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Reviewers	RI, GF, TA	AT, TS, PS, AI	SS, PJ, KT	CC, SO, PW	AT, GF, PN	AT, SS, RI, PN	RI, GF, PN
Vaccine	CoronaVac	mRNA-1273	BNT162b2 mRNA Covid-19	ChAdOx1nCoV-19	NVX-CoV2373	Ad26.COV2.S or JNJ-78436735	Sputnik V rAd26/5 Gam-COVID-Vac
Technique	Inactivated virus	mRNA	mRNA	Viral vector	Recombinant Nanoparticle spike protein	Viral vector	Viral vector
Dosage	2 doses, 14 days apart	2 doses, 28 days apart	2 doses, 21 days apart	2 doses, 4-12 weeks apart	2 doses, 21 days apart	Single dose	2 doses of: first - rAd26 and second - rAd5, 21 days apart
Cost per dose	15-30 USD	32-37 USD	18.30-19.50 USD	2-5 USD	16 USD	10 USD	10-13 USD
Storage/Logistic	2 to 8 °C up to 3 years	*Short term storage:* 2 to 8 °C up to 30 days Room temperature: 8 hours before administration *Long term storage:* -25 to -15 °C	*Short term storage:* After thawed: 2 to 8 °C up to 5 days (undiluted) up to 6 hours (diluted) *Long term storage:* -80 to -60 °C up to 10 days	2 to 8 °C up to 6 months	2 to 8 °C	2 to 8 °C up to 2 years -20 °C up to 3 months	2 to 8 °C *Long term storage:* -18°C
Phase I, II results (Immunogenicity)	Seroconversion of neutralizing antibodies at day 28 3 mcg: 92% 6 mcg: 98%	For 100 mcg Anti-S-2P geometric mean titer: 782,719 (619,310-989,244) (day 57) Systemic AEs:	For 30 mcg S1-Binding IgG: geometric mean titer (U/ml): - 18-55 years: 9,136 (day 28), 8147 (day 35)	>99% of 209 boosted participants had neutralizing antibody responses after 14 days No serious	For 2 doses of 5 mcg (+ Matrix M1 adjuvant) at day 35: geometric mean anti-spike IgG: 63,160 ELISA unit	100% neutralizing antibody by day 57	Day 42: 100% seroconversion IgG geometric mean titer Frozen: 14703 Lyophilized: 11143 Neutralizing AB Frozen: 49.25

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		- overall: fever, fatigue, or chills 100%	- 65-85 years: 7,985 (day 28), 6,014 (day 35) Systemic AEs: - fever: 8-17% - fatigue: 42-75% - chills: 17-58%	adverse events	Neutralizing antibody GMT: 3,906		Lyophilized: 45.95 Frozen form is used in phase III. Mostly mild to moderate AEs
Phase III trials							
Baseline characteristics of participants in phase III trials							
Countries and COVID-19 prevalence	**UNOFFICIAL RESULTS** Brazil 3.9% Chile 3.4% China 0.007% Indonesia 0.32% Turkey 2.8%	USA 7.3%	USA 7.3% Argentina 3.9% Brazil 3.9% Turkey 2.8% Germany 2.4% South Africa 2.2% (Pooled prevalence: 6.4%)	UK 4.8% Brazil 3.9%	**UNOFFICIAL RESULTS** UK 4.8%	**UNOFFICIAL RESULTS** USA 7.3% Latin America South Africa 2.2%	Moscow, Russia 2.7%
Total sample size	31,020	30,420	43,548	11,636 for Efficacy 23,784 for Safety	15,000+	43,783	21,977
Age, year, median (Range)	18-60+	51.4 (18-95) ≥65 years: 24.8%	52 (16-91) >55 years: 42.2%	18-55 >55 years: 3.8%	18-84 >65 years: 27%	≥ 18 > 60 years: 31.1%	45.3 (18-87) >60 years: 10.8%
Ethnicity	-	White 79.2%, Black 10.2%, Asian 4.6%	White 82.9%, Black 9.4%, Asian 4.3%	White 82.7%, Black 4.1%, Asian 4.4%,	No data	No data	White 98.5% Asian 1.4%
Comorbidities data	-	- Chronic lung disease: 4.8% - Cardiac disease: 4.9% - Severe obesity: 6.7% - Diabetes: 9.5%	- Chronic lung disease: 7.8% - Cardiac disease: 0.5-1% - Obesity: 35.1% - Diabetes: 7.8%	- Respiratory disease: 10-13% - Cardiac disease: 7-12% - Diabetes: 1-3%	No data	No data	Either diabetes, hypertension, ischemic heart disease, obesity: 24.8%

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Healthcare workers	86.2%	25.4%	(Not reported)	79.7%	No data	No data	About 0.45%
Pregnancy	0%	0%	0%	0%	No data	No data	0%
Children	0%	0%	(100 children aged 12-15 years were accidentally enrolled)	0%	0%	0%	0%
Median follow-up	1 year (Protocol)	2 months after the 2nd dose	2 months after the 2nd dose	2 months after the 2nd dose	No data	No data	2 months after 2nd dose
Comparator	Placebo	Saline	Saline	Meningococcal vaccine/Saline	Saline	Saline	Placebo: vaccine buffer

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Validity of phase III trials							
Appraisal using User's Guide	No data	Randomized: Yes Concealment: Yes **Analysis: Per protocol, *Modified intention-to-treat** Balanced baseline: Yes Blinding: Patients, clinicians and assessors **Follow-up complete: Ongoing** ***Excluded 4.15% and 3.77% in vaccine and placebo groups** **Interim analysis**	Randomized: Yes Concealment: Yes **Analysis: Per protocol, Modified intention-to-treat** Balanced baseline: Yes Blinding: Patients, clinicians and assessors **Follow-up complete: Yes But 16.1% not assessed for COVID-19 infection ≥ 7 days after second dose**	Randomized: Yes Concealment: Yes **Analysis: Per protocol, Modified intention-to-treat** Balanced baseline: Yes Blinding: Patients **Follow-up complete: Ongoing** **Protocol violation: half dose** **Interim analysis: n=11,636/23,848**	No data	No data	Randomized: Yes Concealment: Yes **Analysis: Per protocol,** Balanced baseline: Yes Blinding: Patients, clinicians, and assessors **Loss follow-up/ Excluded participant/ missing data rate: 34%** **Interim analysis**
GRADE level of evidence	No data	1B (RCT with important limitations)	1B (RCT with important limitations)	1B (RCT with important limitations)	No data	No data	1B (RCT with important limitations)

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Result of phase III trials							
Outcome assessment	Symptom diary, periodic nasal swab/serology	Electronic symptom diary (and PCR confirmed for symptomatic participants)	Electronic symptom diary (and PCR confirmed for symptomatic participants)	Periodic nasal swab and phone calls	Self report	Electronic symptom diary (and PCR confirmed for symptomatic participants)	Electronic symptom diary (and PCR confirmed for symptomatic participants)
Efficacies in ***asymptomatic*** COVID infection	Unofficial report from Brazil, Indonesia, Turkey: Vaccine group: 1.24 - 1.83% Placebo group: 3.48 - 3.63% **Efficacy: 49.6% - 64.2%** **NNT: 41 – 56** **18-24/1,000 vaccinated patients**	No information	No information	Vaccine group: 0.9% Placebo group: 1.2% **Efficacy: 27.3%** **NNT: 334** **3/1,000 vaccinated patients** Subgroup LD/SD Vaccine group: 0.6% Placebo group: 1.5% **Efficacy: 58.9%** **NNT: 112** **9/1,000 vaccinated patients** Subgroup SD/SD Vaccine group: 1% Placebo group: 1% **Efficacy: 3.8%** **NNT: 0** **0/1,000 vaccinated patients**	No information	No information	No information

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Efficacies in ***symptomatic*** COVID infection	Unofficial report from Brazil, Indonesia, Turkey: Vaccine group: 0.2% Placebo group: 1.2% **Efficacy 78.2%** **NNT 102** **10/1,000 vaccinated patients**	**Per protocol:** Vaccine group: 0.08% Placebo group: 1.31% **Efficacy 94.1%** **NNT 84** **12/1,000 vaccinated patients** **modified ITT** Vaccine group: 0.13% Placebo group: 1.84% **Efficacy 93.0%** **NNT 59** **17/1,000 vaccinated patients**	**Per protocol:** Vaccine group: 0.04% Placebo group: 0.88% **Efficacy 95.0%** **NNT 120** **8/1,000 vaccinated patients** **modified ITT** Vaccine group: 0.23% Placebo group: 1.27% **Efficacy 81.8%** **NNT 97** **10/1,000 vaccinated patients**	Vaccine group: 0.5% Placebo group: 1.7% **Efficacy 70.4%** **NNT 84** **12/1,000 vaccinated patients** Subgroup LD/SD Vaccine group: 0.2% Placebo group: 2.2% **Efficacy 90.0%** **NNT 50** **20/1,000 vaccinated patients** Subgroup SD/SD Vaccine group: 0.6% Control group: 1.6% **Efficacy 62.1%** **NNT 100** **10/1,000 vaccinated patients**	In UK phase III trial **Efficacy: 89.3%** **6 cases in vaccine group** **56 in placebo group**	Prevention of moderate to severe disease: **Over all 66% effective** USA 72% Latin America 66% South Africa 57% (in South Africa > 90% of cases attributed to South Africa Escape Variant)	**Per protocol:** Vaccine group: 0.1% Placebo group: 1.3% **Efficacy 91.5%** **NNT 86** **12/1,000 vaccinated patients** **ITT** Vaccine group: 0.08% Placebo group: 0.86% **Efficacy 90.8%** **NNT 128** **8/1,000 vaccinated patients** (Due to high rate of loss follow-up and missing data, in worst case scenario efficacy can be as low as 18.9%)

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Efficacies in ***moderate to severe*** COVID disease: 1. Hospital admission rate 2. Patients requiring oxygen therapy rate 3. ICU admission rate 4. Mortality rate	1. Efficacy 100% Vaccine = 0/6215 = 0.00% Placebo = 13/5979 = 0.21%	1. Efficacy 100% Vaccine = 0/13934 = 0.00% Placebo = 9/13883 = 0.06% 2. Efficacy 100% Vaccine = 0/13934 = 0.00% Placebo = 28/13883 = 0.02% 3. No information 4. Efficacy 15% Vaccine 6/15184 = 0.039 % Placebo 7/15165 = 0.046 %	Composite of 3/4 Efficacy 74.7% Vaccine group: 1/19,965 (0.005%) Placebo group: 4/20,172 (0.02%) No COVID-19-associated deaths were observed	1. Efficacy 80% Vaccine group: 2/12,021 Control group: 10/11,724 2. Efficacy 100% Vaccine group: 0/12,021 Control group: 10/11,724 3. Efficacy 100% Vaccine group: 0/12,021 (0) Control group: 2/11,724 (0.02%) 4. Efficacy 100% Vaccine group: 0/12,021 Control group: 1/11,724 (0.009%)	No information	Prevention of severe disease 85% effective Complete prevention of hospitalization and death	Moderate to severe cases (contains 2/3) efficacy 100%. 4. Efficacy 0.44% Vaccine group: 3/16,501 Placebo group: 1/5,476

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Efficacy in sub-population	Pregnant: Not included Children: Not included Elderly: No result	Pregnant: Not included Children: Not included Age: ≥ 65 y: 86.4% (61.4-95.2)	Pregnant: Not included Children: No, included by some accidental enrollment Age: ≥ 65 y: 94.7% (66.7, 99.9) ≥ 75 y: 100% (-13.1, 100.0)	(No result)	No information	No information	Pregnant: Not included Children: Not included Age: >60 y: 91.7% (61.1, 98.2)
Efficacy in mutant strains of virus	(No data)	(No data)	(No data)	(No data)	In South Africa phase IIb trial ~ 90% of cases attributed to South Africa Escape Variant Efficacy: 60%	(No data)	(No data)
Vaccine-related adverse events (AE)	Brazil Both arm (n=7913) 1st dose 6803 (87.9%) 2nd dose 2722 (63.1%) Indonesia Vaccine arm (n=405) 1st dose: 245 (60.5%) 2nd dose: 206 (51.9%) Turkey	**Solicited AEs:** Mainly pain. Vaccine vs placebo 1st dose: 84.2% vs 19.8% 2nddose: 88.6% vs 18.8% **Systemic AEs** 1st dose: 54.9% vs 42.4% 2nd dose: 79.4% vs 36.5% Most common: fatigue, headache, myalgia, arthralgia,	**Solicited AEs** Injected site reactions (84.1%), fatigue (62.9%), headache (55.1%), muscle pain (38.3%), chills (31.9%), joint pain (23.6%), fever (14.2%). **Serious adverse events:** <0.5%. Vaccine group: Shoulder injury related to Vaccine administration, Right axillary lymphadenopathy,	**Serious adverse events** Vaccine group: 79/12021 (0.65%) Control group: 89/11724 (0.76%) (ARR -0.001) **Transverse myelitis:** one possible related to vaccine	Low incidence of serious adverse event and comparable between vaccine and placebo	Fever 9% (grade 3 = 0.2%) Serious adverse event: lower in vaccine group No anaphylaxis	**Serious adverse events** Vaccine group: 45/16427 (0.27%) Control group: 23/5435 (0.42%) (ARR -0.149) Deep vein thrombosis (1), Hypertensive crisis (2), Acute myocardial infarction (2). None considered

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	Systemic AE in vaccine arm 1st dose: 373 (of 603; 61.9%) 2nd dose: 180 (of 1221; 14.7%)	chills, nausea/vomiting, and fever. Commonly occurred in younger than older participants Unsolicited adverse events Overall, 23.9% vs 21.6%	Paroxysmal ventricular arrhythmia, and Right leg paresthesia No deaths				associated with vaccination, as confirmed by the independent data monitoring committee
Summary	• Vaccine efficacy and safety have been reviewed indicating Moderna achieved highest relative efficacy in symptomatic subjects, followed by Pfizer, Gumaleya, Novavax, Sinovac, Astra/Oxford, and Johnson & Johnson with relative risk reductions of 93%-94%, 81.8%-95%, 91.6%, 89.3%, 78.2%, 70.4%, and 57-72%, respectively. • If we vaccinate 1000 people with Moderna, Pfizer, Sinovac, and Astra/Oxford, we will be able to prevent Covid-19 infections in 12-17, 8-10, 12, 10, and 12 subjects. • Serious adverse events (i.e., ICU admission and death) are rare, i.e., 0% to 0.039% in all vaccines, and 0% to 0.046% in controls. • These findings are based on Grade IB level of evidences with short term follow-up (2 months), except for Sinovac, Novavax, and Johnson & Johnson data are from unofficial non-peer-reviewed reports, therefore we are awaiting those manufacturers' results • Efficacy in pregnant women, children, older adults are lacking due to lower number of participants in these subgroups • Vaccination strategies should consider efficacy, number of patients that can prevented, level of evidence, side effects, administration, storage, and availability aspects.						

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