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## NEWS ANALYSIS

# Covid-19: Where are we on vaccines and variants?

Nearly a year after WHO declared the covid-19 pandemic, **Elisabeth Mahase** reports on the latest developments in vaccines, variants, and diplomacy

Elisabeth Mahase

### Have any new variants emerged?

We've heard a lot about B.1.1.7 (first detected in the UK), B.1.351 (first detected in South Africa), and P.1 (detected in Manaus, Brazil), but other variants have also emerged, including one in New York. Named B.1.526, the variant contains the same E484K mutation that has caused so much concern in B.1.351. This mutation is thought to allow the virus to escape some of the body's immune response. Vaccines developed against the original virus have also been

found to be less effective against B.1.351 (table 1). In a preprint released on 25 February,<sup>20</sup> researchers said the variant was "surging, alarmingly, in our patient population over the past few weeks" and that patients with this novel variant "were on average older and more frequently hospitalised." They added that further analysis showed that the B.1.526 variant was "scattered in the northeast of US, and its unique set of spike mutations may also pose an antigenic challenge for current interventions."

Table 1 | Main vaccines that have been approved or rolled out in some capacity (such as for emergency use)

Manufacturers (vaccine name)	Technology used	Doses	Efficacy against symptomatic disease*	Safety profile (from phase III trials)	Efficacy against variants*		Are updated versions being made to target variants?	Reported effectiveness from mass rollout
					B.1.1.7. (first detected in UK)	B.1.351 (first detected in South Africa)		
Pfizer and BioNTech (Comirnaty)	mRNA	2	95% <sup>1</sup>	Of the covid-19 vaccine group, 27% of participants reported any adverse event, compared with 12% taking a placebo. This was mainly due to transient reactogenicity events, such as injection site pain. Few people in either group had severe or serious adverse events.	Unknown	Unknown	Yes	Reduced symptomatic cases by 94%, hospital admissions by 87%, and severe covid-19 by 92% in Israel <sup>2</sup>
Oxford and AstraZeneca (AZD1222)	Viral vector	2	82.4% (12 weeks between doses) <sup>3</sup>	Serious adverse events occurred in 168 participants: 79 in the vaccine group and 89 in the controls. Two cases of transverse myelitis were originally reported as potentially related to the vaccine but later determined to be unlikely to be related.	74.6% <sup>4</sup>	TBC (unconfirmed reports as low as 10%) <sup>5</sup>	Yes	In Scotland, risk of hospital admission for covid-19 fell by up to 94% four weeks after first doses administered <sup>6</sup>
Moderna and NIH (mRNA-1273)	mRNA	2	94.5% <sup>7</sup>	Solicited adverse events at the injection site occurred much more often in the vaccine than in the placebo group. Serious adverse events were rare, with incidence similar in the two groups.	Unknown (but reports of decrease in neutralising antibodies) <sup>8</sup>	Unknown	Yes <sup>9</sup>	TBC
Gamaleya (Sputnik V)	Viral vector	2	91.6% <sup>10</sup>	Forty five of 16 427 participants in the vaccine group and 23 of 5435 in the placebo group had serious adverse events, but none were considered associated with vaccination.	Unknown	Unknown	Unknown	TBC
CanSinoBio (Convidecia)	Viral vector	1	65.7% <sup>11</sup>	Unknown	Unknown	Unknown	Unknown	TBC

Table 1 | Main vaccines that have been approved or rolled out in some capacity (such as for emergency use) (Continued)

Manufacturers (vaccine name)	Technology used	Doses	Efficacy against symptomatic disease*	Safety profile (from phase III trials)	Efficacy against variants*	Are updated versions being made to target variants?	Reported effectiveness from mass rollout	
Novavax (NVX-CoV2373)	Protein	2	95.6% <sup>12</sup>	A preliminary review of the safety database showed that severe, serious, and medically attended adverse events occurred at low levels and were balanced between vaccine and placebo groups. <sup>13</sup>	85.6%	60%	Yes <sup>14</sup>	TBC
Johnson & Johnson (Ad26.COV2.S)	Viral vector	1	72%	More serious adverse events were reported in participants who received placebo than in the vaccine group. <sup>15</sup>	Unknown	57% <sup>16</sup>	Unknown	TBC
Sinopharm (BBIBP-CorV)	Inactivated virus	2	79.34% <sup>17</sup>	Unknown	Unknown	Unknown (but reports of weekend effect) <sup>18</sup>	Unknown	TBC
Sinovac (CoronaVac)	Inactivated virus	2	50.4% <sup>19</sup>	Unknown	Unknown	Unknown	Unknown	TBC
Bharat Biotech (Covaxin)	Inactivated virus	2	Unknown	Unknown	Unknown	Unknown	Unknown	TBC

\* Vaccines' efficacy cannot be directly compared because of differing clinical trial designs

### What about the variant found in Finland?

The Fin-796H variant, identified by researchers from Vita laboratories and the Institute of Biotechnology at the University of Helsinki, is reported to have mutations similar to those seen in B.1.1.7 and B.1.351. Additionally, it also has a mutation in one of the regions (N) recognised by PCR testing. However, experts said this should not cause major problems, as most PCR testing relies on two or three different assays that detect different parts of the virus.<sup>21</sup> A similar issue was seen with the B.1.1.7 variant, which escaped the assay that detects the S gene of the virus.<sup>22</sup>

### Are the vaccines being updated to target new variants?

Pfizer and Oxford-AstraZeneca are reported to be in discussions regarding updating their vaccines to target new variants. Meanwhile, Moderna has said it is waiting on approval from regulators to start trialling a modified version of its vaccine that will target the B.1.351 variant.<sup>23</sup>

### How is the rollout going in Israel?

A published study assessing Israel's vaccination rollout between 20 December and 1 February showed that two doses of the Pfizer-BioNTech vaccine reduced symptomatic cases by 94%, hospital admissions by 87%, and severe covid-19 by 92%.<sup>24</sup> The paper also suggested that the vaccine was effective against the B.1.1.7 variant. The lack of data on B.1.351 cases means there is no information on vaccine effectiveness against this variant.

### What about Germany?

Despite having stock, Germany is having problems getting people to turn up to appointments, as many citizens and healthcare workers

are rejecting the Oxford-AstraZeneca vaccine. This hesitancy came after a German newspaper caused international upset when it insisted that the vaccine was ineffective in older people, on the basis of a single anonymised source and without evidence.<sup>25</sup> The country's regulator then approved the vaccine only for adults under 65. Two weeks after 1.45 million doses of the vaccine were delivered, only 271 000 have been administered.<sup>26</sup> Chancellor Angela Merkel has since stated she will not have the Oxford-AstraZeneca vaccine as it is not recommended for her age group.<sup>27</sup>

This was despite the European Medicines Agency,<sup>28</sup> and many other countries, approving the vaccine for the over 65s, including, most recently, Canada. The Canadian drug regulator said that the vaccine's efficacy in this age group was supported by factors outside clinical trials.<sup>29</sup> This came after early evidence from the rollout to healthcare workers and elderly people in Scotland showed that the vaccine reduced the risk of admission to hospital by up to 94%, four weeks after the first dose was administered.<sup>30</sup> These findings may have prompted a change to the recommendations in France, where the vaccine is now approved for adults up to 75, after originally being restricted to those under 65.<sup>31</sup>

### When will the Johnson & Johnson vaccine be rolled out?

The single dose covid-19 vaccine made by Janssen, the pharmaceutical arm of Johnson & Johnson, has now been given emergency use authorisation by the US Food and Drug Administration (27 February).<sup>32</sup> The FDA said its analysis of data from 39 321 adults with no previous signs of infection reported the efficacy as 66.1% (95% confidence interval 55% to 74.8%) for preventing moderate to severe or critical covid-19, 28 days after vaccination. Johnson & Johnson previously reported that the vaccine

provided 72% protection against moderate to severe covid-19 infection in the US, but the proportion fell to 66% in Latin America and 57% in South Africa, 28 days after vaccination.<sup>33</sup>

The US is expected to begin rolling out the first three to four million of its 100 million dose order this week. In the UK the Medicines and Healthcare Products Regulatory Agency is reviewing the vaccine under its rolling review system. The UK has ordered 30 million doses.

The vaccine could also soon be made available to low income countries through the Covax programme, which has an agreement with Johnson & Johnson for up to 500 million doses.<sup>34</sup> Covax is a collaboration among organisations such as Gavi (the global alliance for vaccines and immunisation), the World Health Organization, the Coalition for Epidemic Preparedness Innovations, Unicef, and the World Bank, focused on ensuring that lower income countries can get covid-19 vaccines.

### Are countries getting better at sharing vaccine stock?

Equitable access has been a major concern during the pandemic, with many healthcare leaders warning that vaccine nationalism would allow the virus to continue thriving and lead to even more worrying variants.<sup>35 36</sup>

There have been some small but positive developments in this area. Portugal has announced it will send 5% (1.75 million doses) of its covid-19 vaccines to a group of Portuguese speaking African countries and East Timor in the second half of 2021.<sup>37</sup> These countries, including Angola (population 32 million) and Mozambique (30 million), are former colonies of Portugal. Portugal has just over 10 million people but is entitled to 35 million vaccine doses as part of the EU scheme.

Meanwhile, shipments of the Oxford-AstraZeneca vaccine supplied through Covax have been delivered to Ghana (600 000 doses) and Ivory Coast (504 000).<sup>38</sup> These first deliveries were part of an effort to deliver at least two billion doses of covid-19 vaccines by the end of 2021.<sup>39</sup>

Israel has also reportedly begun sending excess vaccine stock to countries with which it hopes to improve diplomatic relations, including Czech Republic, Honduras, and Guatemala.<sup>40</sup> However, at the same time the country has been criticised for not sharing vaccine supplies with occupied Palestinian territories, where current stock levels are insufficient even to cover all healthcare workers.<sup>41</sup>

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