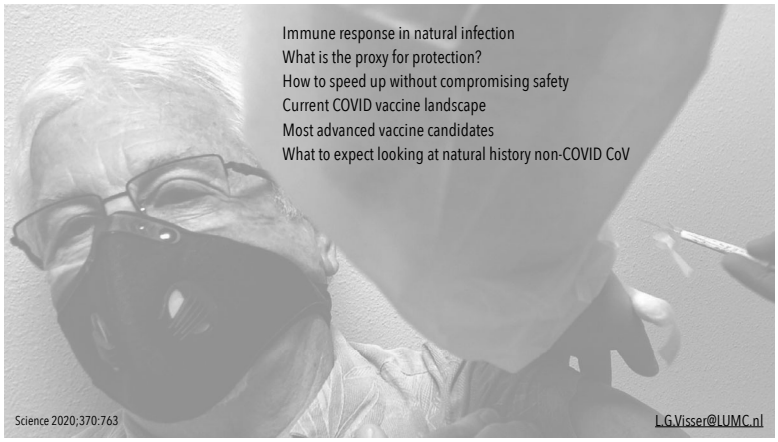
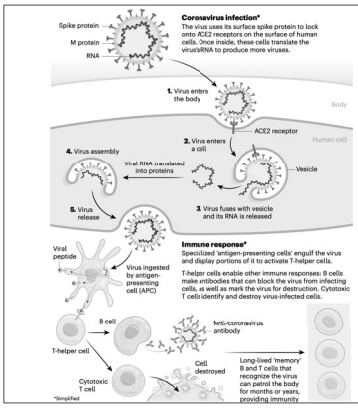
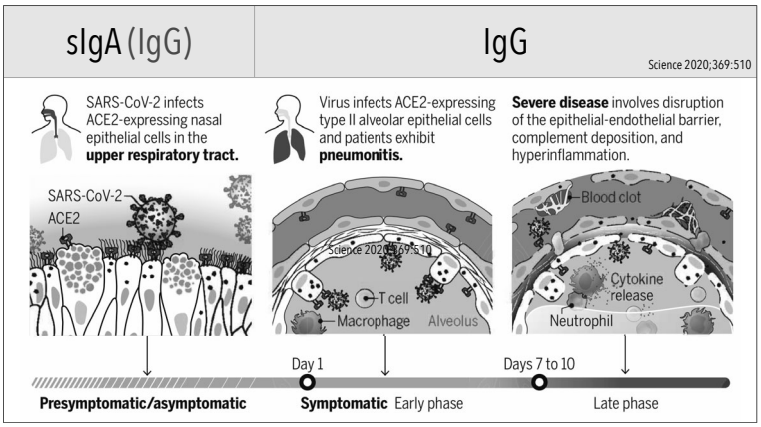


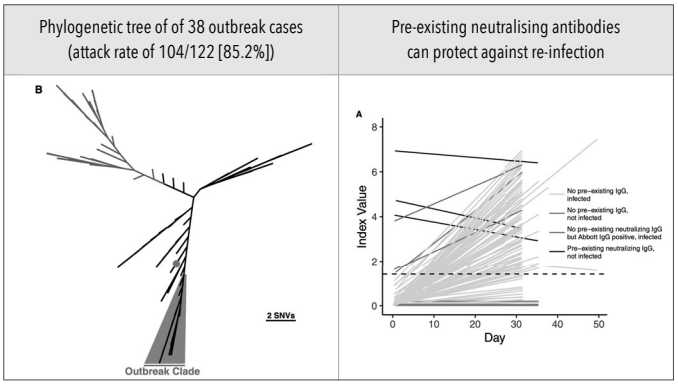


Spike protein locks onto ACE2 and pulls the virus into the cell
B-cells will make antibodies that can block virus from entry into cells
Natural infection induces mucosal sIgA and systemic IgG
Cytotoxic T-cells destroy virus-infected cells
Long-lived memory B- and T-cells patrol the body providing immunity upon re-exposure

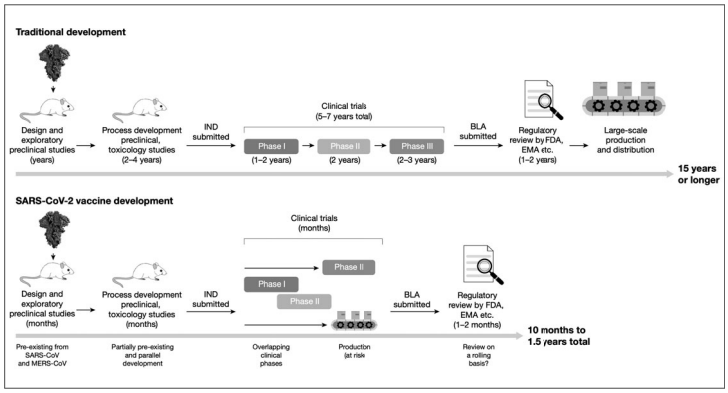
Nature 2020; 580:576



*McMahan et al. Nature 2020, 4 December



J Clin Microbiol 2020;58:e02107



Nature 2020; 580:516

Continuous safety evaluation ensures vaccine safety	
Long-standing experience vaccine development	Rigorous pre-clinical and clinical testing
Cutter incident (1955) Inadequate inactivation polio vaccine virus	All batches are tested for safety
Vaccine associated enhanced respiratory disease Formaline inactivated RSV vaccine (1960) No neutralising antibodies	Understanding mechanisms of action vaccine and correlates of immune protection
Additional testing if serious event are detected pre- and post-licensure Rotavirus vaccine and intussusception (1998)	Rare severe adverse events trigger a safety pause to trial or use
	Continuing surveillance of potential vaccine-related adverse events post-licensure and post-marketing

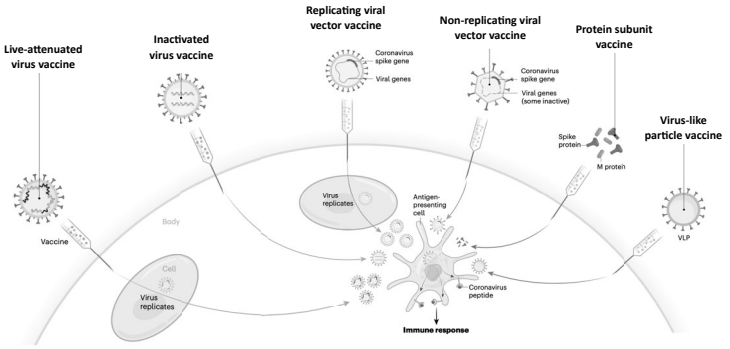
Science 2020, 17 November

Potential risks associated with vaccine development for COVID-19

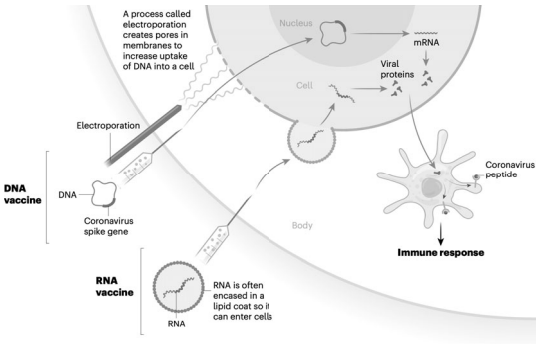
	Antibody-mediated		T cell–mediated
	ADE	VAERD	VAERD
Mechanism	Fc-mediated increase in viral entry	Immune complex formation and complement deposition	T_H2-biased immune response
Effectors	Macrophage activation and inflammatory cytokines	Complement activation and inflammatory cytokines	Allergic inflammation and T_H2 cytokines
Mitigation	Conformationally correct antigens and high-quality neutralizing antibody		T_H1-biasing immunization and $CD8^+$ T cells

Science 2020;368:945

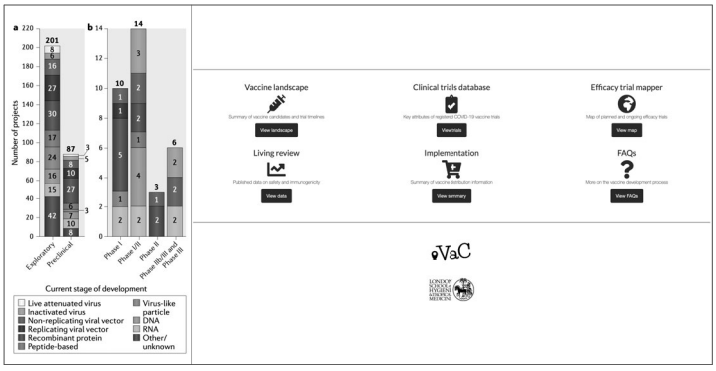
Protein-based vaccines	Gene-based vaccines
Inactivated whole virus	Live-attenuated virus vaccine
Virus like particle	Replicating recombinant vector virus (Measles vaccine virus strain)
Replication-incompetent vector virus (Adenovirus)	Nucleic acid (mRNA)
Spike protein	



Nature 2020; 580:576



Nature 2020; 580:576



Nature Rev Drug Discovery 2020;19:667

https://vac-lshtm.shinyapps.io/ncov_vaccine_landscape/#

Table 1 | Overview of NHP results

Company (ref.)	Vaccine candidate (type)	Dose range (route)	Neut. titre after prime	Neut. titre after boost	T cell response	Challenge dose (route)	URT protection	LRT protection	Species
Sinovac[34]	PiCoVacc (inactivated virion + aluminium hydroxide)	3–6 μg (i.m.)	None[a]	1:10 range[a] after first boost; 1:50 range[a] after second boos	ND	10^6 $TCID_{50}$ (i.t.)	Partial[b]	Partial (low dose)[b] Complete (high dose)	Rhesus macaques
Pfizer	mRNA-BNT162b2	30-100 μg (i.m.)	80-100	962-1,689 range	Yes	1.05 x 10^6 PFU (i.n., i.t.)	Complete (2x)	Complete (2x)	Rhesus macaques
AstraZeneca[49]	ChAdOxnCoV-19 (non-replicating AdV)	2.4×10^{10} VP; 1× cr 2× (i.m.)	1:5–1:40 range[a]	1:10–1:160 range[a]	Yes	2.6 × 10^6 $TCID_{50}$ (i.t., oral, i.n., ocular)	Non₃ (1×)[c] Non₃ (2×)[c]	Partial (1×)[c] Complete (2×)[c]	Rhesus macaques
Janssen[41]	Ad26COVS1 (non-replicating AdV)	1 × ^{0}[11] VP (i.m.)	1:100 range[d]	NA	Low	10^5 $TCID_{50}$ (i.n, i.t.)	Complete in S.ᗤP group[c]	Complete in S.PP group[c]	Rhesus macaques
Moderna[57]	mRNA-1273 (mRNA via LNPs)	2× 10–100 μg (i.m.)	ND[e]	1:501–1:3,481 range[d]	Yes, CD4, T_{FH}	7.6 × 10^5 $TCID_{50}$ (i.n., i.t.)	Non₃ (10 μg)[c] Partial (100 μg)[c]	Partial (10 μg)[c] Complete (100 μg)[c]	Rhesus macaques
Novavax[79]	NVX CoV2373 (spike protein + Matrix-M)	2×2.5–25 μg	Not reported	17,920–23,040 range[e]	ND	10^4 plaque-forming units (i.n., i.t.)	Partial (lowdose)[c] Complete (higher doses)[c]	Complete[c]	Cynomolgus macaques

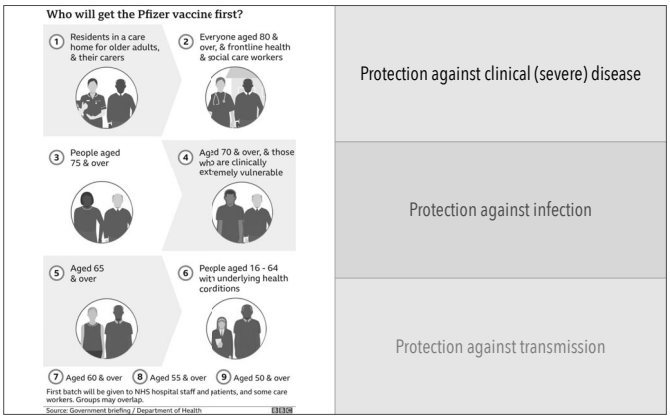
Nature 2020; 580:516 (modified results BioNTech added bioRxiv Sept 8, 2020)

BNT162b2 (Pfizer)	mRNA-1273 (Moderna)	NVX-CoV2373 (Novavax)	ChAdOx1 nCoV-19 (Astra Zeneca)	CoronaVac (SinoVac)
mRNA in lipid nanoparticles	mRNA in lipid nanoparticles	recombinant spike protein	Replication deficient vector	Inactivated whole virus
full-length spike protein with 2 stabilizing mutations	full-length spike protein with 2 stabilizing mutations	full-length spike protein with 2 stabilizing mutations	full-length wild-type version spike protein	
		saponin-containing Matrix-M		$AlOH_3$
3-week prime-boost	4-week prime-boost	3-week prime-boost	4-week prime-boost	4-week prime-boost
Medium range VNA	Medium range VNA	High range VNA	Medium range VNA	Lower range VNA
70% fever	40% fever after booster dose	Malaise, fatigue, headache	Fatigue, headache, feverish	Excellent safety
Lower reactogenicity and immunogenicity in older people				Lower antibody titres in older persons

	BioNTech BNT162 (b1/b2)	Moderna mRNA-1273	Oxford ChAdOx1-S
Developer(s)	BioNTech, Fosun Pharma, Pfizer	Moderna, NIAID	University of Oxford, AstraZeneca
Platform	RNA	RNA	Non-replicating viral vector
Dosing	2 doses, intramuscular	2 doses, intramuscular	2 doses, intramuscular
Description	Lipid nanoparticle-formulated mRNA encoding full-length spike (S) protein	Lipid nanoparticle-encapsulated mRNA encoding pre-fusion spike (S) protein	Simian adenovirus vector containing codon-optimised spike (S) protein
Efficacy data	Vaccine efficacy against COVID-19 reported to be 95% based on primary efficacy analysis of 170 confirmed cases (18 Nov 2020). These included 10 cases of severe COVID-19, 9 of which occurred in the placebo group.	Vaccine efficacy against COVID-19 reported to be 94.5% based on interim data from 95 cases (16 Nov 2020). These included 11 cases of severe COVID-19, all of which occurred in the placebo group.	Vaccine efficacy against COVID-19 reported to be 62–90% based on interim data from 131 cases (23 Nov 2020).
Storage requirements	Ultra-cold (-60°C to -80°C)	Refrigeration (2°C to 8°C) for up to 30 days or frozen (-15°C to -25°C) for long-term storage	Refrigeration (2°C to 8°C)
ONE Vaccine Access Test score	BioNTech and Pfizer given scores of 1 out of 15 and 2.8 out of 15, respectively	Moderna given score of 1.7 out of 15	AstraZeneca given score of 8.6 out of 15
Manufacture projections	50 million doses in 2020 and up to 1.3 billion doses in 2021 (30 Nov 2020)	500 million to 1 billion doses per year (26 Oct 2020)	3 billion doses in 2021 (23 Nov 2020)
Approval/licensure	Granted approval for emergency use in the UK (02 Dec 2020)	Not yet approved for widespread use	Not yet approved for widespread use

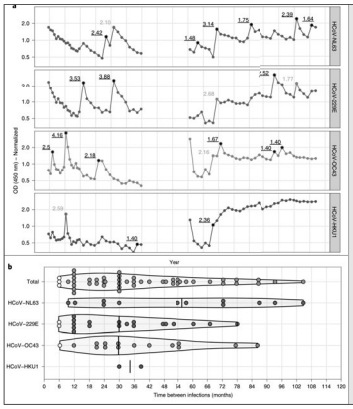
Vaccines undergoing phase III efficacy testing are included (see **Clinical trials** and **Trial mapper** tabs for further details). Information on storage requirements obtained from Poland et al (2020).

https://vac-lshtm.shinyapps.io/ncov_vaccine_landscape/#



‘Because none of us is safe until all of us is safe’

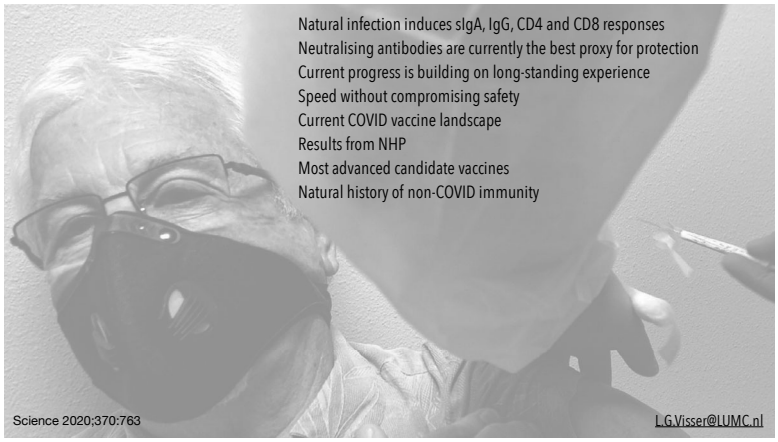
https://www.one.org/international/vaccine-access-test/



Reinfections with common cold corona virus occurs regularly over the years

1. Infections with different strains of CoV
2. Infections with same strain but antigen drift (HCoV-229De)

Nature Med 2020;26:1691


Natural infection induces sIgA, IgG, CD4 and CD8 responses
Neutralising antibodies are currently the best proxy for protection
Current progress is building on long-standing experience
Speed without compromising safety
Current COVID vaccine landscape
Results from NHP
Most advanced candidate vaccines
Natural history of non-COVID immunity
Science 2020;370:763
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