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VACCINATION

Data and distrust hamper Russia's vaccination programme

Russia has approved three homegrown vaccines against covid-19, but data from clinical trials have been hard to obtain, and the Russian public are hesitant to get their shots, reports **Polina Loseva**

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In August 2020, Russian president Vladimir Putin announced that the Ministry of Health had approved use of Sputnik V, the first Russian developed vaccine against SARS-CoV-2, for people at high risk of covid-19. Russia was between two waves of infection; lockdowns were over, restrictions had been relaxed.

No trial data were published for Sputnik V. Only a couple of reports were available about the phase I and II trials, in which mostly military men reported feeling well after vaccination, and vaccine developers from the Gamaleya Institute injected themselves as the pre-clinical trials started. According to a statement from the Association of Clinical Research

Organisations¹ (a Russian non-profit organisation that includes drug companies) testing was “a gross violation of the very foundations of conducting clinical trials, Russian legislation, and generally recognised international norms.” Still, Putin sought to reassure to the public by declaring that one of his daughters (he never mentioned her name) had already received her shot and had a high antibody titre.

This was not enough to convince the Russian public: less than 40% would agree to get vaccinated, according to periodic independent polls (fig 1).

Fig 1 | Percentage of people willing to get a Russian vaccine. Source: Levada Center

Data for the phase I and II trials were published in the *Lancet* in September 2020,² and raised further questions. Critics noted the small cohort size and limited characterisation of the convalescent plasma controls, but also suspicious patterns that appeared repeatedly in several figures.³ “It seems to us,” a group of scientists wrote in a note of concern, “that on the grounds of simple probabilistic evaluations, the fact of observing so many data points preserved among different experiments is highly unlikely.”

A phase III trial was expected to shed light on these issues. Meanwhile, the first healthcare workers received their shots.

The preliminary phase III trial data were released on 11 November,⁴ just days after Pfizer/BioNTech and Moderna declared their candidate mRNA vaccines to be effective in phase III trials. Sputnik V’s effectiveness, claimed as 92%, was similar to that of Pfizer/BioNTech and Moderna. President Putin announced a national vaccination campaign on 2 December, hours after the UK had made a similar declaration. “I know the industry and the [medical] network are generally ready,” Putin said, “Let’s take this first step.”

Within a few days, healthcare workers and teachers were able to get jabs, and within a month, older people, social workers, and journalists. By mid

January, vaccination became available to everyone, which effectively brought clinical trials to a halt. Trial participants, unsure which group they were in, started to ask for the guaranteed medicine. But among the wider public, demand for the vaccine appeared low.

In February 2021, the developers of Sputnik V claimed in a paper in the *Lancet* that the vaccine “showed 91.6% efficacy against covid-19 and was well tolerated in a large cohort.”⁵ Yet, according to one poll, about 20% of Russian citizens were willing to travel abroad to get a foreign vaccine instead. Another 40% intended to wait for a foreign vaccine to be approved and available in Russia. At the time of writing, none are.

A year on, the Ministry of Health still refuses to publish long term data on Sputnik V, as these results “contain commercially confidential information.” The Ministry also avoids disclosing the death rate among vaccinated people, citing the “impracticality” of doing so, “as this data does not reflect any interrelation between the lethal case and the vaccination and may provoke negative attitude towards vaccination.” Data on side effects⁶ and virus neutralisation⁷ were available only as part of a study from Argentina.

Data scrutiny

By spring 2021, about 3% of Russians had received covid-19 vaccines (compared with almost 30% of people in the UK). More than 60% of those polled said they had no trust in the Russian vaccination campaign.

Two more Russian developed vaccines received swift domestic approval with no clinical data. Both became widely available just as the phase III trials began.

EpiVacCorona—the patent for which is held by a group including the head of the Russian Federal State Agency for Health and Consumer Rights—consists of artificially synthesised protein subunits. CoviVac—developed by the Chumakov Institute—is a classic “dead” virus preparation. The absence of viral vectors in both vaccines led experts to suggest that they would be less likely to cause side effects than the adenovirus based Sputnik V. Many people rushed to get a shot of EpiVacCorona or CoviVac, which created queues and shortages never seen for Sputnik V.

In March 2021, the Kremlin announced that Vladimir Putin had been vaccinated. Officials declined to name the vaccine, stating only that all three available vaccines were effective and reliable. Only one report⁸ on the phase I and II trials for EpiVacCorona appeared by the end of March in *Infection and Immunity*, a Russian journal founded by an institution under the Russian Federal State Agency for Health and Consumer Rights, which also manages Vector, the developer of EpiVacCorona. The report stated that the vaccine had

“100% immunogenicity”, although the data were impossible to verify. Vector used its own test system to assess the antibody titre and claimed that no other system was suitable for such measurements. However, as no culture test results were provided, it remains unknown whether those antibodies actually protected the cells from infection.

By June 2021, several citizen science groups (groups of specialists collaborating separately from the government) had reported their data on EpiVacCorona and CoviVac.⁹ The true immunogenicity of EpiVacCorona appeared to be lower than declared (70% versus the 100% claimed in official statements). Moreover, as a preprint stated, “immunisation with this vaccine did not lead to emergence of neutralising antibodies in healthy volunteers.” Two further^{10 11} preprints have since been issued (one by a group of epidemiologists from St Petersburg, the other by a scientist and a science journalist), both claiming negative efficacy for EpiVacCorona. This could also be because of the small size of the cohort studied, or because of the tendency in vaccinated people to be less cautious about spreading infection, preprint authors suggested.

The immunogenicity of CoviVac also appears¹² to be lower than officially claimed (less than 50% versus the 75% claimed). But, as the citizen scientist reported, it does seem to work well as a primer or booster for Sputnik V. The developers of CoviVac have issued a preprint on the phase I-II trials beginning February 2022,¹³ but developers of both vaccines have still to present clinical data from phase III.

Mandatory vaccination

In June 2021, Vladimir Putin disclosed it was the Sputnik V vaccine he had received, rebutting rumours that it had been Pfizer or Moderna. But Russians had other worries: the delta variant had emerged, pushing the government to introduce mandatory vaccination.

First, companies were obliged¹⁴ to get 60% of their staff vaccinated and another 30% to work remotely. Then, a QR code covid passport system was introduced: a code was generated for every person vaccinated, recovered, or recently tested negative. This was required to access public places, except for grocery stores, pharmacies, and public transport, although implementation varied from region to region.

These measures seemed to work. Vaccination numbers reached 15% of the population by July and 35% by the end of August 2021 (fig 2). However, the true number of people vaccinated is a point of contention: trade in fake vaccination certificates peaked as the QR codes were introduced, with certificate prices as high as several thousand roubles (£100, €118, \$135).

Fig 2 | Rate of vaccination in Russia

After a short respite, case numbers started to rise again, and autumn 2021 brought new restrictions and lockdowns. In early November, a fourth wave of covid-19 provoked another period of “non-working days”—the term the Russian government uses instead of “lockdown.” To ensure greater consistency between regions, the government proposed plans to unify QR code requirements for access to public places, and separately for intercity and international travel. This sparked anger and sometimes unrest around the country.¹⁵ According to the National Anxiety Index survey (which ranks issues by the volume of discussion in social networks and media) by the end of 2021, Russians feared the QR code system more than SARS-CoV-2.

Russia enters 2022 with three two-shot vaccines (and one booster, Sputnik Light, which is a single dose of the normally two-dose Sputnik V). Sputnik V has proved to be effective, though lacks long term data. EpiVacCorona appears to be ineffective, and the effectiveness of CoviVac is still unknown. No other vaccines are accepted to obtain a QR code.

At the time of writing, less than 50%¹⁶ of the Russian population is vaccinated (most with Sputnik V), although the real rate might be lower. According to Viktor Kabanov, who analyses vaccination statistics for the “Watching COVID-19” Facebook community, “the rough estimate of fake certificates is by order of millions” (fig 3). The QR code laws are being continuously postponed as much of the Russian population remains opposed to restrictions.

Fig 3 | Number of websites selling fake vaccination certificates. First peak corresponds to introduction of QR codes. Second peak corresponds to point at which the QR code law was introduced. Source: Novaya Gazeta

Meanwhile, the pandemic continues. As of January 2022, the government reported more than 300 000 deaths from covid-19. Studies that include excess mortality suggest that the real number is more than a million, which would place Russia as the highest worldwide (in absolute numbers).¹⁷

Parallels with flu

Russia's approach to developing and distributing the covid vaccine looks much like its strategy for influenza. In the past, Russia developed several flu vaccines, which—like their covid counterparts—were approved despite a paucity of available data. One such vaccine was registered for use despite being shown to be ineffective against previous strains of flu. Others contain three times less the amount of antigen recommended by the World Health Organization to stimulate an immune response.¹⁸ These vaccines include adjuvants that are supposed to compensate for antigen deficiency; however, at least one of those—azoximer bromide—is of unknown efficacy.

Flu vaccination in Russia is mandatory only for certain groups, such as teachers and healthcare workers. The number of flu related deaths has not been published for several years. The latest public data, issued by the Ministry of Health in 2019, indicated several hundred victims yearly.

Fewer than 50% of Russians are vaccinated against flu, a rate similar to that for covid-19. In 2019 it was reported that fewer than half of Russian citizens planned to get a flu vaccine. A survey noted greater trust in foreign shots, although these have been in short supply in Russia for several years, and none are available at present.

Flu season usually ends around May in Russia, but covid has no such timeline. With the omicron variant spreading quickly, the country is encountering more than 150 000 cases daily (the previous peak was 41 335 cases in autumn 2021).

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