PSK, CB, AD, MG, US, DK, and BG are employees of SIIPL. JV and EJK are employees of AstraZeneca. All other authors declare no competing interests."
	Protocol: *
	Statistical plan: *
	Data-sharing stated: *

Madhi 2021a (results for this trial are also included in Voysey 2021)

Trial: NCT04444674, PACTR202006922165132, Madhi S, Lancet, 2021 (published in peer reviewed journal), first published as preprint Madhi S, ResearchSquare,2021

Methods	RCT
	Phase 1-2
	Blinding: double blinding
	Date of study: 08/17/2020 to 11/12/2020
	Location: Multicenter / South Africa
	Follow-up duration (months): 2
	Vaccine group: ChAdOx1 nCoV-19 (n = 52); Placebo (n = 52)
Participants	**Population randomized:** 104 participants (n1=52 / n2=52)
	Characteristics of participants Type of participants: People living with HIV N=104 Children: 0 Pregnant women: 0 Immunocompromised patients: 103 Age mean: NR Age range: NR Men: 27
	Description of participants Adults living with HIV in 7 centers in South Africa

	Inclusion criteria • 18–65 years • People living with HIV-1 (PLWH) in receipt of antiretroviral treatment for ≥3 months and an HIV-1 viral load <1000 copies/mL within 2 weeks of randomization • Test seronegative for hepatitis B surface antigen
	Exclusion criteria • Grade ≥2 abnormalities in full blood count, urea and electrolytes tests, or liver function tests, according to the Division of AIDS Grading Criteria
	Withdrawals: 0 withdrawal due to adverse events
Interventions	**Intervention:** ChAdOx1 - 2 IM doses of 5x10^10 vp (D0/28)
	Control: Placebo
Outcomes	**Primary outcome of the trial:** **In the report:** • Local and systemic reactogenicity and adverse events for 7 and 28 days following vaccination • Cellular and humoral immunogenicity of ChAdOx1 nCoV-19, as assessed by quantification of serum antibody (IgG) to SARS-CoV-2 full-length spike (FLS) protein, receptor-binding domain (RBD), and virus neutralizing antibody (NAb) assays against live and/or pseudotyped SARS-CoV-2 virus for 7 days after receipt of vaccine **In the register:** • Incidence of adverse events (intervention-related and intervention-unrelated) [Time Frame: Up to 12 months post enrollment]; • Cellular Immunogenicity [Time Frame: Up to 12 months post enrollment] • Humoral immunogenicity [Time Frame: Up to 12 months post enrollment]
Notes	**Funding**: Public/non profit (The Bill & Melinda Gates Foundation, South African Medical Research Council, UK Research and Innovation, UK National Institute for Health Research)
	Conflict of interest: Yes. Quote: "Oxford University has entered into a partnership with AstraZeneca for further development of ChAdOx1 nCoV-19 (AZD1222). AstraZeneca reviewed the data from the trial and the final manuscript before submission, but the authors retained editorial control. SCG is cofounder of Vaccitech (a collaborator in the early development of this vaccine candidate) and named as an inventor on a patent covering use of ChAdOx1-vectored vaccines (PCT/GB2012/000467) and a patent application covering this SARS-CoV-2 vaccine (GB2003670.3, 13.03.2020). TL is named as an inventor on a patent application covering this SARS-CoV-2 vaccine and was consultant to Vaccitech. TLV and JV are employees of AstraZeneca."
	Protocol: English
	Statistical plan: Yes
	Data-sharing stated: Yes

Madhi 2021b (results for this trial are also included in Voysey 2021)

Trial: NCT04444674, Madhi S, N Engl J Med, 2021 (published in peer reviewed journal)

Methods	RCT
	Phase 1-2
	Blinding: double blinding
	Date of study: 06/24/2020 to 11/08/2020
	Location: Multicenter / South Africa
	Follow-up duration (months): 6.73
	Vaccine group: 0.33 to 0.5 ml ChAdOx1, 2 doses (n=1013); Placebo, 2 doses (n=1013)
Participants	**Population randomized:** 2026 participants (n1=1013 / n2=1013)
	Characteristics of participants Type of participants: Healthy volunteers N=2026 Children: 0 Pregnant women: 0 Immunocompromised patients: 0 Age mean: NR Age range: 18-65 Men: 1142
	Description of participants Healthy adult volunteers that were HIV-negative and SARS-CoV-2 infection-free in 7 centres in South Africa
	Inclusion criteria • Healthy adults aged 18-65 years • Documented result of not being infected with HIV (including screening by a rapid HIV antibody test) within two weeks of randomization into the study for Group-1 and Group-2 participants only • Able and willing (in the Investigator's opinion) to comply with all study requirements. • Willing to allow investigators review available medical records, and review all medical and laboratory records if participant is admitted to hospital with respiratory tract infection suspected or confirmed to be COVID-19 • For females only, willingness to practice continuous effective contraception (see below) during the study and a negative pregnancy test on the day(s) of screening (within 14 days of randomization) or vaccination • For Group-3 only (i.e. HIV-infected), need to have been on anti-retroviral treatment for at least three months and HIV-1 viral load is <1,000 copies/ml within two weeks of randomization • Agreement to refrain from blood donation during the course of the study. Provide written informed consent

	Exclusion criteria • Planned receipt of any vaccine other (licensed or investigational) than the study intervention within 30 days before and after each study vaccination • Use of any unproven registered and unregistered treatments for COVID-19 • Prior receipt of an investigational or licensed vaccine likely to impact on interpretation of the trial data (e.g., Adenovirus vectored vaccines, any coronavirus vaccines) • Administration of immunoglobulins and/ or any blood products within the three months preceding the planned administration of the vaccine candidate • HBSAg positivity on the screening sample • Grade 2 or higher level of abnormality for FBC, U&E or LFT based on DAIDS Grading Criteria (Version 2.1, July 2017) • History of allergic disease or reactions likely to be exacerbated by any component of the ChAdOx1 nCoV-19 vaccine • Any history of hereditary angioedema or idiopathic angioedema • Any history of anaphylaxis in relation to vaccination • Pregnancy, lactation or willingness/intention to become pregnant during the study • History of cancer (except basal cell carcinoma of the skin and cervical carcinoma in situ). • History of serious psychiatric condition likely to affect participation in the study • Bleeding disorder (e.g. factor deficiency, coagulopathy or platelet disorder), or prior history of significant bleeding or bruising following IM injections or venipuncture • Any other serious chronic illness requiring hospital specialist supervision • Chronic respiratory diseases, including asthma • Chronic cardiovascular disease, gastrointestinal disease, liver disease, renal disease, endocrine disorder and neurological illness • Seriously overweight (BMI ≥ 40 Kg/m2) • Suspected or known current alcohol abuse as defined by an alcohol intake of greater than 42 units every week • Suspected or known injecting drug abuse in the 5 years preceding enrollment. • Any clinically significant abnormal finding on screening urinalysis • Any other significant disease, disorder or finding which may significantly increase the risk to the participant because of participation in the study, affect the ability of the participant to participate in the study or impair interpretation of the study data • History of laboratory confirmed COVID-19 illness or known contact with a person that was infected with SARS-COV-2 • New onset of fever or a cough or shortness of breath in the 30 days preceding screening and/or enrollment • Travel history to any other country with widespread epidemic since January 2020 • In addition to above, Group 1 & 2 participants need to fulfill the following exclusion criteria: Any confirmed or suspected immunosuppressive or immunodeficient state, including HIV infection, asplenia, recurrent severe infections and chronic use (more than 14 days) immunosuppressant medication within the past 6 months (topical steroids are allowed) • Any confirmed or suspected immunosuppressive or immunodeficient state (except HIV infection for Group-3), asplenia, recurrent severe infections and chronic use (more than 14 days) immunosuppressant medication within the past 6 months (topical steroids are allowed)
	Withdrawals: 0 withdrawal due to adverse events
Interventions	**Intervention:** ChAdOx1 - 2 IM doses of 5 x 10^10vp (D0/28)
	Control: Placebo

Outcomes	**Primary outcome of the trial:** **In the report:** • Efficacy against nucleic acid amplification test–confirmed symptomatic Covid-19 with onset more than 14 days after the second injection in participants who were seronegative at randomization • Occurrence of solicited local and systemic reactogenicity within the first 7 days after an injection, unsolicited adverse events within 28 days after an injection, changes from baseline in safety laboratory measures, and serious adverse events **In the register:** • Assess the incidence of adverse events (intervention-related and intervention-unrelated) in HIV-negative adults aged 18-65 year receiving candidate ChAdOx1 nCoV-19 vaccine or placebo (safety) [Time Frame: Up to 12 months post enrollment] • Determine if there is a reduction of severe and non-severe COVID-19 disease in HIV-negative adults who receive candidate vaccine ChAdOx1 nCoV-19 compared to placebo recipients (efficacy) [Time Frame: Up to 12 months post enrollment] • Assess the incidence of adverse events (intervention-related and intervention-unrelated) in HIV-positive adults aged 18-65 year receiving candidate ChAdOx1 nCoV-19 vaccine or placebo (safety) [Time Frame: Up to 12 months post enrollment] • Assess cellular Immunogenicity of ChAdOx1 nCoV-19 in people living with HIV (immunogenicity) [Time Frame: Up to 12 months post enrollment] • Assess humoral immunogenicity of ChAdOx1 nCoV-19 in people living with HIV [Time Frame: Up to 12 months post enrollment]
Notes	**Funding**: Mixed (UK Research and Innovation (For Vaccine supply only), The Bill and Melinda Gates Foundation and South African Medical Research Council)
	Conflict of interest: Yes. Quote: "SCG is co-founder of Vaccitech (collaborators in the early development of this vaccine candidate) and named as an inventor on a patent covering use of ChAdOx1-vectored vaccines and a patent application covering this SARS-CoV-2 vaccine (PCT/GB2012/000467), AJP is chair of the UK Department of Health and Social Care's (DHSC) Joint Committee on Vaccination & Immunisation (JCVI), but does not participate in discussions on COVID-19 vaccines, and is a member of WHO's SAGE. AJP is a National Institute for Health Research (NIHR) Senior Investigator. The views expressed in this Article do not necessarily represent the views of the DHSC, JCVI, NIHR, or WHO."
	Protocol: English
	Statistical plan: Yes
	Data-sharing stated: Yes

Voysey 2021

Trial: NCT04324606; ISRCTN89951424; NCT04400838; NCT04444674, Voysey M, Lancet, 2021 (published in peer reviewed journal)

NCT04324606 was published separately -Folegatti P M, LANCET, 2020

Methods	RCT
	Phase 1/2/3
	Blinding: single blinding
	Date of study: 04/23/2020 (end date not reported)
	Location: Multicenter / Brazil, South Africa, UK
	Follow-up duration (months): 3.94
	Vaccine group: ChAdOx1 (n=12408); Control (n = 12014)
Participants	**Population randomized:** 24422 participants (n1=12408 / n2=12014)
	Characteristics of participants Type of participants: Adults N=24422 Children: 0 Pregnant women: 0 Immunocompromised patients: 104 Age mean: NR Age range: NR Men: 7492
	Description of participants Adults seronegative at baseline from four studies in multiple centres in Brazil, South Africa, and the UK
	Inclusion criteria • Healthy adults aged 18-55 years (COV001), Healthy adults aged ?18 years with priority given to health professionals and adults with high potential for exposure to SARS-CoV-2 aged ?18 years (COV002), health professionals and adults with high potential for exposure to SARS-CoV-2 aged ?18 years (COV003), adults aged 18-65 years (COV005) • Able and willing (in the Investigator's opinion) to comply with all study requirements • Willing to allow the investigators to discuss the volunteer's medical history with their General Practitioner/personal doctor and access all medical records when relevant to study procedures • For females of childbearing potential only, willingness to practice continuous effective contraception during the study and a negative pregnancy test on the day(s) of screening and vaccination • Agreement to refrain from blood donation during the course of the study • Provide written informed consent • Health professionals and/or adults at high risk of exposure to SARS-CoV-2

	Exclusion criteria • Participation in COVID-19 prophylactic drug trials for the duration of the study • Participation in SARS-CoV-2 serological surveys where participants are informed of their serostatus for the duration of the study • Receipt of any vaccine (licensed or investigational) other than the study intervention within 30 days before and after each study vaccination, with the exception of the licensed seasonal influenza vaccination and the licensed pneumococcal vaccination. Participants will be encouraged to receive these vaccinations at least 7 days before or after their study vaccine • Prior or planned receipt of an investigational or licensed vaccine or product likely to impact on interpretation of the trial data (e.g. Adenovirus vectored vaccines, any coronavirus vaccines) • Administration of immunoglobulins and/or any blood products within the three months preceding the planned administration of the vaccine candidate • Any confirmed or suspected immunosuppressive or immunodeficient state, asplenia, recurrent severe infections and use of immunosuppressant medication within the past 6 months, except topical steroids or short-term oral steroids (course lasting ?14 days) • History of allergic disease or reactions likely to be exacerbated by any component of ChAdOx1 nCoV-19 or MenACWY • Any history of angioedema • Any history of anaphylaxis • Pregnancy, lactation or willingness/intention to become pregnant during the study • Current diagnosis of or treatment for cancer (except basal cell carcinoma of the skin and cervical carcinoma in situ) • History of serious psychiatric condition likely to affect participation in the study • Bleeding disorder (e.g. factor deficiency, coagulopathy or platelet disorder), or prior history of significant bleeding or bruising following IM injections or venepuncture • Continuous use of anticoagulants, such as coumarins and related anticoagulants (i.e. warfarin) or novel oral anticoagulants (i.e. apixaban, rivaroxaban, dabigatran and edoxaban) • Suspected or known current alcohol or drug dependency • Any other significant disease, disorder or finding which may significantly increase the risk to the volunteer because of participation in the study, affect the ability of the volunteer to participate in the study or impair interpretation of the study data • Severe and/or uncontrolled cardiovascular disease, respiratory disease, gastrointestinal disease, liver disease, renal disease, endocrine disorder and neurological illness (mild/moderate well controlled comorbidities are allowed)
	Withdrawals: 0 withdrawal due to adverse events
Interventions	**Intervention:** ChAdOx1 (low/standard or standard/standard) - 2 IM doses of 2.2 or 5.5x10^10 vp ChAdOx1 (D0/28)
	Control: MenACWY vaccine or saline placebo
Outcomes	**Primary outcome of the trial:** **In the report** • Symptomatic COVID-19 disease defined as a NAAT+ swab combined with at least one qualifying symptom (fever 37.8C; cough; shortness of breath; anosmia or ageusia) **In the register** • Virologically confirmed symptomatic COVID-19 disease, defined as a nucleic acid amplification test (NAAT)-positive swab combined with at least one qualifying symptom (fever 37·8°C, cough, shortness of breath, anosmia, or ageusia)

Notes	**Funding**: Mixed (UKRI, NIHR, CEPI, the Bill & Melinda Gates Foundation, the Lemann Foundation, Rede D'OR, the Brava and Telles Foundation, NIHR Oxford Biomedical Research Centre, Thames Valley and South Midland's NIHR Clinical Research Network, and Astra Zeneca)
	Conflict of interest: Yes. Quote: "Oxford University has entered into a partnership with Astra Zeneca for further development of ChAdOx1 nCoV-19. SCG is co-founder of Vaccitech (collaborators in the early development of this vaccine candidate) and named as an inventor on a patent covering use of ChAdOx1-vectored vaccines and a patent application covering this SARS-CoV-2 vaccine. TL is named as an inventor on a patent application covering this SARS-CoV-2 vaccine and was a consultant to Vaccitech for an unrelated project. PMF is a consultant to Vaccitech. AJP is Chair of UK Dept. Health and Social Care's (DHSC) Joint Committee on Vaccination & Immunisation (JCVI), but does not participate in discussions on COVID-19 vaccines, and is a member of the WHO's SAGE. AJP and SNF are NIHR Senior Investigator. The views expressed in this article do not necessarily represent the views of DHSC, JCVI, NIHR or WHO. AVSH reports personal fees from Vaccitech, outside the submitted work and has a patent on ChAdOx1 licensed to Vaccitech, and may benefit from royalty income to the University of Oxford from sales of this vaccine by AstraZeneca and sublicensees. MS reports grants from NIHR, non-financial support from AstraZeneca, during the conduct of the study; grants from Janssen, grants from GlaxoSmithKline, grants from Medimmune, grants from Novavax, grants and non-financial support from Pfizer, grants from MCM, outside the submitted work. CG reports personal fees from the Duke Human Vaccine Institute, outside of the submitted work. SNF reports grants from Janssen and Valneva, outside the submitted work. ADD reports grants and personal fees from AstraZeneca, outside of the submitted work. In addition, ADD has a patent manufacturing process for ChAdOx vectors with royalties paid to AstraZeneca, and a patent ChAdOx2 vector with royalties paid to AstraZeneca. The other authors declare no competing interests."
	Protocol: English
	Statistical plan: Yes
	Data-sharing stated: Yes

Gam-COVID-Vac - Gamaleya Research Institute

Comparison: Gam-COVID-Vac vs Placebo

Logunov 2021

Trial: NCT04530396, Logunov D, Lancet, 2021 (published in peer reviewed journal)

Methods	RCT
	Phase 3
	Blinding: triple blinding
	Date of study: 09/07/2020 to 11/24/2020
	Location: Multicenter / Russia
	Follow-up duration (months): 2.56
	Vaccine group: Gam-COVID-Vac (n=16501); Placebo (n=5476)
Participants	**Population randomized:** 21977 participants (n1=16501 / n2=5476)
	Characteristics of participants Type of participants: Adults N=21977 Children: 0 Pregnant women: 0 Immunocompromised patients: 0 Age mean: 45.3 Age range: NR Men: 12158
	Description of participants SARS-CoV-2- and HIV infection-free adult volunteers at 25 centers in Russia
	Inclusion criteria • Age 18 years or older • Negative HIV, hepatitis B and C, and syphilis test results • Negative anti-SARS-CoV-2 IgM and IgG antibody and SARS-CoV-2 PCR tests • No history of COVID-19 • No contact with anyone with COVID-19 in the preceding 14 days • Consent to use effective contraceptive methods • Negative urine pregnancy test (for women of child-bearing potential) • Negative drug and alcohol tests at screening visit • No history of vaccine-induced reactions • No acute infectious or respiratory disease in the 14 days before enrolment

	Exclusion criteria • Any vaccination in the 30 days before enrolment • Steroids or immunoglobulins in the 30 days before enrolment • Immunosuppression in the 3 months before enrolment • Pregnancy or breastfeeding • Acute coronary syndrome or stroke in the year before enrolment • Tuberculosis or chronic systemic infections • Allergy or hypersensitivity to the drug or components • Neoplasms • Blood donation in the 2 months before enrolment • Splenectomy • Neutropenia, agranulocytosis, significant blood loss, severe anaemia, or immunodeficiency in the 6 months before enrolment • Active form of a disease caused by HIV, syphilis, or hepatitis B or C • Anorexia or protein deficiency • Large tattoos at the injection site • History of alcohol or drug addiction • Participation in any other clinical trial • Study center staff or other employees directly involved in the trial or their families • Any other condition deemed a problem by the study physician
	Withdrawals: 0 withdrawal due to adverse events
Interventions	**Intervention:** Gam-COVID-Vac - 1 IM dose of rAd26-S 10^11 vp followed by 1 IM dose of rAd5-S 10^11 vp (D0/21)
	Control: Placebo (Vaccine buffer composition)
Outcomes	**Primary outcome of the trial:** **In the report:** • Proportion of participants with COVID-19 confirmed by PCR from day 21 after receiving the first dose. **In the register:** • Percentage of trial subjects with coronavirus disease 2019 (COVID-19) developed within 6 months after the first dose, confirmed with PCR
Notes	**Funding**: Mixed (Moscow City Health Department, Russian Direct Investment Fund, Sberbank, and RUSAL)
	Conflict of interest: Yes. Quote: "OVZ, TAO, IVD, OP, DVS, DMG, ASD, AIT, DNS, IBE, EAT, AGB, ASE, ASS, SVB, DYL, BSN, and ALG report patents for an immunobiological expression vector, pharmaceutical agent, and its method of use to prevent COVID-19. All other authors declare no competing interests."
	Protocol: English
	Statistical plan: Yes
	Data-sharing stated: Yes

Ad26.COV2.S - Janssen Pharmaceutical Companies

Comparison: Ad26.COV2.S vs Placebo

Sadoff 2021a

Trial: NCT04436276, Sadoff J, N Engl J Med, 2021 (published in peer reviewed journal)

First published as Sadoff J , medRxiv, 2020

Methods	RCT
	Phase 1-2
	Blinding: double blinding
	Date of study: 07/22/2020 to 08/24/2020
	Location: Multicenter / Belgium, USA
	Follow-up duration (months): 2.33
	Vaccine group: **≥18 to ≤55 years (Cohort 1a)** • Ad26.COV2.S 5×1010 vp (n = 153) • Ad26.COV2.S 1×1010 vp (n = 150) • Placebo 1 (n = 77) **≥18 to ≤55 years (Cohort 1b)** • Ad26.COV2.S 5×1010 vp (n = 10) • Ad26.COV2.S 1×1010 vp (n = 10) • Placebo 1 (n = 5) **≥65 years (Cohort 3)** • Ad26.COV2.S 5×1010 vp (n = 161) • Ad26.COV2.S 1×1010 vp (n = 162) • Placebo 2 (n = 82) At the time of this analysis, enrollment of Cohort 2 had not started.
Participants	**Population randomized:** 810 participants (n1=324 / n2=322 / n3=164)
	Characteristics of participants Type of participants: Healthy volunteers N=810 Children: 0 Pregnant women: 0 Immunocompromised patients: 0 Age mean: NR Age range: 18-83 Men: 391
	Description of participants Healthy SARS-CoV-2 nucleic acid negative adults 18-55 years old and elderly >65 years old in multiple centres in Belgium and the US
	Inclusion criteria

	• Participant must sign an informed consent form (ICF) indicating that he or she understands the purpose, procedures, and potential risks and benefits of the study, and is willing to participate in the study • All female participants of childbearing potential must have a negative highly sensitive urine pregnancy test at screening and have a negative highly sensitive urine pregnancy test immediately prior to each study vaccine administration • Participant must have a body mass index (BMI) less than or equal to (<=) 30.0 kilograms per squaremeter (kg/m^2) • Applicable to Cohorts 1 and 2 only: Participant must be healthy, in the investigator's clinical judgment,as confirmed by medical history, physical examination, clinical laboratory assessments, and vital signs performed at screening, and must not have comorbidities related to an increased risk of severe coronavirus disease-2019 (COVID-19). • Applicable to Cohort 3 only: In the investigator's clinical judgment, participant must be either in good or stable health Participants may have underlying illnesses such as hyperlipoproteinemia or hypothyroidism, as long as their symptoms and signs are medically controlled and not considered to be comorbidities related to an increased risk of severe COVID-19 (participants may have medical conditions of mild severity (according to the Toxicity Grading Scale),including hypertension or high blood pressure, as long as their symptoms and signs are stable and medically controlled as defined by no change in medication over the past 6 months [except for issues of tolerability or use of similar drug with same mechanism of action, for example, thiazides, Beta blockers, Alpha blockers at the same effective dose]). If they are on medication for a condition, the medication dose must have been stable for at least 12 weeks preceding vaccination and expected to remain stable for the duration of the study. Participants will be included on the basis of physical examination, clinical laboratory assessments medical history, and vital signs (participants can be enrolled with Grade 1 or Grade 2 values for vital signs measurements) • Participant agrees to not donate bone marrow, blood, and blood products from the first study vaccine administration until 3 months after receiving the last dose of study vaccine
	Exclusion criteria • Participant has a clinically significant acute illness (this does not include minor illnesses such as diarrhea or mild upper respiratory tract infection) or temperature greater than or equal to (>=) 38.0degree Celsius within 24 hours prior to the planned first dose of study vaccine • Randomization at a later date is permitted at the discretion of the investigator and after consultation with the sponsor • Participant has a history of malignancy within 5 years before screening (exceptions are squamous and basal cell carcinomas of the skin and carcinoma in situ of the cervix, or malignancy, which is considered cured with minimal risk of recurrence) • Participant has a history of any neurological disorders or seizures including Guillain-Barre syndrome, with the exception of febrile seizures during childhood • Participant has a positive diagnostic test result for SARS-CoV-2 infection confirmed by polymerase chain reaction (PCR) at screening • Participants with comorbidities that are or might be associated with an increased risk of progression to severe COVID-19, that is, participants with moderate-to-severe asthma • Chronic lung diseases such as chronic obstructive pulmonary disease (COPD) (including emphysema and chronic bronchitis), idiopathic pulmonary fibrosis and cystic fibrosis • Diabetes (including type 1, type 2, or gestational) • Serious heart conditions, including heart failure, coronary artery disease, congenital heart disease, cardiomyopathies, and (pulmonary) hypertension or high blood pressure • Obesity (BMI >= 30 kg/m^2) • Chronic kidney disease being treated with dialysis • Participants who are immunocompromised (as outlined in other exclusion criteria)

	• Chronic liver disease, including cirrhosis • Sickle cell disease • Thalassemia • Cerebrovascular disease • Neurologic conditions (dementia) • Smoking • Participants who live in nursing homes or long-term care facilities • Investigators must refer to the complete list of conditions that increase the risk of progression to severe COVID-19 available at the Centers for Disease Control and Prevention (CDC) website. • Applicable to Cohort 3 only: Participants may have medical conditions of mild severity (according to the Toxicity Grading Scale), including hypertension or high blood pressure, as long as their symptoms and signs are stable and medically controlled in the judgment of the investigator • Applicable to Cohorts 1 and 3 only: Participant currently working in an occupation with a high risk of exposure to SARS-CoV-2 (for example, health care worker or emergency response personnel) or considered at the investigator's discretion to be at increased risk to acquire COVID-19 for any other reason
	Withdrawals: 0 withdrawal due to adverse events
Interventions	**Intervention** • Ad26.COV2.S - 1 or 2 IM low dose of 5x10^10 vp Ad26.COV2.S (D0/56) • Ad26.COV2.S - 1 or 2 IM high dose of 1x10^11 vp Ad26.COV2.S (D0/56)
	Control: Placebo
Outcomes	**Primary outcome of the trial:** **In the report:** • Safety and reactogenicity of each dose schedule. Follow-up visits to evaluate reactogenicity, safety, and immunogenicity were scheduled on days 7, 28, and 71 after vaccination in each cohort. **In the register:** • Number of Participants with Solicited Local Adverse Events (AEs) for 7 Days after First and Second Vaccination • Number of Participants with Solicited Systemic AEs for 7 Days after First and Second Vaccination • Number of Participants with Unsolicited AEs for 28 Days after First and Second Vaccination • Number of Participants with Serious Adverse Events (SAEs) from the First Vaccination until 1 Year after the Second Vaccination
Notes	**Funding**: Mixed (This project was sponsored by Johnson and Johnson and funded, in part, by the Department of Health and Human Services Biomedical Advanced Research and Development Authority)
	Conflict of interest: Yes. Quote: "Janssen Pharmaceuticals and the US Army have a cooperative research agreement (Cooperative Research and Development Agreement, CRADA). Under the terms of the agreement, Janssen may provide financial resources to support work; there is no personal financial benefit from the arrangement. JS, MLG, GS, DH, CT, MG, JS, ST, EC, GS, JH, FS, MD,

	JVH and HS are all employees of Janssen Pharmaceuticals and may be Johnson & Johnson stockholders."
	Protocol: English
	Statistical plan: Yes
	Data-sharing stated: No

Sadoff 2021b

Trial: NCT04505722, Sadoff J, N Engl J Med, 2021 (published in peer reviewed journal)

First published as FDA breifing document Ad26.COV2.S (COVID-19) Vaccine

Methods	RCT
	Phase 3
	Blinding: double blinding
	Date of study: 09/21/2020 (end date not reported)
	Location: Multicenter / Argentina, Brazil, Chile, Colo
	Follow-up duration (months): 1.84 median
	Vaccine group: Ad26.COV2.S (5×10^10 vp), 1 dose (n=22174); Placebo (0.9% sodium chloride solution), 1 dose (n=22151)
Participants	**Population randomized:** 44325 participants (n1=22174 / n2=22151)
	Characteristics of participants Type of participants: Adults N=44325 Children: 0 Pregnant women: 0 Age mean: 50.7 Age range: 18-100 Men: 24053
	Description of participants Adults >18 years of age at 213 centers in Argentina, Brazil, Chile, Colombia, Mexico, Peru, South Africa and USA
	Inclusion criteria • Stages 1a and 1b: Participant is ≥18 to <60years of age on the day of signing the ICF. Stages 2a and 2b: Participant is ≥60years of age • BMI <30kg/m2 • In the investigator's clinical judgement, participant must be either in good or stable health • Participants may have underlying illnesses (not associated with increased risk of progression to severe COVID-19a,13 as specified in Exclusion Criterion 15), as long as their symptoms and signs are stable and well-controlled.

	• Contraceptive (birth control) use should be consistent with local regulations regarding the acceptable methods of contraception for those participating in clinical studies • All participants of childbearing potential must: have a negative highly sensitive urine pregnancy test at screening • Have a negative highly sensitive urine pregnancy test immediately prior to each study vaccine administration • Participant agrees to not donate bone marrow, blood, and blood products from the first study vaccine administration until 3 months after receiving the last dose of study vaccine • Must be willing to provide verifiable identification, has means to be contacted and to contact the investigator during the study • Must be able to read, understand, and complete questionnaires in the electronic clinical outcome assessment (eCOA) (that is, the coronavirus disease-2019 [COVID 19] signs and symptoms surveillance question, the e-Diary, and the electronic patient-reported outcomes (ePROs). Note: Participants with visual impairment are eligible for study participation and may have caregiver assistance in completing the electronic clinical outcome assessment (eCOA) questionnaires

	Exclusion criteria • Participant has a clinically significant acute illness (this does not include minor illnesses such as diarrhea or mild upper respiratory tract infection) or temperature greater than or equal to (≥) 38.0 degree Celsius (100.4-degree Fahrenheit) within 24 hours prior to the planned first dose of study vaccine • Randomization at a later date is permitted at the discretion of the investigator and after consultation with the sponsor • Participant received or plans to receive: (a) licensed live attenuated vaccines - within 28 days before or after planned administration of study vaccine and (b) other licensed (not live) vaccines - within 14 days before or after planned administration of study vaccine • Participant previously received a coronavirus vaccine • Participant received an investigational drug (including investigational drugs for prophylaxis of COVID-19) within 30 days or used an invasive investigational medical device within 30 days or received investigational immunoglobulin or monoclonal antibodies within 3 months, or received convalescent serum for COVID-19 treatment within 4 months or received an investigational vaccine (including investigational Adenoviral-vectored vaccines) within 6 months before the planned administration of the first dose of study vaccine or is currently enrolled or plans to participate in another investigational study during the course of this study • Participant has a known or suspected allergy or history of anaphylaxis or other serious adverse reactions to vaccines or their excipients • Participant has abnormal function of the immune system • Participant received treatment with Ig in the 3 months or exogenous blood products (autologous blood transfusions are not exclusionary) in the 4 months before the planned administration of the study vaccine or has any plans to receive such treatment during the study • Participant has a history of an underlying clinically significant acute or chronic medical condition or physical examination findings for which, in the opinion of the investigator, participation would not be in the best interest of the participant • Major psychiatric illness • Comorbidities that are or might be associated with an increased risk of progression to severe COVID-19a,13, ie, participants with moderate to severe asthma • Chronic lung diseases such as chronic obstructive pulmonary disease (COPD) (including emphysema and chronic bronchitis), idiopathic pulmonary fibrosis and cystic fibrosis • Diabetes (including type 1ortype 2) • Serious heart conditions, including heart failure, coronary artery disease, congenital heart disease, cardiomyopathies, and pulmonary hypertension • Moderate to severe high blood pressure • Obesity (body mass index [BMI] ≥30kg/m2) • Chronic liver disease, including cirrhosis • Sickle cell disease • Thalassemia • Cerebrovascular disease • Neurologic conditions (dementia) • End stage renal disease • Organ transplantation • Cancer • HIV infection and other immunodeficiencies • Hepatitis B infection • Sleep apnea • Malignancy within 1 year before screening • Surgery requiring hospitalization (defined as inpatient stay for longer than 24 hours or overnight stay), within 12 weeks before vaccination

	Withdrawals: 0 withdrawal due to adverse events
Interventions	**Intervention:** Ad26.COV2.S - 1 IM dose Ad26.COV2.S (D0)
	Control: Placebo
Outcomes	**Primary outcome of the trial:** **In the report:** • Vaccine efficacy against moderate to severe–critical coronavirus disease 2019 (Covid-19) with an onset at least 14 days and at least 28 days after administration among participants in the per-protocol population who had tested negative for SARS-CoV-2. • Vaccine safety **In the register:** • Number of Participants with First Occurrence of Molecularly Confirmed Moderate to Severe/Critical Coronavirus Disease (COVID-19) with Seronegative Status [Time Frame: 14 Days post-vaccination (Day 15) to end of study (2 years and 1 month)] • Number of Participants with First Occurrence of Molecularly Confirmed Moderate to Severe/Critical Coronavirus Disease (COVID-19) with Seronegative Status [Time Frame: 28 Days post-vaccination (Day 29) to end of study (2 years and 1 month)]
Notes	**Funding**: Mixed (Janssen Research and Development, and in whole or in part by federal funds from the Office of the Assistant Secretary for Preparedness and Response, Biomedical Advanced Research and Development Authority, and from the National Institute of Allergy and Infectious Diseases (NIAID), National Institutes of Health.)
	Conflict of interest: Yes. Quote: "Vicky Cárdenas is a shareholder of JnJ stock. Sadoff J is a full time Janssen employee."
	Protocol: English
	Statistical plan: Yes
	Data-sharing stated: Yes

Inactivated Virus

CoronaVac Sinovac

Comparison: CoronaVac vs Placebo

Zhang 2020 (This trial reports results for Phase 1 and 2, we present them in separate tables)

Trial: NCT04352608, Zhang Y, Lancet Infect Dis, 2020 (published in peer reviewed journal)

Methods	RCT
	Phase 1
	Blinding: double blinding
	Date of study: 04/16/2020 to 04/25/2020
	Location : Single center / China
	Follow-up duration (months): 1.41
	Vaccine group: CoronaVac 3 mcg (n=24); Placebo (n=12); CoronaVac 6 mcg (n=24); Placebo (n=12); CoronaVac 3 mcg (n=24); Placebo (n=12); CoronaVac 6 mcg (n=24); Placebo (n=12)
Participants	**Population randomized:** 144 participants (n1=24 / n2=24 / n3=24 / n4=24 / n5=24 / n6=24)
	Characteristics of participants Type of participants: Healthy volunteers N=144 Children: 0 Pregnant women: 0 Immunocompromised patients: 0 Age mean: 42.1 Age range: NR Men: 63
	Description of participants Healthy SARS-CoV-2 serology/DNA negative adults in a single centre in China
	Inclusion criteria • Healthy adults aged 18-59 years • Proven legal identity • Participants should be capable of understanding the informed consent form, and such form should be signed prior to enrolment
	Exclusion criteria • Travel history / residence history of Wuhan city and surrounding areas, or other communities with case reports within 14 days • History of contact with a SARS-CoV-2 infection (positive in nucleic acid test) within 14 days • Have contacted patients with fever or respiratory symptoms from Wuhan and surrounding areas, or from communities with case reports within 14 days • Have contacted patients with fever or respiratory symptoms from Wuhan and surrounding areas, or from communities with case reports within 14 days • Self-reported history of SARS • Self-reported history of new coronavirus infection • Positive in serum antibodies (IgG or IgM) screening of COVID-19 • Positive in nasopharyngeal swabs or anal swabs through RT-PCR • Women who are breastfeeding, pregnant or planning to become pregnant during the study period • BMI>35 kg/m2

	• History of asthma, history of allergy to the vaccine or vaccine components, or serious adverse reactions to the vaccine, such as urticaria, dyspnea, and angioedema • Congenital malformations or developmental disorders, genetic defects, severe malnutrition, etc. • Autoimmune disease or immunodeficiency / immunosuppression • Suffering from severe chronic diseases, severe cardiovascular diseases, hypertension and diabetes that cannot be controlled by drugs, liver and kidney diseases, malignant tumors, etc. • Severe neurological disease (epilepsy, convulsions or convulsions) or mental illness • Thyroid disease or history of thyroidectomy, spleenlessness, functional spleenlessness, spleenlessness or splenectomy resulting from any condition • Diagnosed abnormal blood coagulation function (eg, lack of blood coagulation factors, blood coagulopathy, abnormal platelets) or obvious bruising or blood coagulation • Immunosuppressive therapy, cytotoxic therapy, inhaled corticosteroids (excluding allergic rhinitis corticosteroid spray therapy, acute non-complicated dermatitis superficial corticosteroid therapy) in the past 6 months • Abnormal laboratory test results in the physical examination such as clinically significant abnormal hematology and biochemistry beyond the reference value range (only applicable to Phase I clinical trials) • History of alcohol or drug abuse • Receipt of blood products within in the past 3 months • Receipt of other investigational drugs in the past 30 days • Receipt of attenuated live vaccines in the past 14 days • Receipt of inactivated or subunit vaccines in the past 7 days • Attacks of acute diseases or chronic diseases in the past 7 days • Axillary temperature >37.0°C • According to the investigator's judgment, the subject has any other factors that are not suitable for participating in the clinical trial
	Withdrawals: 0 withdrawal due to adverse events
Interventions	**Intervention** • CoronaVac - 2 IM doses of 3mcg per dose (D0/14) • CoronaVac - 2 IM doses of 6mcg per dose (D0/14) • CoronaVac - 2 IM doses of 3mcg per dose (D0/28) • CoronaVac - 2 IM doses of 6mcg per dose (D0/28)
	Control: Placebo (aluminum hydroxide)
Outcomes	**Primary outcome of the trial:** **In the report**: • Any adverse reactions within 28 days after each dose of study drug • Seroconversion of neutralising antibodies to live SARS-CoV-2 at day 14 after the last dose in the days 0 and 14 vaccination cohort, or day 28 after the last dose in the days 0 and 28 vaccination cohort **In the register:** • Safety indexes of adverse reactions [Time Frame: From the beginning of the vaccination to 28 days after the whole schedule vaccination] • Immunogenicity indexes of neutralizing-antibody seroconversion rates for the emergency vaccination schedule day (0,14) [Time Frame: The 14th day after two doses of vaccination] • Immunogenicity indexes of neutralizing-antibody seroconversion rates for the routine vaccination schedule (day 0,28) [Time Frame: The 28th day after two doses of vaccination]
Notes	**Funding**: Mixed (National Key Research and Development Program, Beijing Science and Technology Program)

	Conflict of interest: Yes. Quote: "QG is an employee of Sinovac Life Sciences. GZ, YaH, WH, WY, and YuH are employees of Sinovac Biotech. All other authors declare no competing interests."
	Protocol: NR
	Statistical plan: NR
	Data-sharing stated: Yes

Zhang 2020 (This trial reports results for Phase 1 and 2, we present them in separate tables)

Trial: NCT04352608, Zhang Y, Lancet Infect Dis, 2020 (published in peer reviewed journal)

Methods	RCT
	Phase 2
	Blinding: double blinding
	Date of study: 03/05/2020 to 05/05/2020
	Location: Single center / China
	Follow-up duration (months): 1.41
	Vaccine group: 3 µg at d0/14 (n = 120); 6 µg at d0/14 (n = 120); Placebo d0/14 (n = 60); 3 µg at d0/28 (n = 120); 6 µg at d0/28 (n = 120); Placebo d0/28 (n = 60)
Participants	**Population randomized:** 600 participants (n1=120 / n2=120 / n3=60 / n4=120 / n5=120 / n6=60)
	Characteristics of participants Type of participants: Healthy volunteers N=600 Children: 0 Pregnant women: 0 Immunocompromised patients: 0 Age mean: 42.1 Age range: 18-59 Men: 283
	Description of participants Healthy SARS-CoV-2 serology/DNA negative adults in a single center in China
	Inclusion criteria • Healthy adults aged 18-59 years • Proven legal identity • Participants should be capable of understanding the informed consent form, and such form should be signed prior to enrolment
	Exclusion criteria • Travel history / residence history of Wuhan city and surrounding areas, or other communities with case reports within 14 days • History of contact with a SARS-CoV-2 infection (positive in nucleic acid test) within 14 days • Have contacted patients with fever or respiratory symptoms from Wuhan and surrounding areas, or from communities with case reports within 14 days • Have contacted patients with fever or respiratory symptoms from Wuhan and surrounding areas, or from communities with case reports within 14 days • Self-reported history of SARS • Self-reported history of new coronavirus infection • Positive in serum antibodies (IgG or IgM) screening of COVID-19 • Positive in nasopharyngeal swabs or anal swabs through RT-PCR

	• Women who are breastfeeding, pregnant or planning to become pregnant during the study period • BMI≥35 kg/m2 • History of asthma, history of allergy to the vaccine or vaccine components, or serious adverse reactions to the vaccine, such as urticaria, dyspnea, and angioedema • Congenital malformations or developmental disorders, genetic defects, severe malnutrition, etc. • Autoimmune disease or immunodeficiency / immunosuppression • Suffering from severe chronic diseases, severe cardiovascular diseases, hypertension and diabetes that cannot be controlled by drugs, liver and kidney diseases, malignant tumors, etc. • Severe neurological disease (epilepsy, convulsions or convulsions) or mental illness • Thyroid disease or history of thyroidectomy, spleenlessness, functional spleenlessness, spleenlessness or splenectomy resulting from any condition • Diagnosed abnormal blood coagulation function (eg, lack of blood coagulation factors, blood coagulopathy, abnormal platelets) or obvious bruising or blood coagulation • Immunosuppressive therapy, cytotoxic therapy, inhaled corticosteroids (excluding allergic rhinitis corticosteroid spray therapy, acute non-complicated dermatitis superficial corticosteroid therapy) in the past 6 months • Abnormal laboratory test results in the physical examination such as clinically significant abnormal hematology and biochemistry beyond the reference value range (only applicable to Phase I clinical trials) • History of alcohol or drug abuse • Receipt of blood products within in the past 3 months • Receipt of other investigational drugs in the past 30 days • Receipt of attenuated live vaccines in the past 14 days • Receipt of inactivated or subunit vaccines in the past 7 days • Attacks of acute diseases or chronic diseases in the past 7 days • Axillary temperature >37.0°C • According to the investigator's judgment, the subject has any other factors that are not suitable for participating in the clinical trial
	Withdrawals: 0 withdrawal due to adverse events
Interventions	**Intervention** • CoronaVac - 2 IM doses of 3mcg per dose (D0/14) • CoronaVac - 2 IM doses of 6mcg per dose (D0/14) • CoronaVac - 2 IM doses of 3mcg per dose (D0/28) • CoronaVac - 2 IM doses of 6mcg per dose (D0/28)
	Control: Placebo (aluminum hydroxide)
Outcomes	**Primary outcome of the trial:** **In the report:** • Any adverse reactions within 28 days after each dose of study drug • Seroconversion of neutralising antibodies to live SARS-CoV-2 at day 14 after the last dose in the days 0 and 14 vaccination cohort, or day 28 after the last dose in the days 0 and 28 vaccination cohort **In the register:** • Safety indexes of adverse reactions [Time Frame: From the beginning of the vaccination to 28 days after the whole schedule vaccination] • Immunogenicity indexes of neutralizing-antibody seroconversion rates for the emergency vaccination schedule (day 0,14) [Time Frame: The 14th day after two doses of vaccination] • Immunogenicity indexes of neutralizing-antibody seroconversion rates for the routine vaccination schedule (day 0,28) [Time Frame: The 28th day after two doses of vaccination]
Notes	**Funding**: Mixed (National Key Research and Development Program, Beijing Science and Technology Program)

	Conflict of interest: Yes. Quote: "QG is an employee of Sinovac Life Sciences. GZ, YaH, WH, WY, and YuH are employees of Sinovac Biotech. All other authors declare no competing interests."
	Protocol: NR
	Statistical plan: NR
	Data-sharing stated: Yes

Bueno 2021

Trial: NCT04651790, Bueno S, Clin Infect Dis, 2021 (published in peer reviewed journal)

First published as preprint Bueno S, medRxiv, 2021

Methods	RCT
	Phase 3
	Blinding: double blinding
	Date of study: 11/27/2020 to 02/10/2021
	Location: Multicenter / Chile
	Follow-up duration (months): 1.4
	Vaccine group: CoronoVac (3 mcg) (n=270); Placebo (aluminum hydroxide adjuvant) (n=164)
Participants	**Population Randomized:** 434 participants (n1=270 / n2=164)
	Characteristics of participants Type of participants: People in close contact with COVID-19 patients, Healthcare workers. N=434 Children: 0 Pregnant women: 0 Immunocompromised patients: 0 Age mean: 40.4 Age range: NR Men: 166
	Description of participants Adult healthcare workers with no history of confirmed symptomatic SARS-CoV-2 infection who were in contact with possible or confirmed cases of COVID-19 in 8 sites in Chile.
	Inclusion criteria • Healthcare workers who were in contact with possible or confirmed cases of COVID-19 • ≥18 years old

	Exclusion criteria • History of confirmed symptomatic SARS-CoV-2 infection • Pregnancy • Allergy to vaccine components • Immunocompromised conditions • Uncontrolled neurological, cardiac, pulmonary, hepatic, or renal disease, according to anamnesis or physical examination • Behavioral, cognitive, or psychiatric illness that, in the opinion of the principal investigator or his medical representative, affects the participant's ability to understand and collaborate with the requirements of the study protocol • Use of immunosuppressive therapies six months before inclusion in the study or its scheduled use within two years of inclusion • Have received an immunosuppressive dose of corticosteroids in the last three months before inclusion in the study or scheduled administration of an immunosuppressive dose of corticosteroids for the three months following inclusion in the study • History of asplenia, either anatomic or functional • History of bleeding disorders • Any alcohol or drug abuse in the last 12 months before inclusion in the study that has caused medical, professional, or family problems, as indicated by clinical history • Have received blood products (transfusions or immunoglobulins) in the last three months before inclusion in the study • Have received any vaccine with a live attenuated virus in the last 28 days or inactivated vaccine in the last 14 days before their inclusion in the study, or have immunization scheduled for the first 28 days after their inclusion in the study • Participation in another clinical trial with product administration under investigation during the six months before its inclusion in the study or scheduled participation in another clinical trial in the two years following inclusion • Previous participation in a COVID-19 vaccine evaluation study or previous exposure to a COVID-19 vaccine • Fever (>37.8°C) within 72 hours before vaccination • Any other condition that, in the opinion of the principal investigator or his medical representative, could jeopardize the safety or rights of a potential participant or that would prevent him from complying with this protocol.
	Withdrawals: 0 withdrawal due to adverse events
Interventions	**Intervention:** CoronaVac - 2 IM doses of 3 mcg (D0/14)
	Control: Adjuvant (D0/14)

Outcomes	**Primary outcome of the trial:** **In the report:** • To evaluate the frequency of solicited and unsolicited AEs that occur during 7 days after each dose, stratified by age group (aged 18-59 and ≥60) **In the register:** • Frequency of solicited and unsolicited adverse events that occur during the period of one week after each dose of the vaccine in two vaccination schedules: 0,14 and 0,28 days stratified by age group (18-59 years, and 60 or more years). [Time Frame: During the first 7 days after each dose of vaccine] • Incidence of symptomatic cases of virologically confirmed COVID-19 two weeks after the second dose of each vaccination schedule. [Time Frame: Two weeks after second dose up to one year after first dose] • Vaccine efficacy to prevent virologically confirmed COVID-19 two weeks after the second dose of each vaccination schedule will be determined
Notes	**Funding**: Public/non-profit (Ministry of Health of the Chilean Government; Confederation of Production and Commerce, Chile; Consortium of Universities for Vaccines and Therapies against COVID-19, Chile; Millennium Institute on Immunology and Immunotherapy.)
	Conflict of interest: Yes. Quote: "A.S. is a consultant for Gritstone, Flow Pharma, Merck, Epitogenesis, Gilead and Avalia. LJI has filed for patent protection for various aspects of T cell epitope and vaccine design work. All other authors declare no conflict of interest."
	Protocol: English
	Statistical plan: Yes
	Data-sharing stated: Yes

Han 2021

Trial: NCT04551547, Han B, SSRN, 2021 (Preprint)

Methods	RCT
	Phase 1-2
	Blinding: double blinding
	Date of study: 10/31/2020 to 12/30/2020
	Location: Single center / China
	Follow-up duration (months): 4.1
	Vaccine group: 1.5 mcg CoronaVac (n = 219); 3 mcg CoronaVac (n = 219); Adjuvant (n = 114)
Participants	**Population randomized:** 552 participants (n1=219 / n2=219 / n3=114)
	Characteristics of participants Type of participants: Children N=552 Children: 552 Pregnant women: 0 Immunocompromised patients: 0 Age mean: NR Age range: 03-17 Men: 297
	Description of participants Healthy children and adolescents aged 3-17 years with no history of SARS-CoV-2 infection in a single centre in China.

	Inclusion criteria • Healthy children and adolescents aged 3-17 years
	Exclusion criteria • High-risk epidemiology history within 14 days before enrollment (eg, travel or residence history in communities with case reports, or contact history with someone infected with SARS-CoV-2) • History of severe acute respiratory syndrome or SARS-CoV-2 infection • Axillary temperature of more than 37·0°C • History of allergy to any vaccine component
	Withdrawals: 0 withdrawal due to adverse events
Interventions	**Intervention** • CoronaVac - 2 IM doses of 1.5 mcg CoronaVac (D0/28) • CoronaVac - 2 IM doses of 3.0 mcg CoronaVac, (D0/28)
	Control: Placebo
Outcomes	**Primary outcome of the trial:** **In the report**: • Adverse reactions within 28 days after each injection in all participants who received at least one dose. • Seroconversion rate at 28 days after the second injection **In the register:** • Safety index-incidence of adverse reactions [Time Frame: Day 0-28 after each dose vaccination] • Immunogenicity index-seroconversion rates of neutralizing antibody [Time Frame: The 28th day after the second dose vaccination]
Notes	**Funding**: Public/non profit (Chinese National Key Research and Development Program and Beijing Science and Technology Program)
	Conflict of interest: Yes. Quote: "QG and XL are employees of Sinovac Life Sciences Co., Ltd. YS, WY and LW are employees of Sinovac Biotech Ltd. All other authors declare no competing interests."
	Protocol: NR
	Statistical plan: NR
	Data-sharing stated: Yes

Fadlyana 2021

Trial: NCT04508075 ; INA-WXFM0YX, Fadlyana E, Vaccine, 2021 (published in peer reviewed journal)

Methods	RCT
	Phase 3
	Blinding: double blinding
	Date of study: 08/11/2020 to 10/21/2020
	Location : Single center / Indonesia
	Follow-up duration (months): 3
	Vaccine group: CoronaVac (n = 810); Placebo (n = 810)
Participants	**Population randomized** 1620 participants (n1=810 / n2=810)
	Characteristics of participants Type of participants: Healthy adults N=1620 Children: 0 Pregnant women: 0 Immunocompromised patients: 0 Age mean: NR Age range: NR Men: 1046
	Description of participants Healthy adults aged 18 - 59 years, seropositive and seronegative, at a single center in Indonesia
	Inclusion criteria • Clinically healthy adults aged 18 - 59 years • Informed consent • commit to comply with the instructions of the investigator and the schedule of the trial
	Exclusion criteria • Evolving mild, moderate, or severe illness, especially infectious disease or fever (body temperature ≥ 37.5°C) • Positive result from a nasopharyngeal swab RT-PCR test • Reactive IgG and IgM for SARS-CoV-2 • Lactating, pregnant or planning to become pregnant during the study period • Serious chronic diseases (serious cardiovascular disease, uncontrolled hypertension and diabetes, liver and kidney disease, malignant tumors, or any condition which according to the investigator may interfere with the assessment of the trial objectives) • Uncontrolled coagulopathy or blood disorders • History of asthma • History of allergy to vaccines or vaccine ingredients • History of confirmed or suspected immunosuppressive or immunodeficient state, or received in the previous 4 weeks a treatment likely to alter the immune response [intravenous immunoglobulins, blood-derived products, or long-term corticosteroid therapy (>2 weeks)] • History of uncontrolled epilepsy or other progressive neurological disorders • Having received any vaccination within 1 month before or after administration of the study vaccine

	Withdrawals: 0 withdrawal due to adverse events
Interventions	**Intervention:** CoronaVac - 2 IM doses of 3mcg (D0/14)
	Control: Placebo
Outcomes	**Primary outcome of the trial:** **In the report:** • Incidence of laboratory confirmed-symptomatic COVID-19 cases starting at 14 days following the second dose **In the register:** • Incidence of laboratory-confirmed COVID-19 after the second dose [Time Frame: 14 days to 6 months after the second dose]
Notes	**Funding**: Mixed (PT Bio Farma and Sinovac Life Sciences Co., Ltd.)
	Conflict of interest: Quote: "The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. "
	Protocol: NR
	Statistical plan: NR
	Data-sharing stated: No

Palacios 2021

Trial: NCT04456595, Palacios R, SSRN, 2021 (Preprint)

Methods	RCT
	Phase 3
	Blinding: double blinding
	Date of study: 07/21/2020 to 12/16/2020
	Location: Multicenter / Brazil
	Follow-up duration (months): 12
	Vaccine group: CoronaVac (n=6201); Placebo (n=6207)
Participants	**Population randomized:** 12408 participants (n1=6201 / n2=6207)
	Characteristics of participants Type of participants: Healthcare workers N=12408 Children: 0 Pregnant women: 0 Immunocompromised patients: 0 Age mean:39.5 Age range: NR Men: 4441
	Description of participants Healthcare professionals with or without previous COVID-19 infection caring for COVID-19 patients at 16 centers in Brazil.
	Inclusion criteria • 18 years of age or older • Work as healthcare professional caring for COVID-19 patients • Sign the informed consent form

	Exclusion criteria • Pregnant or lactating women • Unstable chronic disease • Previous use of any COVID-19 vaccines • Acute disease symptoms including COVID-19 in the previous 72 hours
	Withdrawals: 0 withdrawal due to adverse events
Interventions	**Intervention:** CoronaVac - 2 IM doses of 3mcg CoronaVac (D0/14)
	Control: Adjuvant D0/14
Outcomes	**Primary outcome of the trial:** **In the report:** • Efficacy of CoronaVac against confirmed symptomatic COVID-19 with onset at least 14 days after the second injection in the per protocol population • Incidence of adverse reactions within 7 days after injection. **In the register:** • Incidence of COVID-19 cases after two-doses immunization schedule [Time Frame: Two weeks after second dose up to one year after first dose] • Frequency of adverse events up to seven days after immunization [Time Frame: Seven days after each immunization]
Notes	**Funding**: Public/non-profit (Fundação Butantan, Instituto Butantan, and São Paulo Research Foundation (FAPESP))
	Conflict of interest: COI. Quote: "Instituto Butantan is non-profit public research institute that is part of the Secretary of Health of the State of São Paulo and acted as sponsor of the study and is Market Authorization Holder of CoronaVac in Brazil under authorization of Sinovac Life Sciences. Ricardo Palacios, Ana Paula Batista, Camila Nascimento Santos Albuquerque, Elizabeth Gonzalez Patiño, Joane do Prado Santos, Mônica Tilli Reis Pessoa Conde and Roberta de Oliveira Piorelli are full-time employees of Fundação Butantan, a non-profit organization supporting activities from Instituto Butantan. Viviane Fongaro Botosso is full-time researcher at Instituto Butantan. None of us received shares or any kind monetary compensation linked to the distribution of CoronaVac in Brazil, or have any share or financial interests in Sinovac Life Sciences or parent companies. The other investigators of the study in Brazil Ana Lúcia Lyrio de Oliveira, André Machado de Siqueira, Cor Jesus Fernandes Fontes, Danise Senna Oliveira, Eduardo Barbosa Coelho, Esper Georges Kallás, Fabiano Ramos, Fábio Eudes Leal, Francisco Hideo Aoki, Gecilmara Cristina Salviato Pileggi, Gustavo Adolfo Sierra Romero, Luis Fernando Aranha Camargo, Luiz Carlos Pereira Junior, Maurício Lacerda Nogueira, Mauro Martins Teixeira, Sonia Mara Raboni, and Danielle Bruna Leal de Oliveira received shares or any kind monetary compensation linked to the distribution of CoronaVac in Brazil, or have any share or financial interests in Sinovac Life Sciences or parent companies. Gang Zeng and Qianqian Xin are full-time employees of Sinovac Biotech Co. Ltd."
	Protocol: English
	Statistical plan: Yes
	Data-sharing stated: Yes

Tanriover 2021

Trial: NCT04582344, Tanriover M, Lancet, 2021 (published in peer reviewed journal)

Methods	RCT
	Phase 3
	Blinding: double blinding
	Date of study: 09/15/2020 to 01/06/2021
	Location: Multicenter / Turkey
	Follow-up duration (months): 6
	Vaccine group: 3 mcg CoronaVac (n=6650); Placebo (adjuvant) (n=3568)
Participants	**Population randomized:** 10218 participants (n1=6650 / n2=3568)
	Characteristics of participants Type of participants: Adults, Healthcare workers N=10218 Children: 0 Pregnant women: 0 Immunocompromised patients: 0 Age mean: NR Age range: 18-59 Men: 5907
	Description of participants Healthy healthcare workers and adults aged 18–59 years with no history of COVID-19 from 24 centres in Turkey
	Inclusion criteria • 18-59 years of age • For only K1 cohort, health care workers such as medical doctor, nurse, ward boy, cleaner, hospital technician, administrative personnel who work in any department of a healthcare unit • Signed informed consent
	Exclusion criteria • Previously PCR positive for COVID-19 • IgG or IgM is positive • For females: Pregnancy (confirmed by positive beta-hCG test), breastfeeding or intent to engage in sexual relations with reproductive intent without use of birth control methods in the three months following vaccination • Known allergy to components of the study vaccine or control • Use of immunosuppressant therapy regimens within the six months prior to enrollment in the study or planned use within the two years following enrollment. Immunosuppressant therapy regimens include antineoplastic chemotherapy, radiation therapy and immunosuppressants to induce transplant tolerance, among others • Use of immunosuppressive doses of corticosteroids within the three months prior to the enrollment in the study and planned use of immunosuppressive doses of corticoids within the three months following enrollment in the study. Immunosuppressive doses of corticosteroids will be considered the equivalent prednisone 20 mg/day for adults, for longer than one week. Continued use of topical or nasal corticosteroids is not considered an immunosuppressant • History of asplenia • History of bleeding disorder (e.g., factor deficiency, coagulopathy or platelet disorder), or prior history of significant bleeding or bruising following IM injections or venipuncture

	• Any alcohol or drug abuse over the 12 months prior to enrollment in the study that has caused medical, professional or family problems, indicated by clinical history • Administration of immunoglobulins and/or any blood products within the three months preceding the planned administration of the vaccine candidate • Participation in another clinical trial with an investigational product in the six months prior to enrollment in the study or planned participation in another clinical trial within the two years following enrollment • Received live attenuated virus vaccine 14 days prior to enrollment in the study • Inactivated vaccine or sub unit vaccine 7 days prior to enrollment in the study • Fever (oral temperature >37.2°C, axillary temperature will not be accepted) within the past 24 hours • Any other condition that, in the opinion of the principal investigator or his/her representative physician, could put the safety/rights of potential participants at risk or prevent them from complying with this protocol • Any confirmed or suspected autoimmune disease or immunodeficiency disease, including human immunodeficiency virus (HIV) infection
	Withdrawals: 5 withdrawal due to adverse events
Interventions	**Intervention:** CoronaVac - 2 IM doses of 3mcg, (D0/14)
	Control: Placebo
Outcomes	**Primary outcome of the trial:** **In the report:** • Symptomatic COVID-19 cases confirmed by RT-PCR at least 14 days after the second dose of vaccination, assessed in the per protocol population **In the register:** • Protection Indexes of Two Vaccine Doses For Symptomatic COVID-19 [Time Frame: 2 weeks afterthe second dose of vaccination]
Notes	**Funding**: Public/non-profit (Turkish Health Institutes Association (TUSEB))
	Conflict of interest: No. Quote: "We declare no competing interests."
	Protocol: English
	Statistical plan: NR
	Data-sharing stated: Yes

Wu 2021

Trial: NCT04383574, Wu Z, Lancet Infect Dis, 2021 (published in peer reviewed journal)

Methods	RCT
	Phase 1-2
	Blinding: triple blinding
	Date of study: 05/22/2020 to 06/15/2020
	Location: Single center / China
	Follow-up duration (months): 1.84
	Vaccine group: 1.5 mcg CoronaVac (n=100); 3 mcg CoronaVac (n=124); 6 mcg CoronaVac (n=124); Placebo (n =74)
Participants	**Population randomized:** 422 participants (n1=100 / n2=124 / n3=124 / n4=74)

	Characteristics of participants Type of participants: Older adults N=422 Children: 0 Pregnant women: 0 Immunocompromised patients: 0 Age mean: NR Age range: NR Men: 206
	Description of participants Healthy adults aged 60 years and older with no history of SARS-CoV-2 infection in a single center in China
	Inclusion criteria • Healthy adults aged 60 years or older.
	Exclusion criteria • High-risk epidemiological history within 14 days before enrolment (eg, travel to or residence in Wuhan and surrounding areas or other communities with reports of COVID-19 cases, or contact with someone infected with SARS-CoV-2) • History of severe acute respiratory syndrome or SARS-CoV-2 infection • Axillary temperature of more than 37·0°C • History of allergy to any vaccine component
	Withdrawals: 0 withdrawal due to adverse events
Interventions	**Intervention** • CoronaVac - 2 IM doses of 1.5mcg per dose (D0/28) • CoronaVac - 2 IM doses of 3mcg per dose (D0/28) • CoronaVac - 2 IM doses of 6mcg per dose (D0/28)
	Control: Aluminum hydroxide placebo
Outcomes	**Primary outcome of the trial:** **In the report:** • Vaccine-related adverse event (adverse reaction) within 28 days after the administration of each dose of vaccine or placebo • Seroconversion rate of neutralizing antibodies to live SARS-CoV-2 at day 28 after the second dose **In the register:** • Safety index-incidence of adverse reactions [Time Frame: Day 0-28 after each dose vaccination] • Immunogenicity index-seroconversion rates of neutralizing antibody [Time Frame: The 30th day after the second dose vaccination]
Notes	**Funding**: Public/non-profit (The National Key Research and Development Program; the Beijing Science and Technology Program)
	Conflict of interest: Yes. Quote: "GC is an employee of Sinovac Life Sciences. YH, WYa, GC, LW, and WYi are employees of Sinovac Biotech. All other authors declare no competing interests. "
	Protocol: English
	Statistical plan: Yes
	Data-sharing stated: Yes

WIBP-CorV -Sinopharm

Comparison: WIBP-CorV vs Placebo

Al Kaabi 2021 (This trial reports results for 2 different comparisons, we present them in separate tables)

Trial: NCT04510207, ChiCTR2000034780, Al Kaabi N, JAMA, 2021 (published in peer reviewed journal)

Methods	RCT
	Phase 3
	Blinding: double blinding
	Date of study: 07/16/2020 to 12/20/2020
	Location: Multicenter / United Arab Emirates, Bahrain
	Follow-up duration (months): 5
	Vaccine group: Inactivated SARS-CoV-2 vaccine WIV04 (n=13,470); Inactivated SARS-CoV-2 vaccine HB02 (n=13,470); Placebo (alum adjuvant) (n=13,471)
Participants	**Population randomized:** 40411 participants (n1=13470 / n2=13470 / n3=13471)
	Characteristics of participants Type of participants: Healthy adults N=40411 Children: 0 Pregnant women: 0 Immunocompromized patients: 0 Age mean: NR Age range: NR Men: 34135
	Description of participants Healthy adults free of known COVID-19 or HIV infection at 3 centres in United Arab Emirates and Bahrain
	Inclusion criteria • Age range: healthy people aged 18+ years old • General good health as established by medical history and physical examination • Women of childbearing age are not pregnant (negative urine pregnancy test), are not breastfeeding, do not have pregnancy plan within the three months after enrollment, and have already taken effective contraceptive measures two weeks before enrollment • Participants are able and willing to complete the whole research procedure in about 14 months • Participants have the ability to understand the research procedures, to sign the informed consent voluntarily after explanation, and can comply with the requirements of the clinical research program
	Exclusion criteria • History of SARS-CoV, SARS-CoV-2 or MERS virus infection (identified through self-report or on-site inquiry) • Those with fever (axillary temperature >37.0 °C), dry cough, fatigue, nasal obstruction, runny nose, sore throat, myalgia, diarrhea, shortness of breath, and dyspnea within 14 days before inoculation • Axillary temperature ≥37.0 °C (or ear or forehead temperature ≥37.0 °C) before inoculation • Those who have experienced severe allergic reactions (such as acute anaphylaxis, urticaria, eczema, dyspnea, neurovascular edema, or abdominal pain), or those who are allergic to the known gradients of COVID-19 inactivated vaccine

	• Those with history or family history of convulsion, epilepsy, encephalopathy, or mental illness • Those with congenital malformation, developmental disorder, genetic defect, or severe malnutrition, etc. • Those with confirmed or suspected serious respiratory diseases, serious cardiovascular disease, severe liver or renal diseases, malignant tumors, uncontrolled hypertension (systolic blood pressure ≥150 mmHg, diastolic blood pressure ≥90 mmHg), diabetes complications, malignant tumors, or various acute or chronic diseases (acute attack stage) • Those diagnosed with congenital or acquired immunodeficiency, HIV infection, lymphoma, leukemia, or other autoimmune diseases • Those with a history of abnormal coagulation (such as lack of coagulation factors or coagulation diseases) • Those receiving anti-TB treatment • Those receiving immune-enhancement or inhibitor treatment (p.o. or gtt.) over 14 days within 3 months (continuous oral or infusion for more than 14 days) • Those receiving live-attenuated vaccines within one month before inoculation or other vaccines within 14 days before inoculation • Those receiving blood products within 3 months before inoculation • Those receiving other study drugs within 6 months before inoculation • Those under other conditions not suitable for the clinical trial (evaluated by researchers)
	Withdrawals: 24 withdrawal due to adverse events
Interventions	**Intervention** • SARS-CoV-2 strain WIV04 - 2 IM doses of 5 mcg (D0/22) • SARS-CoV-2 strain HBO2 - 2 IM doses of 4 mcg (D0/22)
	Control: Placebo
Outcomes	**Primary outcome of the trial:** **In the report**: • Laboratory-confirmed symptomatic COVID-19 cases that occurred at least 14 days after receipt of the second vaccine dose **In the register** • Incidence of COVID-19 cases after two-doses of vaccination - Time Frame: From 14 days after the second dose to 6 months after the second dose (NCT) • Protective efficacy against COVID 19 14 days after the full course of vaccination (ChiCTR)
Notes	**Funding**: Mixed (National Key Research and Development Project of China, China National Biotec Group Company Limited)
	Conflict of interest: Yes. Quote: "Dr Xiaoming Yang, Dr Yuntao Zhang, Ms Y Yang, Ms Xuqin Yang, Mr Lai, Ms Q. Wang, Mr T. Yang, and Mr Liu are employees of the China National Biotec Group Company Limited"
	Protocol: English
	Statistical plan: Yes
	Data-sharing stated: Yes

Guo 2021

Trial: ChiCTR2000031809, Guo W, EClinicalMedicine, 2021 (published in peer reviewed journal First published as Xia S, JAMA, 2020

Methods	RCT
	Phase 1-2
	Blinding: double blinding
	Date of study: 04/12/2020 to 05/17/2020
	Location : Multicenter / China
	Follow-up duration (months): 4.77
	Vaccine group: 2·5 mcg on days 0, 28, and 56 = 168; 5 mcg on days 0, 28, and 56 = 168; 10 mcg on days 0, 28, and 56 = 168; Placebo on days 0, 28, and 56 = 168; 5 mcg on days 0 and 14 = 84; Placebo on days 0 and 14 = 28; 5 mcg on days 0 and 21 = 84; Placebo on days 0 and 21 = 28; 5 mcg on days 0 and 28 = 84; Placebo on days 0 and 28 = 28; 10 mcg on day 0 = 84; Placebo on day 0 = 28. (Placebo = adjuvant)
Participants	**Population randomized:** 1120 participants (n1=168 / n2=168 / n3=168 / n4=168 / n5=84 / n6=28 / n7=84 / n8=28 / n9=84 / n10=28 / n11=84 / n12=28)
	Characteristics of participants Type of participants: Healthy volunteers, Adults N=1120 Children: 0 Pregnant women: 0 Immunocompromised patients: 0 Age mean: NR Age range: NR Men: 522
	Description of participants Healthy adults with no history of COVID-19 at 5 centers in China.
	Inclusion criteria • Healthy, non-pregnant adults • Aged 18 years or older • No known history of SARS-CoV-1 (via on-site inquiry) or SARS-CoV-2 infection (via serological and nucleic acid test) • Had not been to Hubei province, regions outside China, or other regions with confirmed COVID-19 cases • Had not contacted with confirmed or suspected cases
	Exclusion criteria • Respiratory diseases or symptoms within 14 days before vaccination • Abnormalities in laboratory examinations • History of severe allergic reaction or allergy to ingredients in the vaccine • Taking certain treatments or medications or other vaccines before the study as specified in Supplementary Appendix • History of severe comorbidities that may affect the adherence
	Withdrawals: 0 withdrawal due to adverse events

Interventions	**Intervention** • Inactivated vaccine - 3 IM doses of 2.5 mcg (D0/28/56) • Inactivated vaccine - 3 IM doses of 5 mcg (D0/28/56) • Inactivated vaccine - 3 IM doses of 10 mcg (D0/28/56) • Inactivated vaccine - 2 IM doses of 5 mcg (D0/14) • Inactivated vaccine - 2 IM doses of 5 mcg (D0/21) • Inactivated vaccine - 2 IM doses of 5 mcg (D0/28) • Inactivated vaccine - 1 IM dose of 10 mcg (D0)
	Control: Placebo
Outcomes	**Primary outcome of the trial:** **In the report:** • 7-day adverse reactions; • Neutralizing antibody titres and specific IgG binding antibody titres measured on days 28 and 90 after the whole-course vaccination **In the register** • Incidence of adverse reactions/events 0-7 days after each dose of vaccination
Notes	**Funding**: Public/non profit (National Program on Key Research Project of China; Major Science and Technology Project of the National New Drug Development of China)
	Conflict of interest: Yes. Quote: "Xiaoming Yang report grants from National Program on Key Research Project of China during the conduct of the study; and has patent 202,010,559,132.3 pending. Shengli Xia and Wanshen Guo reports grants from National Program on Key Research Project of China, grants from Major Science and Technology Project of the National New Drug Development of China, during the conduct of the study."
	Protocol: English
	Statistical plan: Yes
	Data-sharing stated: Yes

BBIBP-CorV -Sinopharm-Beijng

Comparison: BBIBP-CorV vs Placebo

Al Kaabi 2021 (This trial reports results for 2 different comparisons, we present them in separate tables)

Trial: NCT04510207, ChiCTR2000034780, Al Kaabi N, JAMA, 2021 (published in peer reviewed journal)

Methods	RCT
	Phase 3
	Blinding: double blinding
	Date of study: 07/16/2020 to 12/20/2020
	Location : Multicenter / United Arab Emirates, Bahrain
	Follow-up duration (months): 5
	Vaccine group: Inactivated SARS-CoV-2 vaccine WIV04 (n=13,470); Inactivated SARS-CoV-2 vaccine HB02 (n=13,470); Placebo (alum adjuvant) (n=13,471)
Participants	**Population randomized** 40411 participants (n1=13470 / n2=13470 / n3=13471)
	Characteristics of participants Type of participants: Healthy adults N=40411 Children: 0 Pregnant women: 0 Immunocompromised patients: 0 Age mean: NR Age range: NR Men: 34135
	Description of participants Healthy adults free of known COVID-19 or HIV infection at 3 centres in United Arab Emirates and Bahrain
	Inclusion criteria • Age range: healthy people aged 18+ years old • General good health as established by medical history and physical examination • Women of childbearing age are not pregnant (negative urine pregnancy test), are not breastfeeding, do not have pregnancy plan within the three months after enrollment, and have already taken effective contraceptive measures two weeks before enrollment • Participants are able and willing to complete the whole research procedure in about 14 months • Participants have the ability to understand the research procedures, to sign the informed consent voluntarily after explanation, and can comply with the requirements of the clinical research program
	Exclusion criteria • History of SARS-CoV, SARS-CoV-2 or MERS virus infection (identified through self-report or on-site inquiry) • Those with fever (axillary temperature >37.0 °C), dry cough, fatigue, nasal obstruction, runny nose, sore throat, myalgia, diarrhea, shortness of breath, and dyspnea within 14 days before inoculation • Axillary temperature ≥37.0 °C (or ear or forehead temperature ≥37.0 °C) before inoculation

	• Experienced severe allergic reactions (such as acute anaphylaxis, urticaria, eczema, dyspnea, neurovascular edema, or abdominal pain), or those who are allergic to the known gradients of COVID-19 inactivated vaccine • History or family history of convulsion, epilepsy, encephalopathy, or mental illness • Congenital malformation, developmental disorder, genetic defect, or severe malnutrition, etc. • Confirmed or suspected serious respiratory diseases, serious cardiovascular disease, severe liver or renal diseases, malignant tumors, uncontrolled hypertension (systolic blood pressure ≥150 mmHg, diastolic blood pressure ≥90 mmHg), diabetes complications, malignant tumors, or various acute or chronic diseases (acute attack stage) • Diagnosed with congenital or acquired immunodeficiency, HIV infection, lymphoma, leukemia, or other autoimmune diseases • History of abnormal coagulation (such as lack of coagulation factors or coagulation diseases) • Receiving anti-TB treatment • Receiving immune-enhancement or inhibitor treatment (p.o. or gtt.) over 14 days within 3 months (continuous oral or infusion for more than 14 days) • Receiving live-attenuated vaccines within one month before inoculation or other vaccines within 14 days before inoculation • Receiving blood products within 3 months before inoculation • Receiving other study drugs within 6 months before inoculation • Under other conditions not suitable for the clinical trial (evaluated by researchers)
	Withdrawals: 24 withdrawal due to adverse events
Interventions	**Intervention** • SARS-CoV-2 strain WIV04 - 2 IM doses of 5 mcg (D0/22) • SARS-CoV-2 strain HBO2 - 2 IM doses of 4 mcg (D0/22)
	Control: Placebo
Outcomes	**Primary outcome of the trial:** **In the report:** • Laboratory-confirmed symptomatic COVID-19 cases that occurred at least 14 days after receipt of the second vaccine dose **In the register:** • Incidence of COVID-19 cases after two-doses of vaccination - Time Frame: From 14 days after the second dose to 6 months after the second dose (NCT) • Protective efficacy against COVID 19 14 days after the full course of vaccination (ChiCTR)
Notes	**Funding**: Mixed (National Key Research and Development Project of China)
	Conflict of interest: Yes. Quote: "Dr Xiaoming Yang, Dr Yuntao Zhang, Ms Y Yang, Ms Xuqin Yang, Mr Lai, Ms Q. Wang, Mr T. Yang, and Mr Liu are employees of the China National Biotec Group Company Limited"
	Protocol: English
	Statistical plan: Yes
	Data-sharing stated: Yes

Xia 2020

Trial: ChiCTR2000032459, Xia S, Lancet Infect Dis, 2020 (published in peer reviewed journal)

Methods	RCT
	Phase 2
	Blinding: double blinding
	Date of study: 05/18/2020 to 07/30/2020
	Location : Single center / China
	Follow-up duration (months): 1
	Vaccine group: 8 mcg BBIBP-CorV once-off (n=84) ; Placebo (n=28); 4 mcg BBIBP-CorV D0/D14 (n=84); Placebo (n=28) ;4 mcg BBIBP-CorV D0/D21 (n=84); Placebo (n=28) ;4 mcg BBIBP-CorV D0/D28 (n=84); Placebo (n=28) (Placebo = adjuvant)
Participants	**Population randomized** 448 participants (n1=84 / n2=28 / n3=84 / n4=28 / n5=84 / n6=28 n7=84 / n8=28)
	Characteristics of participants Type of participants: Healthy adults N=448 Children: 0 Pregnant women: 0 Immunocompromised patients: 0 Age mean: NR Age range: 18-59 Men: NR
	Description of participants Healthy SARS-CoV-2 serology negative adults 18-59 years old in a single centre in China
	Inclusion criteria • Healthy subjects aged ≥18 years • No travel to Hubei province, outside the country or in a village/community where there has been an outbreak since December 2019 • No exposure to a person infected with or suspected of COVID-19 • Female subjects with childbearing age not pregnant at the time of recruitment and are not nursing • Effective contraceptive measures taken within 2 weeks before inclusion • Able to informed consent, and comply with the requirements of the clinical study protocol
	Exclusion criteria • Confirmed, suspected or asymptomatic cases with COVID-19 • Positive in serum antibodies (IgG and IgM) screening of COVID-19 • History of SARS virus infection (self-reported, site information) • Fever, dry cough, fatigue, nasal obstruction, runny nose, sore throat, myalgia, diarrhea, shortness of breath and dyspnea within 14 days before administration • Abnormal indicators, such as blood biochemistry, blood routine and urine routine, which might show clinical meaning, before administration (only refers to Phase I) • History of severe allergic reactions or allergy to known composition of COVID-19 vaccine • History of convulsion, epilepsy, encephalopathy or mental illness or family history • congenital malformations or developmental disorders, genetic defects, severe malnutrition, etc.

	• Severe liver and kidney diseases, uncontrollable hypertension, diabetic complications, malignant tumors, acute diseases or acute onset of chronic diseases • Congenital or acquired immune deficiency, HIV infection, lymphoma, leukemia or other autoimmune diseases • History of coagulation dysfunction • Receiving anti-TB treatment • Receiving immunotherapy or inhibitor therapy within 3 months • Vaccinated with live attenuated vaccine within 1 month, or other vaccine within 14 days before vaccination • Receiving blood products within 3 months before administration • Receiving other research drugs within 6 months before vaccination
	Withdrawals: 0 withdrawal due to adverse events
Interventions	**Intervention** • BBIBP-CorV - 2 IM doses of 8 mcg (D0) • BBIBP-CorV - 2 IM doses of 4 mcg (D0/D14) • BBIBP-CorV - 2 IM doses of 4 mcg (D0/D21) • BBIBP-CorV - 2 IM doses of 4 mcg (D0/D28)
	Control: Placebo
Outcomes	**Primary outcome of the trial:** **In the report:** • Adverse reactions within 7 days after the first and second vaccinations **In the register:** • Incidence of adverse reactions/events 0-7 days after each dose of vaccination
Notes	**Funding**: Mixed (National Program on Key Research Project of China, National Mega projects of China for Major Infectious Diseases, National Mega Projects of China for New Drug Creation, and Beijing Science and Technology Plan. The China National Biotec Group and the Beijing Institute of Biological Products provided the study product, and oversaw all trial operations.)
	Conflict of interest: Yes. Quote: "Yunkai Yang, Hui Wang, Wei Wang, Na Li, Ling Ding, Yuxiu Zhao, Xu Yang, Yang Liu, and Qian Wang were involved in safety and immunogenicity data analysis and interpretation and are employees of the Beijing Institute of Biological Products, which developed the candidate vaccine."
	Protocol: NR
	Statistical plan: NR
	Data-sharing stated: Yes

Xia 2021

Trial: ChiCTR2000032459, Xia S , Lancet, 2021 (published in peer reviewed journal)

Methods	RCT
	Phase 1-2
	Blinding: triple blinding
	Date of study: 08/14/2020 to 09/24/2020
	Location : Single center / China
	Follow-up duration (months): 2.9
	Vaccine group: 2 mcg BBIBP-CorV (n=252) ; 4 mcg BBIBP-CorV (n=252); 8 mcg BBIBP-CorV (n=252) Placebo (n=252) (Placebo = adjuvant)
Participants	**Population randomized** 1008 participants (n1=252 / n2=252 / n3=252 / n4=252)
	Characteristics of participants Type of participants: Healthy adults N=1008 Children: 1008 Pregnant women: 0 Immunocompromised patients: 0 Age mean: NR Age range: 3-18 Men: 525
	Description of participants Healthy children and adolescents aged 3 to 17 years free from SARS-CoV-2 infection and antibodies at a single center in China
	Inclusion criteria • Healthy individuals aged 3–17 years • Negative for serum-specific IgM or IgG antibodies against SARS-CoV-2 N and S proteins
	Exclusion criteria • History of travelling to Hubei, regions outside of China, or regions within China with any reported COVID-19 cases since December, 2019 • History of infection with SARS-CoV • Fever (axillary temperature more than 37·3°C if aged older than 14 years, and axillary temperature of more than 37·5°C if aged 14 years or younger), respiratory syndromes, diarrhea, dyspnea, or tachypnoea within 14 days before vaccination • Abnormal results in laboratory tests (blood biochemistry tests [alanine aminotransferase, aspartate aminotransferase, total bilirubin, creatinine, urea nitrogen], routine blood tests [hemoglobin, white blood cell count], and routine urine tests [protein, urine sugar, blood cells—microscopic examination]) • Allergy to any ingredient included in the vaccine • History of seizures or mental illness (defined as a history of convulsion, epilepsy or psychosis) • Being unable to comply with the study schedule
	Withdrawals: 1 withdrawal due to adverse events

Interventions	**Intervention** • BBIBP-CorV - 3 IM doses of 2 mcg (D0/28/56) • BBIBP-CorV - 3 IM doses of 4 mcg (D0/28/56) • BBIBP-CorV - 3 IM doses of 8 mcg (D0/28/56)
	Control: Placebo (adjuvant)
Outcomes	**Primary outcome of the trial:** **In the report:** • Adverse reactions within 7 days after each vaccination **In the register:** • Incidence of adverse reactions/events 0-7 days after each dose of vaccination
Notes	**Funding**: Private (Beijing Institute of Biological Products)
	Conflict of interest: Yes. Quote: "XMY, YTZ, YKY, HW, WW, NL, XJZ, LD, YXZ, JZ, MM, YLQ, SHZ, JJC, QQL, HF, YX, and XTZ are employees of Beijing Institute of Biological Products, which developed the vaccine and funded the trial. All other authors declare no competing interests."
	Protocol: NR
	Statistical plan: NR
	Data-sharing stated: Yes

BBV152 -Bharat Biotech

Comparison: BBV152 vs Placebo

Ella 2021a

Trial: NCT04471519; CTRI/2, Ella R, Lancet Infect Dis, 2021 (published in peer reviewed journal) First published as preprint Ella R, medRxiv, 2020

Methods	RCT
	Phase 1
	Blinding: double blinding
	Date of study: 07/13/2020 to 07/30/2020
	Location: Multicenter / India
	Follow-up duration (months): 6.38
	Vaccine group: 3 mcg BBV152 + Algel-IMDG (n = 100); 6 mcg BBV152 + Algel-IMDG (n = 100); 6 mcg BBV152 + Algel (n = 100); Placebo (n = 75)
Participants	**Population randomized:** 375 participants (n1=100 / n2=100 / n3=100 / n4=75)
	Characteristics of participants Type of participants: Healthy volunteers N=375 Children: 0 Pregnant women: 0 Immunocompromised patients: 0 Age mean: NR Age range: 18-55 Men: 297
	Description of participants Healthy SARS-CoV-2 serology/PCR negative adults in 11 centers in India
	Inclusion criteria • Ability to provide written informed consent • Participants of either gender of age between ≥18 to ≤55 years • Good general health as determined by the discretion of investigator (vital signs (heart rate ≥60 to ≤100 bpm • Blood pressure systolic ≥90 mm Hg and <140 mm Hg • Diastolic ≥ 60 mm Hg and <90 mm Hg • Oral temperature <100.4ºF), medical history, and physical examination) • Expressed interest and availability to fulfill the study requirements • For a female participant of child-bearing potential, planning to avoid becoming pregnant (use of an effective method of contraception or abstinence) from the time of study enrolment until at least four weeks after the last vaccination • Male subjects of reproductive potential: Use of condoms to ensure effective contraception with the female partner from first vaccination until 3 months after last vaccination • Male subjects agree to refrain from sperm donation from the time of first vaccination until 3 months after last vaccination • Participants must refrain from blood or plasma donation from the time of first vaccination until 3 months after last vaccination • Agrees not to participate in another clinical trial at any time during the study period • Agrees to remain in the study area for the entire duration of the study • Willing to allow storage and future use of biological samples for future research
	Exclusion criteria

	• History of any other COVID-19 investigational vaccination • Unacceptable laboratory abnormality from screening (prior to first vaccination) or safety testing, as listed below [Abnormal Complete Blood Count (CBC), Random blood sugar level, Renal function test (serum urea and Creatinine), liver function tests, urine analysis report, Positive serology for hepatitis C or HIV antibody or hepatitis B surface antigen]. (Subjects will be informed if their results are positive for hepatitis C, HIV 1 & 2 antibody or hepatitis B surface antigen (HBsAg) and will be referred to a primary care provider for follow up of these abnormal laboratory tests.) • Confirmed SARS-CoV-2 at the time of screening using RT-PCR and ELISA method • Health care workers • For women, a positive serum pregnancy test (during screening within 45 days of enrolment) or positive urine pregnancy test (within 24 hours of administering each dose of vaccine) • Temperature >38.0°C (100.4°F) or symptoms of an acute self-limited illness such as an upper respiratory infection or gastroenteritis within three days prior to each dose of vaccine • Medical problems as a result of alcohol or illicit drug use during the past 12 months • Receipt of an experimental agent (vaccine, drug, device, etc.) within 60 days before enrollment or expects to receive an investigational agent during the study period • Receipt of any licensed vaccine within four weeks before enrolment in this study • Known sensitivity to any ingredient of the study vaccines, or a more severe allergic reaction and history of allergies in the past • Receipt of immunoglobulin or other blood products within the three months prior to vaccination in this study • Immunosuppression as a result of an underlying illness or treatment with immunosuppressive or cytotoxic drugs, or use of anticancer chemotherapy or radiation therapy within the preceding 36 months • Long-term use (> 2 weeks) of oral or parenteral steroids (glucocorticoids) or high-dose inhaled steroids (>800 mcg/day of beclomethasone dipropionate or equivalent) within the preceding six months (nasal and topical steroids are allowed) • Any history of hereditary angioedema or idiopathic angioedema • Any history of anaphylaxis in relation to vaccination • Any history of albumin-intolerance • Pregnancy, lactation, or willingness/intention to become pregnant during the study • History of any cancer • History of psychiatric severe conditions likely to affect participation in the study • A bleeding disorder (e.g., factor deficiency, coagulopathy or platelet disorder, or prior history of significant bleeding or bruising following IM injections or venipuncture • Any other serious chronic illness requiring hospital specialist supervision • Chronic respiratory diseases like severe acute respiratory syndrome (SARS), including mild asthma • Chronic cardiovascular disease, gastrointestinal disease, liver disease, renal disease, endocrine disorder, and neurological illness • Morbidly obese (BMI≥35 kg/m2) or underweight (BMI ≤18 kg/m2) • Living in the same household of any COVID-19 positive person • Any other condition that in the opinion of the investigator would jeopardize the safety or rights of a volunteer participating in the trial or would render the subject unable to comply with the protocol • Re-Vaccination Exclusion Criteria 27. Pregnancy • Anaphylactic reaction following administration of the investigational vaccine • Virologically confirmed cases of COVID-19
	Withdrawals: 0 withdrawal due to adverse events

Interventions	**Intervention** • BBV152 nCoV-19 vaccine + Algel-IMDG adjuvant - 2 IM doses of 3-mcg BBV152 with 0.5mL Algel-IMDG (alum) adjuvant (D0/14) • BBV152 nCoV-19 vaccine + Algel-IMDG adjuvant - 2 IM doses of 6-mcg BBV152 with 0.5 mL Algel-IMDG (alum) adjuvant (D0/14) • BBV152 nCoV-19 vaccine + Algel adjuvant - 2 IM doses of 6-mcg BBV152 with 0.5 mL Algel (alum) adjuvant (D0/14)
	Control • Algel (alum) - 0.5mL (D0/14)
Outcomes	**Primary outcome of the trial:** **In the report**: • Solicited local and systemic reactogenicity events at 2 h and 7 days after vaccination and throughout the full study duration, including serious adverse events **In the register:** • Occurrence of adverse events and Serious Adverse events [Time Frame: Through study completion, an average of 6 months]
Notes	**Funding**: Private (Bharat Biotech International Limited)
	Conflict of interest: Yes. Quote: "RE, HJ, BG, KMV, SPr, VS, KE, and SR are employees of Bharat Biotech, with no stock options or incentives. KE is the Chairman and Managing Director of Bharat Biotech. PY, GS, PA, NG, SPa, and BB are employees of The Indian Council of Medical Research. All other authors declare no competing interests."
	Protocol: NR
	Statistical plan: NR
	Data-sharing stated: Yes

Ella 2021b

Trial: NCT04641481, Ella R, medRxiv, 2021 (Preprint)

Methods	RCT
	Phase 3
	Blinding: double blinding
	Date of study: 11/16/2020 to 01/07/2021
	Location: Multicenter / India
	Follow-up duration (months): 12
	Vaccine group: BBV152B (n=12,899); Placebo (adjuvant) (n=12,899)
Participants	**Population randomized:** 25778 participants (n1=12889 / n2=12889)
	Characteristics of participants Type of participants: Adults N=25778 Children: 0 Pregnant women: 0 Immunocompromised patients: 0 Age mean: Age range: 18-92 Men: 17285
	Description of participants Adults with no history of SARS-CoV-2 infection who were healthy or had stable chronic medical conditions at 25 centers in India
	Inclusion criteria • Ability to provide written informed consent and availability to fulfill the study requirement • Participants of either gender of aged 18 years and above • Participants with good general health as determined by the discretion of the investigator, or participants with stable medical conditions. A stable medical condition is defined as a disease not requiring significant change in therapy or hospitalization or worsening disease during the 3 months before enrolment • For a female participant of child-bearing potential, planning to avoid becoming pregnant (use of an effective method of contraception or abstinence) from the time of study enrolment until at least eight weeks after the last vaccination • Male subjects of reproductive potential: Use of condoms to ensure effective contraception with the female partner and to refrain from sperm donation from first vaccination until at least 3 months after the last vaccination • Agrees not to participate in another clinical trial at any time during the study period • Agrees not to take any COVID-19 licensed vaccination for the entire duration of the study • Agrees to remain in the study area for the entire duration of the study • Willing to allow storage and future use of biological samples for future research
	Exclusion criteria • History of any other COVID-19 investigational or licensed vaccination • Known history of SARS-CoV-2 infection, as declared by the subject • For women, positive urine pregnancy test before the first dose of vaccination, or any time during the study period • Temperature >38.0°C (100.4°F) or symptoms of an acute self-limited illness such as an upper respiratory infection or gastroenteritis within three days prior to each dose of vaccine • Resident of COVID-19 infection in the same household

	• Known case of HIV, hepatitis B, or hepatitis C infection • Receipt of any licensed/experimental vaccine within four weeks before enrolment in this study • Receipt of immunoglobulin or other blood products within the three months before vaccination in this study • Immunosuppression as a result of an underlying illness or treatment with immunosuppressive or cytotoxic drugs, or use of anticancer chemotherapy or radiation therapy within the preceding 36 months • Immunoglobulins, anti-cytokine antibodies, and blood products within 6 months prior to study vaccination, during, and 21 days following the last dose of vaccination • Pregnancy, lactation, or willingness/intention to become pregnant during the first 6 months after enrolment • Severe and/or uncontrolled cardiovascular disease, respiratory disease, gastrointestinal disease, liver disease, renal disease, an endocrine disorder, and neurological illness (mild/moderate well-controlled comorbidities are allowed)
	Withdrawals: 19 withdrawal due to adverse events
Interventions	**Intervention:** BBV152 - 2 IM doses of 6 mcg (D0/28)
	Control: Placebo
Outcomes	**Primary outcome of the trial:** **In the report**: • Efficacy of the BBV152 vaccine in preventing a first occurrence of symptomatic COVID-19 (any severity) with onset at least 14 days after the second dose in the per-protocol population composed of participants who were SARS-CoV-2 negative by PCR and serology at baseline, had no major protocol deviations, and followed-up for at least two weeks after the second dose **In the register**: • First occurrence of virologically confirmed (RT-PCR positive) symptomatic cases of COVID-19. [Time Frame: Day 42 to Month 12] (RT-PCR positive) symptomatic cases of COVID-19
Notes	**Funding**: Mixed (Bharat Biotech International Limited and the Indian Council of Medical Research)
	Conflict of interest: Yes. Quote: "RE, KMV, SPr, SRe, VA and V.S. are employees of Bharat Biotech, with no stock options or incentives. Co-author, K.E., is the Chairman and Managing Director of Bharat Biotech. WB is an independent statistical development consultant. VP, PY, GS, PA, NG, and BB are employees of The Indian Council of Medical Research. SK, SR, PRe, SV, CS, SR, SM, AP, PRa, RG, MM, SM, PB, and LK were principal investigators representing the study sites."
	Protocol: NR
	Statistical plan: NR
	Data-sharing stated: Yes

Protein Subunit

NVX-CoV2373 Novavax

Comparison: NVX-CoV2373 vs Placebo

Keech 2020

Trial: NCT04368988, Keech C, N Engl J Med, 2020 (published in peer reviewed journal)

Methods	RCT
	Phase 1
	Blinding: double blinding
	Date of study: 05/27/2020 to 06/06/2020
	Location: Multicenter / Australia
	Follow-up duration (months): 1.15
	Vaccine group: 25mcg/25mcg rSARS-CoV-2 (n=25); 5mcg/5mcg + 50mcg Matrix-M1 adjuvant rSARS-CoV-2 (n=25); 25mcg/25mcg + 50mcg Matrix-M1 adjuvant rSARS-CoV-2 (n=25); 25mcg+ 50mcg Matrix-M1 adjuvant rSARS-CoV-2 (n=25); Placebo (n=25)
Participants	**Population randomized:** 134 participants (n1=26 / n2=29 / n3=28 / n4=26 / n5=25)
	Characteristics of participants Type of participants: Healthy volunteers N=134 Children: 0 Pregnant women: 0 Immunocompromised patients: 0 Age mean: 30.8 Age range: NR Men: 64
	Description of participants Healthy adult volunteers, SARS-CoV-2 infection-free and no history of SARS-CoV-2 infection in two centres in Australia
	Inclusion criteria • Healthy adult males or females between 18 and 59 years of age, inclusive, at screening • Healthy status, determined by the investigator based on medical history, clinical laboratory results, vital sign measurements, and physical examination at screening • Body mass index 17 to 40 kg/m^2 • Willing and able to give informed consent prior to study enrollment and comply with study procedures • Female subjects of childbearing potential (defined as any female who has experienced menarche and who is NOT surgically sterile [ie, hysterectomy, bilateral tubal ligation, or bilateral oophorectomy] or postmenopausal [defined as amenorrhea at least 12 consecutive months or documented plasma follicle-stimulating hormone level ≥40 mIU/mL]) must agree to be heterosexually inactive from at least 21 days prior to enrollment and through 6 months after the last vaccination OR agree to consistently use any of the following methods of contraception from at least 21 days prior to enrollment and through 6 months after the last vaccination: Condoms (male or female) with spermicide (if acceptable in country)m diaphragm with spermicide, cervical cap with spermicided, intrauterine device, oral or patch contraceptives (Norplant®, Depo-Provera®, or other in country regulatory-approved contraceptive method that is designed to protect against pregnancy)
	Exclusion criteria

	• Any ongoing, symptomatic acute or chronic illness requiring medical or surgical care, inclusive of changes in medication in the past 2 months indicating that chronic illness/disease is not stable (at the discretion of the investigator), including any current workup of undiagnosed illness that could lead to a new condition
	• Chronic disease inclusive of:
	  o Hypertension uncontrolled for age according to JNC 8 guidelines
	  o Congestive heart failure by NYHA functional classification of >II
	  o Chronic obstructive pulmonary disease by GOLD classification of >2, recent (within 6 months prior to first study vaccination)
	  o Exacerbation of coronary artery disease as manifested by cardiac intervention
	  o Addition of new cardiac medications for control of symptoms, or unstable angina
	  o Asthma (diagnosed by spirometry showing reversibility of disease and must meet at least the Step 1 classification with current prescription/use of medications to control symptoms)
	  o Diabetes requiring use of medicine (insulin or oral) or not controlled with diet
	• Participation in research involving an investigational product (drug/biologic/device) within 45 days prior to first study vaccination
	• History of a confirmed diagnosis of SARS or COVID-19 disease (confirmed by a specific test for each disease) or known exposure to a SARS-CoV-2 positive confirmed close contact (e.g., family member, housemate, daycare provider, aged parent requiring care), at the discretion of the investigator

	Withdrawals: 1 withdrawal due to adverse events
Interventions	**Intervention** • NVX-CoV2373 – 2 IM doses 25 µg NVX-CoV2373/0 µg Matrix-M1 (D0/21) • NVX-CoV2373 – 2 IM doses 5 µg NVX-CoV2373/50 µg Matrix-M1 (D0/21) • NVX-CoV2373 – 2 IM doses 25 µg NVX-CoV2373/50 µg Matrix-M1 (D0/21) • NVX-CoV2373 – 1 IM dose 25 µg NVX-CoV2373/50 µg Matrix-M1, followed by placebo dose (D0/21)
	Control: Placebo
Outcomes	**Primary outcome of the trial:** **In the report:** • Reactogenicity • Safety laboratory values • Immunoglobulin G (IgG) anti-spike protein response **In the register:** • Subjects with solicited AEs • Safety Laboratory Values (serum chemistry, hematology) • Serum IgG antibody levels specific for the SARS-CoV-2 rS protein antigen(s)
Notes	**Funding**: Mixed (Novavax/Funded by the Coalition for Epidemic Preparedness Innovations/ vaccine NVX-CoV2373, developed by Novavax and manufactured at Emergent Biosolutions (Rockville,Maryland))
	Conflict of interest: Yes. Quote: "Cheryl Keech, and many other authors are employees of Novavax Matthew Frieman, Robert Haupt, James Logue, Marisa McGrath, and Stuart Weston are researchers at the University of Maryland School of Medicine and received a grant from Novavax. Pedro Piedra is a researcher at Baylor University and received non-financial support/materials transfer agreement for spike protein of SARS-Cov-2 and ACE2. Jason Lickliter is an employee of Nucleus Network Pty Ltd and the institution received funding from Novavax to support operation of the clinical trial. Paul Griffin is an employee of Q-Pharm, which was contracted by Nucleus to conduct the clinical trial.

	Jason Lickliter is an employee of Nucleus Network Pty Ltd and the institution received funding from Novavax to support operation of the clinical trial. "
	Protocol: English
	Statistical plan: Yes
	Data-sharing stated: No

Dunkle 2021

Trial: NCT04611802, Dunkle L M, medRxiv, 2021 (Preprint)

Methods	RCT
	Phase 3
	Blinding: quadruple blinding
	Date of study: 12/27/2020 to 02/18/2021
	Location: Multicenter / Mexico, USA
	Follow-up duration (months): 2
	Vaccine group: NVX-CoV2373 (n = 19965); Placebo (n = 9984)
Participants	**Population randomized:** 29949 participants (n1=19965 / n2=9984)
	Characteristics of participants Type of participants: Adults N=29949 Children: 0 Pregnant women: 0 Immunocompromised patients: 0 Age mean: NR Age range: 18-90 Men: 13181
	Description of participants Healthy adults in 113 sites in the USA and 6 in Mexico
	Inclusion criteria • Adults ≥ 18 years of age considered at substantial risk of exposure to and infection with SARS-CoV-2 • Informed consent • Participants of childbearing potential must agree to be heterosexually inactive OR agree to consistently use a medically acceptable method of contraception from at least 28 days prior to enrollment and through 3 months after the last vaccination • Medically stable, as determined by the investigator (based on review of health status, vital signs [to include body temperature], medical history, and targeted physical examination [to include body weight]) • Agree to not participate in any other SARS-CoV-2 prevention trial during the study follow-up
	Exclusion criteria • Unstable acute or chronic illness • Participation in research involving an investigational product (drug/biologic/device) within 45 days prior to first study vaccination • History of a previous laboratory-confirmed diagnosis of SARS-CoV-2 infection or COVID-19 • Received influenza vaccination or any other adult vaccine within 4 days prior to or within 7 days after either study vaccination. Received any vaccine within 4 days prior to first study vaccination or planned receipt of any vaccine before Day 49 (ie, 28 days after second vaccination)

	• Autoimmune or immunodeficiency disease/condition (iatrogenic or congenital) requiring ongoing immunomodulatory therapy • Chronic administration (defined as > 14 continuous days) of immunosuppressant, systemic glucocorticoids, or other immune-modifying drugs within 90 days prior to first study vaccination • Received immunoglobulin, blood-derived products, or immunosuppressant drugs within 90 days prior to first study vaccination • Active cancer (malignancy) on therapy within 1 year prior to first study vaccination (with the exception of malignancy cured via excision, at the discretion of the investigator) • Any known allergies to products contained in the investigational product • Participants who are breastfeeding, pregnant or who plan to become pregnant within 3 months following last study vaccination • Any other condition that, in the opinion of the investigator, would pose a health risk to the participant if enrolled or could interfere with evaluation of the trial vaccine or interpretation of study results • Study team member or first-degree relative of any study team member (inclusive of Sponsor, and study site personnel involved in the study) • Current participation in any other COVID-19 prevention clinical trial.
	Withdrawals: 73 withdrawal due to adverse events
Interventions	**Intervention:** NVX-CoV2373 – 2 IM doses of 5 mcg (D0/21)
	Control: Placebo
Outcomes	**Primary outcome of the trial:** **In the report:** • First episode of reverse transcriptase-polymerase chain reaction (RT-PCR)-confirmed symptomatic mild, moderate, or severe Covid-19 (using FDA criteria) with onset ≥7 days after the second injection **In the register:** • Participants with Symptomatic Mild, Moderate, or Severe Coronavirus Disease 2019 (COVID-19) [Time Frame: Day 28 to Day 750]
Notes	**Funding**: Mixed (Funded by Novavax and the National Institute of Allergy and Infectious Diseases (NIAID), National Institutes of Health)
	Conflict of interest: Yes. Quote: "Lisa M. Dunkle, M.D. [Author Affiliations] From Novavax, Gaithersburg (L.M.D, G.A., K.S., W.W., I.C., G.M.G., F.D.)"
	Protocol: NR
	Statistical plan: NR
	Data-sharing stated: NR

Formica 2021

Trial: NCT04368988, Formica N, PLoS Med, 2021 (published in peer reviewed journal)

First published as preprint Formica N, medRxiv, 2021

Methods	RCT
	Phase 2
	Blinding: double blinding
	Date of study: 08/24/2020 to 09/25/2020
	Location: Multicenter / Australia, USA
	Follow-up duration (months): 1.15
	Vaccine group: Placebo (n = 257) ; NVX-CoV2373 5mcg 2 doses (n = 258); NVX-CoV2373 5mcg 1 dose (n = 257); NVX-CoV2373 25mcg 2 doses (n = 258); NVX-CoV2373 25mcg 1 dose (n = 258)
Participants	**Population randomized:** 1288 participants (n1=258 / n2=257 / n3=258 / n4=258 / n5=257)
	Characteristics of participants Type of participants: Adults N=1288 Children: 0 Pregnant women: 0 Immunocompromised patients: 0 Age mean: Age range: NR Men: 630
	Description of participants Healthy adults (stable comorbidities and confirmed COVID-19 with mild symptoms permitted) aged 18-84 years at 17 centers in Australia and USA
	Inclusion criteria • Men and non-pregnant women 18 to 84 years of age • body mass index of 17 to 35 • participants with underlying medical conditions could be enrolled if the conditions were judged clinically to be stable • participants with confirmed COVID-19 presenting with mild symptomatology could be enrolled
	Exclusion criteria : NR
	Withdrawals: 7 withdrawal due to adverse events
Interventions	**Intervention** • NVX-CoV2373 - 2 IM doses 5-mcg on days (D0/21) • NVX-CoV2373 - 1 IM dose 5-mcg day 0, 1 IM dose placebo (D0/21) • NVX-CoV2373 - 2 IM doses 25-mcg (D0/21) • NVX-CoV2373 - 1 IM dose 25-mcg day 0, 1 IM dose placebo (D0/21)
	Control: Placebo

Outcomes	**Primary outcome of the trial:** **In the report:** • Immunoglobulin G (IgG) anti-spike protein response • 7-day solicited reactogenicity • Unsolicited adverse events. **In the register:** • Serum IgG Antibody Levels Expressed as GMTs (day 35) • Serum IgG Antibody Levels Expressed as GMFRs (day 35) • Serum IgG Antibody Levels Expressed as SCRs (day 35) • Participants with Solicited Adverse Events (AEs) (28 days) • Participants with Unsolicited AEs (35 days)
Notes	**Funding**: Mixed (Coalition for Epidemic Preparedness Innovations; Novavax Inc)
	Conflict of interest: Yes. Quote: "All authors are employees of Novavax, Inc. or were at the time of the study"
	Protocol: NR
	Statistical plan: NR
	Data-sharing stated: NR

Heath 2021

Trial: NCT04583995; EudraCT 2020-004123-16, Heath P, N Engl J Med, 2021 (published in peer reviewed journal)

First published as preprint Heath P, medrxiv, 2021

Methods	RCT
	Phase 3
	Blinding: double blinding
	Date of study: 09/28/2020 to 11/28/2020
	Location: Multicenter / UK
	Follow-up duration (months): 3
	Vaccine group: 5 mcg NVX-CoV2373 (n=7593); Placebo (n=7594)
Participants	**Population randomized :** 15187 participants (n1=7593 / n2=7594)
	Characteristics of participants Type of participants: Adults N=15187 Children: 0 Pregnant women: 0 Age mean: NR Age range: 18-84 Men: 7808
	Description of participants Adults 18 to 84 years old who were healthy or had stable chronic medical conditions with no history of COVID-19 at 33 centres in the UK
	Inclusion criteria • Men and non-pregnant women 18 to 84 years old • Healthy or had stable chronic medical conditions, including but not limited to human immunodeficiency virus (and receiving highly active antiretroviral therapy) and cardiac and respiratory diseases
	Exclusion criteria

	• History of documented Covid-19 • Treatment with immunosuppressive therapy • Diagnosis with an immunodeficient condition
	Withdrawals: 33 withdrawal due to adverse events
Interventions	**Intervention:** NVX-CoV2373 - 2 IM doses 5 mcg (D0/21)
	Control : Placebo
Outcomes	**Primary outcome of the trial:** **In the report:** • Efficacy of the NVX-CoV2373 vaccine against the first occurrence of virologically confirmed symptomatic mild, moderate, or severe Covid-19 with onset at least 7 days after the second dose among participants who were seronegative at baseline, as determined by the results of testing for anti–nucleocapsid antibody **In the register:** • Number of participants, testing serologically negative for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) at baseline, with first occurrence of positive (+) polymerase chain reaction (PCR)-confirmed SARS-CoV-2 illness with symptomatic mild, moderate, or severe COVID-19 with onset from Day 28 through the length of the study
Notes	**Funding**: Private (Novavax, Inc)
	Conflict of interest: Yes. Quote: "COI statement/disclosures not available. Eight authors, including last author, are employees of Novavax Inc."
	Protocol: English
	Statistical plan: Yes
	Data-sharing stated: Yes

Shinde 2021

Trial: NCT04533399; PACTR202009726132275, Shinde V, N Engl J Med, 2021 (published in peer reviewed journal)

First published as preprint Shinde V, medRxiv, 2021

Methods	RCT
	Phase 2
	Blinding: double blinding
	Date of study: 08/17/2020 to 11/25/2020
	Location: Multicenter / South Africa
	Follow-up duration (months): 1.15
	Vaccine group: NVX-CoV2373 5 µg + Matrix-M1 (n=2206); Placebo (n=2200)
Participants	**Population randomized :** 4406 participants (n1=2206 / n2=2200)
	Characteristics of participants Type of participants: Healthy volunteers, Adults, People living with HIV N=4406 Children: 0 Pregnant women: 0 Age mean: NR Age range: NR Men: 2518
	Description of participants HIV-negative adults (18 to 84 years) and medically stable HIV-positive adults (18 to 64 years) at 16 sites in South Africa
	Inclusion criteria • Healthy human immunodeficiency virus (HIV)-negative adults 18 to 84 years of age • Medically stable people living with HIV (PLWH) 18 to 64 years of age.
	Exclusion criteria • Chronic administration of immunosuppressive therapy, autoimmune or immunodeficiency disease (except for medically stable PLWH) • History of prior or current symptomatic Covid-19, or nucleic acid amplification test (NAAT)-confirmed SARS-CoV-2 infection within 5 days prior to anticipated initial dosing
	Withdrawals: 1 withdrawal due to adverse events
Interventions	**Intervention:** NVX-CoV2373 - 2 IM doses of 5 mcg NVX-CoV2373 with 50 mcg Matrix-M1 adjuvant (D0/21)
	Control: Placebo

Outcomes	**Primary outcome of the trial:** **In the report:** • Occurrence of unsolicited adverse events (medically attended, serious, and those of special interest through Day 35 • Solicited local and systemic adverse events evaluated via reactogenicity diary for 7 days following each vaccination • Confirmed symptomatic mild, moderate, or severe Covid-19 in participants seronegative to SARS-CoV-2 at baseline occurring 7 days after receipt of the second study vaccine (ie, after Day 28) **In the register:** • Cohort 1: HIV- Participants with Symptomatic Mild, Moderate, or Severe COVID-19 [Time Frame: Day 28 to Day 386] • Cohort 1: HIV- Participants with Symptomatic Moderate or Severe COVID-19 [Time Frame: Day 28 to Day 386] • Cohort 1: HIV- Participants with Solicited Adverse Events (AEs) [Time Frame: 28 days] • Cohort 1: HIV- Participants with Unsolicited AEs [Time Frame: 35 days] • Cohort 2: HIV+ Participants with Solicited AEs [Time Frame: 28 days] • Cohort 2: HIV+ Participants with Unsolicited AEs [Time Frame: 35 days] • Cohort 2: Serum Immunoglobulin G (IgG) Antibody Levels Expressed as Geometric Mean Titers (GMTs) [Time Frame: Day 35] • Cohort 2: Serum IgG Antibody Levels Expressed as Geometric Mean Fold Rises (GMFRs) [Time Frame: Day 35] • Cohort 2: Serum IgG Antibody Levels Expressed as Seroconversion Rates (SCRs) [Time Frame: Day 35]
Notes	**Funding**: Mixed (Novavax, Bill and Melinda Gates Foundation, Coalition for Epidemic Preparedness Innovations)
	Conflict of interest: Yes. Quote: "BF, ALC, MIB, OH, HJ, RM, SJS, JS, SG, CAD and GDB are Sanofi Pasteur employees and may hold stock. MK, LS and FTDS are employed by the GlaxoSmithKline (GSK) group of companies. MK, LS and FTDS hold restricted shares in the GSK group of companies. IF reports grants from Janssen and personal fees from Gilead and ViiV/ GlaxoSmithKline. PAG, BJE, MCK, MAK, MGD, LDS and HS declare that they have no conflict of interest."
	Protocol: English
	Statistical plan: Yes
	Data-sharing stated: No

FINLAY-FR-2 - Instituto Finlay de Vacunas

Comparison: FINLAY-FR-2 vs Placebo

Toledo-Romani 2021

Trial: RPCEC00000354, Toledo-Romani ME, medRxiv, 2021 (Preprint)

Methods	RCT
	Phase 3
	Blinding: double blinding
	Date of study: 03/08/2021 to 03/31/2021
	Location: Multicenter / Cuba
	Follow-up duration (months): 5.2
	Vaccine group: SOBERANA 02, 2 doses (n = 14679); SOBERANA 02, 2 doses + SOBERANA Plus booster (n = 14 677); Placebo (adjuvant) (n = 14675)
Participants	**Population randomized :** 44031 participants (n1=14675 / n2=14679 / n3=14677)
	Characteristics of participants Type of participants: Adults N=44031 Children: 0 Pregnant women: 0 Immunocompromised patients: 2636 Age mean: Age range: 18-81 Men: 20929
	Description of participants Adults in medically stable condition with no self-reported previous COVID-19 infection at 48 centers in Cuba
	Inclusion criteria • Subjects who give their informed consent to participate in the study in writing • Subjects aged between 19 and 80 years • Women of childbearing age who use contraceptive methods during the study and are willing to use them up to 3 months after the corresponding vaccination schedule has concluded
	Exclusion criteria • Subjects with acute febrile or infectious disease in the 7 days prior to the administration of the vaccine or at the time of its application • Subjects with diminished mental faculties for decision making • Subjects with a history of hypersensitivity to thiomersal or to some of the components of the formulation • Previous or current history of SARS-CoV-2 infection (questioning) • Application of vaccines containing tetanus toxoid in the last 3 months • Subjects previously vaccinated against SARS-CoV-2 • Treatment with immunomodulators in the last 30 days, considering steroids (except topical and inhaled), cytostatics, interferon, immunoferon, transfer factor, Biomodulin T, any gamma globulin, Levamisole, Heberferon, thymosin) or other drugs with immunomodulatory action. In addition, those people who, due to their underlying disease, require immunomodulatory treatment during the development of the study • Pregnancy, puerperium or lactation • Subjects with tattoos in the deltoid region on both arms

	• Decompensated chronic diseases that limit vaccination according to clinical criteria • HIV subjects with detectable viral load, history of opportunistic infection or CD4 less than 200 copies • Subjects with unstabilized malignant disease or who are receiving cytostatic treatment and / or radiotherapy during the time of the study or have been receiving it in the last three months.
	Withdrawals: 0 withdrawal due to adverse events
Interventions	**Intervention** • FINLAY-FR-2-25 mcg - 2 IM doses of 25 mcg (D0/28) • FINLAY-FR-2-25 mcg +FR-1-50 mcg - 2 IM doses of 25 mcg + 1 IM dose of 50 mcg D0/28/56)
	Control: Placebo
Outcomes	**Primary outcome of the trial:** **In the report:** • VE in preventing occurrence of symptomatic COVID-19 confirmed by positive SARS-CoV-2 RT-PCR nasopharyngeal swab (RT-PCR), with onset at least 14 days after the last injection **In the register:** • Virologically confirmed symptomatic infection of Covid-19. Measurement time: from 14 days after the last dose of the candidate until 3 months after this evaluation
Notes	**Funding**: Public/non-profit (Finlay Vaccine Institute, Biocubafarma and Fondo Nacional de Ciencia y Tecnica)
	Conflict of interest: Yes. Quote: "M. M. P, M. C. R. G., B. P. M., R. G.M. R., E. L. M., E.C.G., S. F., Y. C., Y. V.B., D. G.R., V. V. B. [last author] are from Finlay Vaccine Institute the sponsor of the trial"
	Protocol: NR
	Statistical plan: NR
	Data-sharing stated: Yes

Heterologous vaccination scheme

Liu 2021

Trial: ISRCTN69254139, EudraCT: 2020-005085-33, Liu X, Lancet, 2021 (published in peer reviewed journal)

First published as preprint Liu X, SSRN, 2021

Methods	RCT
	Phase 2
	Blinding: single blinding
	Date of study: 02/11/2021 to 02/26/2021
	Location: Multicenter / UK
	Follow-up duration (months): 2
	Vaccine group: ChAdOx1-S/ChAdOx1-S (n=115); ChAdOx1-S/BNT162b2 (n=114); BNT162b2/BNT162b2 (n=119); BNT162b2/ChAdOx1-S (n=115)
Participants	**Population randomized:** 463 participants (n1=114 / n2=115 / n3=115 / n4=119)
	Characteristics of participants Type of participants: Adults N=463 Children: 0 Pregnant women: 0 Immunocompromised patients: 0 Age mean: NR Age range: 50-68 Men: 251
	Description of participants Adults 50 years or older with no previous SARS-CoV-2 infection, no or well-controlled mild-moderate comorbidities and HIV-negative in 8 centers in the UK
	Inclusion criteria • COVID-19 vaccine-naïve adults aged 50 years and over • None or well-controlled mild-moderate comorbidities
	Exclusion criteria • Previous laboratory confirmed SARS-CoV-2 infection • History of anaphylaxis • History of allergy to a vaccine ingredient • Pregnancy • Breastfeeding or intent to conceive • Current use of anticoagulants
	Withdrawals: 0 withdrawal due to adverse events
Interventions	**Intervention** • ChAd/BNT - 1 IM dose of 5.5×10^10 vp ChAdOx1 and 1 IM dose of 30 mcg BNT162b2 (D0/28) • BNT/ChA-28, 1 IM dose of 30 mcg BNT162b2 and 1 IM dose of 5.5×10^10 vp ChAdOx1 (D0/28)
	Control: ChAd/ChAd or BNT/BNT

Outcomes	**Primary outcome of the trial:** **In the report:** • Serum SARS-CoV-2 anti-spike IgG concentration at 28 days post boost for those with a prime-boost interval of 28 days in participants who were seronegative for COVID infection at baseline **In the register:** • Serum level of anti-spike immunoglobulins using ELISA at 56 days
Notes	**Funding**: Public/non profit (UK Vaccine Task Force (VTF) and National Institute for Health Research (NIHR))
	Conflict of interest: Yes. Quote: "MDS acts on behalf of the University of Oxford as an Investigator on studies funded or sponsored by vaccine manufacturers including AstraZeneca, GlaxoSmithKline, Pfizer, Novavax, Janssen, Medimmune, and MCM vaccines. He receives no personal financial payment for this work. JSN-V-T is seconded to the Department of Health and Social Care, England. AMC and DMF are investigators on studies funded by Pfizer and Unilever. They receive no personal financial payment for this work. AF is a member of the Joint Committee on Vaccination and Immunisation and Chair of the WHO European Technical Advisory Group of Experts (ETAGE) on Immunisation. He is an investigator and/or provides consultative advice on clinical trials and studies of COVID-19 vaccines produced by AstraZeneca, Janssen, Valneva, Pfizer and Sanofi and of other vaccines from these and other manufacturers including GSK, VPI, Takeda and Bionet Asia. He receives no personal remuneration or benefits for any of this work. SNF acts on behalf of University Hospital Southampton NHS Foundation Trust as an Investigator and/or providing consultative advice on clinical trials and studies of COVID-19 and other vaccines funded or sponsored by vaccine manufacturers including Janssen, Pfizer, AstraZeneca, GlaxoSmithKline, Novavax, Seqirus, Sanofi, Medimmune, Merck and Valneva vaccines and antimicrobials. He receives no personal financial payment for this work. PTH acts on behalf of St. George's University of London as an Investigator on clinical trials of COVID-19 vaccines funded or sponsored by vaccine manufacturers including Janssen, Pfizer, AstraZeneca, Novavax and Valneva. He receives no personal financial payment for this work. CAG acts on behalf of University Hospitals Birmingham NHS Foundation Trust as an Investigator on clinical trials and studies of COVID-19 and other vaccines funded or sponsored by vaccine manufacturers including Janssen, Pfizer, AstraZeneca, Novavax, CureVac, Moderna, and Valneva vaccines, and receives no personal financial payment for this work. VL acts on behalf of University College London Hospitals NHS Foundation Trust as an Investigator on clinical trials of COVID-19 vaccines funded or sponsored by vaccine manufacturers including Pfizer, AstraZeneca and Valneva. He receives no personal financial payment for this work. TL is named as an inventor on a patent application covering this SARS-CoV-2 vaccine and is an occasional consultant to Vaccitech unrelated to this work. Oxford University has entered into a partnership with AstraZeneca for further development of ChAdOx1 nCoV-19"
	Protocol: English
	Statistical plan: Yes
	Data-sharing stated: Yes

Li 2021 (This trial reports results for 2 different comparisons, we present them in separate tables)

Trial: NCT04892459, Li J, medRxiv, 2021 (Preprint)

Methods	RCT
	Phase 4
	Blinding: triple blinding
	Date of study: 05/25/2021 to 05/26/2021
	Location: Single center / China
	Follow-up duration (months): 1
	Vaccine group: 1 dose CoronaVac + 1 dose Convidecia (n=50); 2 doses CoronaVac (n=50)
Participants	**Population randomized:** 100 participants (n1=50 / n2=50)
	Characteristics of participants Type of participants: Healthy adults N=100 Children: 0 Pregnant women: 0 Age mean: NR Age range: NR Men: 57
	Description of participants Healthy adults with no previous clinical or virologic COVID-19 diagnosis or SARS-CoV-2 infection at one center in China
	Inclusion criteria • Healthy participants • Male or female • Aged between 18 and 59 years • Received one dose of CoronaVac in the past 1-3 months
	Exclusion criteria • Previous clinical or virologic COVID-19 diagnosis or SARS-CoV-2 infection • Women with positive urine pregnancy test
	Withdrawals: 0 withdrawal due to adverse events
Interventions	**Intervention:** CoronaVac/Ad5-vectored - 1 IM dose CoronaVac + 1 IM dose Convidecia 5x10^10 vp, 1-3 months later
	Control: CoronaVac
Outcomes	**Primary outcome of the trial:** **In the report:** • Adverse reactions within 28 days after the vaccination • Geometric mean titers of neutralizing antibodies against live SARS-CoV-2 virus at 14 days after the booster vaccination **In the register:** • Incidence of adverse reactions within 28 days after the booster dose • GMT of neutralizing antibodies against live SARS-CoV-2 virus on day 14 after the booster dose
Notes	**Funding**: Public/non-profit (National Natural Science Foundation of China)
	Conflict of interest: Yes. Quote: "Xue Wang, Jingxuan Wan, Junqiang Li, Tao Zhu are employees of CanSino Biologics. All other authors declare no competing interests."
	Protocol: NR

	Statistical plan: NR
	Data-sharing stated: Yes

Boosters

Bonelli 2021

Trial: EudraCT 2021-002348-57, Bonelli M, medRxiv, 2021 (Preprint)

Methods	RCT
	Phase : NR
	Blinding: double blinding
	Date of study: 05/25/2021 to 07/08/2021
	Location: Single center / Austria
	Follow-up duration (months): 1
	Vaccine group: Third boost dose BNT162b2 or mRNA-1273 (n=30); Third boost dose ChAdOx1 (n=30)
Participants	**Population randomized:** 60 participants (n1=30 / n2=30)
	Characteristics of participants Type of participants: Adults under rituximab therapy N=60 Children: 0 Pregnant women: 0 Immunocompromised patients: 60 Age mean:NR Age range: NR Men: 14
	Description of participants Adults under current rituximab therapy who did not develop humoral response against SARS-CoV-2 after their standard vaccination with Biontech/Pfizer or Moderna in a single center in Austria
	Inclusion criteria • Adults (≥ 18 years) • With chronic-inflammatory rheumatic or neurologic diseases under current rituximab therapy • Without detectable SARS-CoV-2 spike protein antibodies at least four weeks after their second standard vaccination with an mRNA vaccine (BNT162b2 or mRNA-1273)
	Exclusion criteria • Humoral response to the SARS-CoV-2 vaccination • Grade 3 adverse effects from the mRNA vaccination reported • Pregnancy and breast feeding • Signs of SARS-CoV-2 infection (including previous positive PCR testing) • Any other contraindication to any of the study compounds • Urgent need for next rituximab application
	Withdrawals: 1 withdrawal due to adverse events
Interventions	**Intervention:** ChAdOx1 booster, 1 IM booster dose >4 weeks after full primary vaccination schedule
	Control: BNT162b2 or mRNA-1273 booster

Outcomes	**Primary outcome of the trial:** **In the report:** • Difference in antibody seroconversion rates between the vector and mRNA vaccinated groups **In the register:** • Difference in SARS-CoV-2 antibody seroconversion rate by week 4 after vaccination boost at baseline between 3rd mRNA SARS-CoV-2 (Biontech/Pfizer or Moderna) and vector SARS-CoV-2 vaccine (AstraZeneca)
Notes	**Funding**: Public/non profit (Medical University of Vienna; City of Vienna; Medical-Scientific fund of the Mayor of the federal capital Vienna.)
	Conflict of interest: Yes. Quote: "BK has received honoraria for lecturing/consulting from Biogen, BMS Celgene, Johnsson&Johnsson, Merck, Novartis, Roche, Sanofi-Genzyme, Teva. PM reports speaker fees from AbbVie, Janssen and Novartis and research grants from AbbVie, BMS, Novartis, Janssen, MSD and UCB. MB reports about personal fees from Eli-Lilly. DA received grants and consulting fees from AbbVie, Amgen, Lilly, Merck, Novartis, Pfizer, Roche and Sandoz. JS reports about grants, consulting and personal fees from AbbVie, Astra-Zeneca, Lilly, Novartis, Amgen, Astro, Bristol-Myers Squibb, Celgene, Celltrion, Chugai, Gilead, ILTOO, Janssen, Merck Sharp & Dohme, Novartis-Sandoz, Pfizer, Roche, Samsung and UCB. KS received a research grant from Pfizer. MZ received grants and consulting fees from Nabriva, AntibioTxApS, Shionogi, NovoNordisk, Merck, Infectopharm and Pfizer. HH received grants from Glock Health, BlueSky Immunotherapies and Neutrolis. All other authors declare no competing interests."
	Protocol: English
	Statistical plan: NR
	Data-sharing stated: Yes

Hall 2021

Trial: NCT04885907, Hall VG, N Engl J Med, 2021 (published in peer reviewed journal)

Methods	RCT
	Phase : 4
	Blinding: double blinding
	Date of study: 05/25/2021 to 03/06/2021
	Location: Single center / Canada
	Follow-up duration (months): 1
	Vaccine group: Third boost dose mRNA-1273 (n=60); Placebo (n=60)
Participants	**Population randomized:** 120 participants (n1=60 / n2=60)
	Characteristics of participants Type of participants: Adults solid organ transplant recipients with no previous diagnosis of COVID-19 N=120 Children: 0 Pregnant women: 0 Immunocompromised patients: 120 Age mean:NR Age range: NR Men: 79
	Description of participants Solid organ transplant recipients with no previous diagnosis of COVID-19 who has previously received two doses of mRNA-1273 at a single center in Canada
	Inclusion criteria • Adult patients aged ≥18 years • had received an organ transplant (kidney, liver, heart, lung and pancreas, or combined organs) • had a functioning allograft • had already received both doses of the mRNA-1273 vaccine at the 0,1-month interval
	Exclusion criteria • Within 1-month post-transplant • had a febrile illness within 1-week prior • previous microbiologically confirmed COVID-19 infection • active cytomegalovirus (CMV) infection • received intravenous immunoglobulin in the 4 weeks prior • received rituximab in the last 6 months • had treatment for acute rejection in the 30 days prior • an allergic reaction to the previous mRNA-1273 vaccination
	Withdrawals: none reported
Interventions	**Intervention:** A third IM booster dose of mRNA-1273 vaccine, 2 months after the second dose
	Control: 1 IM dose of saline placebo, 2 months after the second dose of mRNA-1273 vaccine

Outcomes	**Primary outcome of the trial:** **In the report:** • Serologic response characterized by an anti–receptor-binding domain (RBD) antibody level of at least 100 U per milliliter at month 4 (measured with an Elecsys Anti-SARS-CoV-2 immunoassay [Roche]) **In the register:** • Anti-RBD antibody titer [Time Frame: 4-6 weeks after intervention]. Percentage of patients that achieve anti-RBD of >=100 U/mL in each arm
Notes	**Funding**: Public/non profit (The Ajmera Transplant Centre and the Di Poce Transplant Fund, University Health Network, University of Toronto)
	Conflict of interest: Yes. Quote: "Deepali Kumar: consultancy, grants, contracts or other with F. Hoffmann-La Roche, GlaxoSmithKline, Merck, Pfizer, SANOFI PASTEUR INC.. Atul Humar: consultancy, grants, contracts with Astellas Pharma, Merck, F. Hoffmann-La Roche. Vathany Kulasingam: consultancy with Abbott Laboratories. Jeffrey Schiff: consultancy with Novartis. All other authors do not have any interests to disclose at this time."
	Protocol: English
	Statistical plan: Yes
	Data-sharing stated: Yes

Li 2021 (This trial reports results for 2 different comparisons, we present them in separate tables)

Trial: NCT04892459, Li J, medRxiv, 2021 (Preprint)

Methods	RCT
	Phase 4
	Blinding: triple blinding
	Date of study: 05/25/2021 to 05/26/2021
	Location: Single center / China
	Follow-up duration (months): 1
	Vaccine group: CoronaVac (2 doses) + CoronaVac booster (n=100); CoronaVac (2 doses) + Convidecia booster (n=100)
Participants	**Population randomized:** 200 participants (n1=100 / n2=100)
	Characteristics of participants Type of participants: Healthy adults N=200 Children: 0 Pregnant women: 0 Age mean: NR Age range: NR Men: 122
	Description of participants Healthy adults with no previous clinical or virologic COVID-19 diagnosis or SARS-CoV-2 infection at one centre in China
	Inclusion criteria • Healthy participants • Male or female • Aged between 18 and 59 years • Received two doses of CoronaVac in the past 3~6 months
	Exclusion criteria • Previous clinical or virologic COVID-19 diagnosis or SARS-CoV-2 infection • women with positive urine pregnancy test
	Withdrawals: 0 withdrawal due to adverse events
Interventions	**Intervention:** CoronaVac/boost Ad5-vectored - 2 IM doses CoronaVac + 1 IM booster dose Convidecia 5×10^10 vp, 3-6 months later
	Control: CoronaVac/boost
Outcomes	**Primary outcome of the trial:** **In the report:** • Adverse reactions within 28 days after the vaccination • Geometric mean titers of neutralizing antibodies against live SARS-CoV-2 virus at 14 days after the booster vaccination **In the register:** • Incidence of adverse reactions within 28 days after the booster dose • GMT of neutralizing antibodies against live SARS-CoV-2 virus on day 14 after the booster dose
Notes	**Funding**: Public/non-profit (National Natural Science Foundation of China)
	Conflict of interest: Yes. Quote: "Xue Wang, Jingxuan Wan, Junqiang Li, Tao Zhu are employees of CanSino Biologics. All other authors declare no competing interests."

	Protocol: NR
	Statistical plan: NR
	Data-sharing stated: Yes

Mok 2021

Trial: NCT04611243, Mok C K P, medRxiv, 2021 (Preprint)

Methods	RCT
	Phase: NR
	Blinding: unclear
	Date of study: 08/18/2021 to 10/26/2021
	Location: Multicenter / China
	Follow-up duration (months): 5.8
	Vaccine group: CoronaVac booster (n = 40); BNT162b2 booster (n = 40)
Participants	**Population randomized :** 80 participants (n1=40 / n2=40)
	Characteristics of participants Type of participants: Adults N=80 Children: 0 Age mean: NR Age range: NR Men: 28
	Description of participants Adults that had received two doses of CoronaVac but had low immune response against SARS-CoV-2 at two centres in Hong Kong, China
	Inclusion criteria • Healthy adults • Had received 2 doses of CoronaVac in previous cohort study • Surrogate virus neutralization test results below 60% in their plasma specimens which were collected at one month after the second dose
	Exclusion criteria: NR
	Withdrawals: 0 withdrawal due to adverse events
Interventions	**Intervention:** CoronaVac/Boost CoronaVac - 2 IM doses of CoronaVac 28 days apart + 1 IM dose of CoronaVac 116 days later (mean)
	Control: CoronaVac/Boost BNT162b2
Outcomes	**Primary outcome of the trial:** **In the report:** • Humoral immunogenicity measured by sVNT, PRNT and ELISA at one month after the third dose of vaccination **In the register:** NR
Notes	**Funding**: Public/non-profit (the Health and Medical Research Fund Commissioned Research on the Novel Coronavirus Disease, Guangdong Province International Scientific and Technological Cooperation Projects, the National Research Foundation of Korea, US National Institutes of Health, National Natural Science Foundation of China (NSFC)/Research Grants Council (RGC) Joint Research Scheme)
	Conflict of interest: No. Quote: "The authors have declared no competing interest."
	Protocol: NR
	Statistical plan: NR
	Data-sharing stated: Unclear

Sablerolles 2021

Trial: NCT04927936, Sablerolles R, medRxiv, 2021 (Preprint)

Methods	RCT
	Phase 3
	Blinding: single blinding
	Date of study: 06/25/2021 (end date not reported)
	Location: Multicenter / The Netherlands
	Follow-up duration (months): 1
	Vaccine group: Ad26.COV2.S boost (n = 116); mRNA-1273 boost (n = 116); BNT162b2 boost (n = 115); No boost (n = 114)
Participants	**Population randomized:** 461 participants (n1=114 / n2=116 / n3=116 / n4=115)
	Characteristics of participants Type of participants: Healthcare workers N=461 Children: 0 Pregnant women: 0 Immunocompromised patients: 0 Age mean: NR Age range: NR Men: 153
	Description of participants Healthcare workers (aged 18-65 years, without severe comorbidities, and no known history of SARS-CoV-2 infection) who received a single Ad26.COV2.S primary vaccination at 4 centers in the Netherlands.
	Inclusion criteria • 18-65 years of age • Health care worker • Without severe comorbidities • No known history of SARS-CoV-2 infection (either laboratory-confirmed or self-reported) • Primed with the Ad26.COV2.S vaccine 3 months before enrollment
	Exclusion criteria • Younger than 18 or older than 65 years • Already vaccinated with other vaccine then Janssen • Previously had a COVID-19 infection • History of allergic reaction likely to be exacerbated by any component of study vaccines (e.g. hypersensitivity to the active substance or any of the ingredients of the Janssen/Pfizer/Moderna vaccine) • Pregnant or have a wish to become pregnant within 6 months • Currently being treated for cancer • Severe kidney failure or dialyses dependent • Status after organ-, stem cell- or bone marrow transplantation • Use of immunosuppressants • Epilepsy • HIV • Bleeding disorder (e.g. factor deficiency, coagulopathy or platelet disorder), or prior history of significant bleeding of bruising following injections of vene puncture • Continuous use of anticoagulants, such as coumarins (e.g. acenocoumarol) or novel oral anticoagulants (i.e. apixaban, dabigatran etc) • Currently participating in another research trial

	• All regular contra-indications of the vaccines will be applied
	Withdrawals: 0 withdrawal due to adverse events
Interventions	**Intervention** • Ad26.COV2.S/Ad26.COV2.S, 1 IM dose Ad26.COV2.S 84 days (−7/+21) after primary Ad26.COV2.S vaccination • Ad26.COV2.S/m-RNA-1273, 1 IM dose mRNA-1273 84 days (−7/+21) after primary Ad26.COV2.S vaccination • Ad26.COV2.S/BNT162b2, 1 IM dose BNT162b2 84 days (−7/+21) after primary Ad26.COV2.S vaccination
	Control: Ad26.COV2.S/No boost
Outcomes	**Primary outcome of the trial:** **In the report:** • SARS-CoV-2-specific binding antibodies at day 0 and 28 days after the boost **In the register:** • Determination of antibodies by a quantitative IgG assay (LIAISON SARS-CoV-2 TrimericS IgG essay) 28 days after booster [Time Frame: 28 days after booster]
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	Conflict of interest: No. Quote: "The authors have declared no competing interest."
	Protocol: English
	Statistical plan: Yes
	Data-sharing stated: Yes