Implementation of covid-19 vaccination in the United Kingdom

Journal:	*BMJ*
Manuscript ID	BMJ-2022-070344
Article Type:	Analysis
Date Submitted by the Author:	28-Jan-2022
Complete List of Authors:	Majeed, Azeem; Imperial College London, Primary Care and Public Health Pollock, Katrina; Imperial College London, Tuberculosis Research Unit Papaluca, Marisa; Imperial College London, Department of Primary Care and Public Health Hodes, Simon; Bridgewater Surgeries, General Practice
Keywords:	COVID-19

Implementation of covid-19 vaccination in the United Kingdom

Azeem Majeed[1]
Katrina Pollock[2]
Simon Hodes[3]
Marisa Papaluca[1]

[1] Department of Primary Care and Public Health, Imperial College London, London W6 8RP
[2] Department of Infectious Diseases, Imperial College London, London W2 1PG
[3] Bridgewater Surgeries, Watford WD18 7QR

Correspondence to:
Professor Azeem Majeed
Department of Primary Care and Public Health, Imperial College London, London W6 8RP
Email: a.majeed@imperial.ac.uk
Phone: 020 7594 3368

KEY MESSAGES

- **The development of safe and effective covid-19 vaccines is one of the great success stories of the covid-19 pandemic.**
- **It is essential that decisions about implementing vaccination programmes in the UK are robust, clear and open to public and professional scrutiny.**
- **A sustainable infrastructure for vaccine delivery is needed that integrates with general practices and pharmacies.**
- **The UK needs to ensure it has the academic and industrial infrastructure to develop and test vaccines for the current and any future pandemic.**

Contributors and sources

Azeem Majeed is a professor of primary care and public health whose general practice is a member of a GP Federation delivering covid-19 vaccines. He has published on areas such as the logistical issues in vaccination programmes and addressing vaccine hesitancy. He works with local and national organisations to improve vaccine uptake.

Katrina Pollock is senior clinical research fellow in vaccinology and honorary consultant physician at Imperial College London. She is chief and principal investigator for clinical trials of novel vaccines including the Imperial College London self-amplifying RNA covid-19 vaccine candidate and the Oxford Astra Zeneca covid-19 vaccine, as well as for experimental medicine studies of prototype immunogens and human immunology studies of vaccine responses. She is leading the Imperial College London vaccine research response to covid-19

Simon Hodes is an NHS GP trainer, appraiser, PCN lead and LMC member based in Watford. He has various opinion pieces and educational modules published on GP topics including continuity of care, advanced care planning and the covid-19 vaccination programme. His practice was a first wave vaccine site.

Marisa Papaluca is a Visiting Professor at Imperial College London. She is former Senior Scientific Advisor at the European Medicines Agency where she worked for over 25 years with a focus on scientific, technical and therapeutic innovation in pharmaceuticals. She published in areas such as biotechnology and nanotechnology based medicinal products, gene therapy, cell therapy, pharmacogenetics, biomarkers, clinical trials methodology.

Acknowledgements

We thank patient collaborators from the NIHR Applied Research Collaboration NW London and the Imperial Vaccines Research Centre for their comments on the article. Imperial College London is grateful for support from the National Institute for Health (NIHR) Research Applied Research Collaboration (ARC) Northwest London. The views expressed in this publication are those of the authors and not necessarily those of the NIHR or the Department of Health and Social Care.

Patient involvement

We received feedback on the on the article from public and patient groups linked to the NIHR Applied Research Collaboration NW London and the Imperial Vaccines Research Centre. The feedback emphasised the importance of clear, positive messages about vaccination for the public; and personalised support for people who were vaccine hesitant or who had concerns about vaccination to help increase vaccine uptake.

Conflicts of Interest

We have read and understood BMJ policy on declaration of interests and have the following interests to declare: No competing interests.

Covid-19 vaccination in the United Kingdom

Standfirst

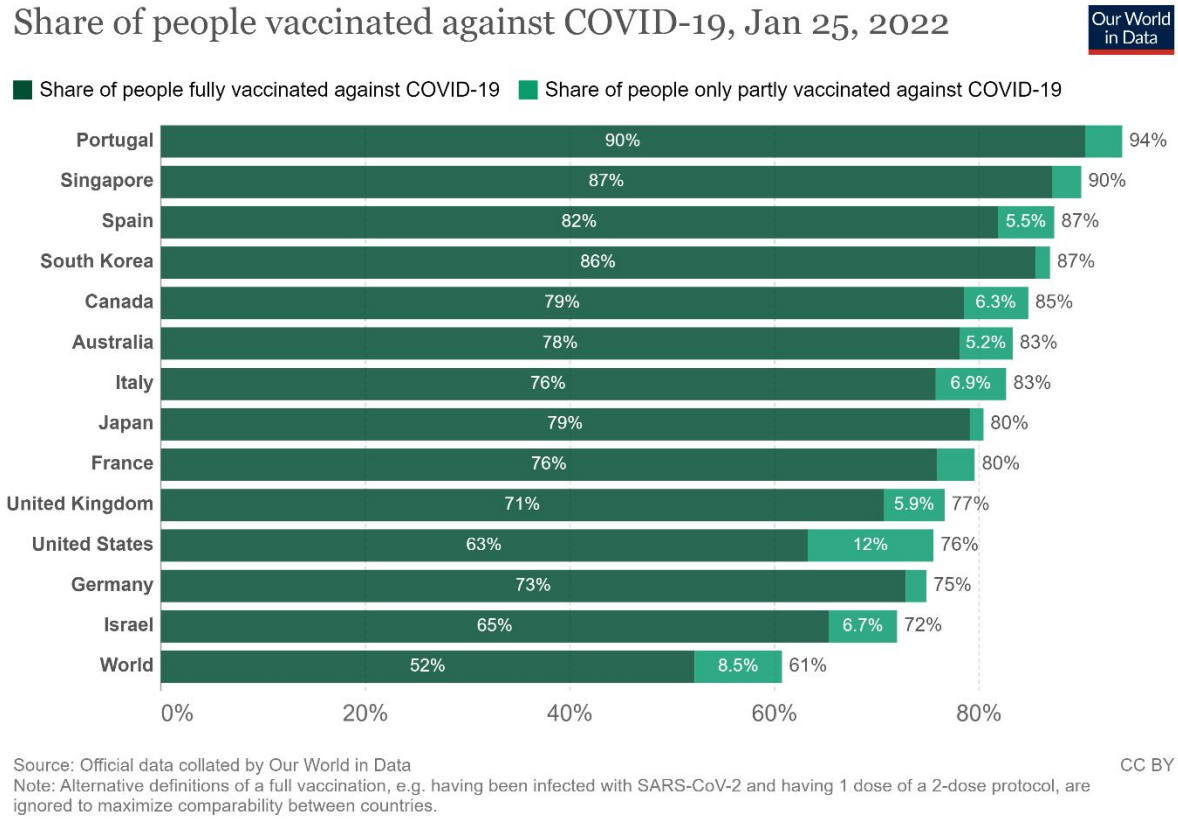
Azeem Majeed and colleagues argue that it is essential that decisions about approving covid-19 vaccines and strategies for their use in the UK are rapid and transparent; and that a sustainable infrastructure is put in place for delivering covid-19 vaccines to the public. This requires data supporting government decisions to be readily accessible and sufficiently detailed to address any questions from the public and professionals. It is also essential that the UK has the capacity to develop, test and manufacture vaccines for the current and any future pandemic at the speed and quantity needed.

Within one year of the genome of the SARS-CoV-2 being sequenced, vaccines had been developed; tested in randomised controlled trials; and rolled out in population-based vaccination programmes across the world. This is one of the great success stories of the covid-19 pandemic. Vaccination offers countries a method of suppressing the number of people with a serious illness that could lead to hospitalisation or death; thereby allowing societies to return to a more normal way of living and working.[1]

The vaccination programme in the United Kingdom (UK) has been heralded by the government as “world-beating” on many occasions.[2] But is this the case? Does the UK remain a world-leader in vaccination; and what can be learned from the approval of vaccines in the UK and the implementation of vaccination programmes by the NHS? We discuss these issues in this article. In terms of implementation, we focus mainly on England because health in the UK is a devolved responsibility, and there were some minor differences in implementation of vaccination programmes between the four UK countries.[3]

Although the covid-19 vaccination programme in the United Kingdom did start well, and more quickly than in other countries, it began to slow down during the summer of 2021 before speeding up again towards the end of 2021, and then slowing down again in early 2022.The UK has now been overtaken by many other countries in the proportion of the population vaccinated with two doses (Figure 1); although the UK does remain ahead of most countries in the proportion of adults who have three vaccinations. The UK was also slower to approve vaccines for use in children than some other countries and by early 2022 was yet to approve vaccination for all 5-11 year old children.

Figure 1.



Development and testing of covid-19 vaccines

With the onset of the covid-19 pandemic, a race began to develop and test covid-19 vaccines. The first vaccines developed fell into two broad groups: mRNA vaccines and viral vector vaccines. Early results from randomised controlled trials of these vaccines showed excellent efficacy against covid-19, and remarkable protection against serious illness and death.[4, 5] There were also no major safety concerns from these studies. Subsequent evaluations using real-world data on much larger populations than in the clinical trials confirmed the general safety and effectiveness of these vaccines in adults.[6, 7] One limitation of current vaccines is that although they are very successful in reducing the number of serious cases of covid-19, they are less effective in preventing infection from SARS-CoV-2; which means that vaccinated people can still become infected and infect others - but at a lower level than in people who are unvaccinated. Early on in the vaccination programme, this was not always communicated well to the public; leading to unrealistic expectations about how well vaccines would work in suppressing the risk of infection.

Approval of vaccines in the UK

Responsibly for licensing vaccines for use in the UK lies with the Medicines and Healthcare products Regulatory Agency (MHRA). The MHRA developed dedicated work programmes to secure the necessary scientific resources to support vaccine developers; and to establish a dialogue on areas such as manufacturing, efficacy and toxicology. They also initiated a new process called “rolling reviews”, which has allowed pharmaceutical companies to submit data to regulators in an ongoing fashion, thus allowing regulators to gain knowledge on the findings emerging from clinical studies. In UK, there are also legal provisions for emergency use authorisation in exceptional circumstances, such as population-wide vaccination campaigns during pandemics.[8]

The UK became the first country in Europe to grant an Emergency Use Authorisation for a covid-19 vaccine when the MHRA gave approval for use of the Pfizer-BioNTech vaccine in adults in the UK on 2 December 2020. The AstraZeneca vaccine was approved for use in adults on 30 December 2020. After MHRA-approval, the Joint Committee on Vaccination and Immunisation (JCVI) then makes recommendations on the use of vaccines by the NHS and prioritisation of different groups for vaccination. The final decision about the implementation of vaccine programmes lies with the government.

Given the limited supply of vaccines available to the UK in the early part of programme, the JCVI produced a priority list for vaccination – largely based on age as modelling data showed that the greatest population benefits from vaccination would come from targeting the elderly. High priority for vaccination was also given to health and care workers, and the residents and staff of care homes.[Box 1] The rationale for this strategy was to vaccinate the groups most at risk from serious illness and death first, along with those at greatest occupational risk of exposure to infection, before moving on to other groups. Overall, the policy was fair but there were criticisms that the prioritisation did not target ethnic minority groups or occupational groups other than health and care workers at higher risk from covid-19, such as people working in public transport or teaching.[9]

Box 1. JCVI advice on priority groups for covid-19 vaccination, 30 December 2020

1. residents in a care home for older adults and their carers
2. all those 80 years of age and over and frontline health and social care workers
3. all those 75 years of age and over
4. all those 70 years of age and over and clinically extremely vulnerable individuals
5. all those 65 years of age and over
6. all individuals aged 16 years[footnote 2] to 64 years with underlying health conditions which put them at higher risk of serious disease and mortality
7. all those 60 years of age and over
8. all those 55 years of age and over
9. all those 50 years of age and over

Shortly after the start of the vaccination programme in the UK, the government took the decision to prioritise delivery of the first dose of covid-19 vaccine over the second dose. Practically, this meant a delay in giving the second dose of vaccine from 3-4 weeks after the first dose to up to 12 weeks. The rationale for this was that prioritising first doses would allow more people to receive one dose of vaccine and thereby gain protection against covid-19. In theory, this would boost protection from SARS-CoV-2 at a population level, albeit at the cost of a short-term reduction in overall protection for individuals whose second dose was delayed. There was also disruption to the immunisation programme that was already underway, with many people having their appointments for their second doses cancelled.

Covid-19 case numbers were also high in the UK for large periods during 2021. This could drive transmission of infection in a partially vaccinated population, leading to the risk of developing SARS-CoV-2 vaccine escape variants. Seen by some as radical, and a departure from the clinical trials evidence, particularly for the mRNA vaccines, this delayed booster approach was not widely adopted by other countries. Subsequent research did however suggest that there were some benefits for individuals in delaying the second vaccine dose; but this did not translate into any major benefits at a population level.

Approval of vaccines for adolescents and children

Although the UK was an early adopter covid-19 vaccines for use in adults, it was slower than many other countries in implementing vaccination in 16-17 year olds and then in 12-15 year olds. Other countries were also quicker to start vaccination in children aged 5-11 years. The delay in authorising vaccination for 12-15 year olds resulted in programmes not beginning until after the start of the 2021-22 school year (August 2021 in Scotland, September 2021

elsewhere in the UK). The programme was then beset by delays (particularly in England), resulting in slow progress with vaccination at a time when many schools faced large covid-19 outbreaks. The policy in the UK was to initially offer one dose to younger people to limit the risks from myocarditis. However, a one-dose policy would reduce the benefits of vaccination, particularly against the delta variant of SARS-CoV-2 that became the predominant strain in the UK in summer 2021 and against the Omicron variant later in the year.[10] In December 2021, a two-dose approach was finally agreed for 12-15 year old children. Booster doses were also later approved for 16-17 year olds.

The JCVI did face considerable criticism for its delay in recommending vaccination for children and adolescents. However, early on, there was a lack of data supporting the unequivocal benefits versus the risks for the use of covid-19 vaccines in children. The vaccines were initially tested in trials designed to analyse safety and efficacy in the prevention of covid-19 in adults. Severe disease is considerably rarer in children (even though infection with SARS-CoV-2 is common) than in the elderly.[11] The risk/benefit analysis is therefore finely balanced, particularly in boys aged 16-19 years where there is a risk of myocarditis after vaccination. As vaccination in children becomes more widespread globally, new data is continually emerging about the risks and benefits of vaccination in this group, which should confirm its safety.

Third primary doses and booster doses

Additional problems arose after the decision to give some immunocompromised people a third primary dose of vaccine.[12] The rationale for this was these people often had a poor response to two doses of vaccine and that a third dose would prime their immune system better and offer improved protection from serious illness. The programme was rolled out with little central or local planning, resulting in considerable confusion amongst both the public and NHS staff; and leading to delays in many eligible people getting their third primary vaccine dose.[13] A key lesson from this component of the vaccination programme was the need to give the NHS adequate time to plan; and to ensure that NHS staff are fully briefed in advance of any public announcement or media briefing about vaccination policy.

Around the same time, the NHS also began to offer selected groups of people a booster vaccine dose. Real-world evaluations of vaccine efficacy suggested that protection from vaccines begins to decline after a few months from the second dose; and that a booster dose offered increased protection from serious illness and death. This is particularly the case for the Omicron variant of SARS-CoV-2. The decline in the efficacy of vaccines is greater for the AstraZeneca vaccine; casting doubt on the longer-term use of this vaccine in the UK

despite its lower cost and easier storage requirements than mRNA vaccines. Currently, we do not know how long the additional protection from a booster dose will last; and whether additional booster doses will be required in the future, possibly with modified vaccines to target new variants, thereby making covid-19 vaccination more like influenza vaccination.

IT Systems

In England, a decision was made at the start of the vaccination programme to record data using separate IT systems (Box 2) rather than directly into a patient's medical record.[3] One of the main reasons for this decision was that not all vaccination sites would have access to the electronic medical record systems used by NHS primary care teams. After vaccination, data was then transferred to the patient's general practice to ensure a record of the vaccination appeared in their electronic primary medical care record. This process sometimes failed, resulting in missing vaccination data for some patients. There were also issues with recording third primary vaccines and vaccines for people who had been vaccinated in another UK country or overseas because of delays in updating IT systems.

Box 2. IT system for Covid-19 vaccination in England

National Booking Service: Use by the public to book vaccination appointments

NHS Foundry: Data collection, processing and visualisation platform

National Immunisation Management System: Records vaccination details and adverse reactions

Outcomes4Health (Pinnacle): Used by community vaccinations sites to record details of vaccinations

National Immunisation and Vaccination System: Used to record vaccinations in hospital sites

GP Electronic Patient Record Systems: Not directly used in the vaccination programme. Vaccination records from other systems are sent electronically to these systems.

Other problems arose in the transfer of vaccination date to the NHS app in England. With proof of full vaccination now often being required for international travel (sometimes referred to as "vaccine passports"), it is essential for vaccination data to show in the NHS app. Because vaccine sites did not usually have full access to patients' medical records, they were not able to deal with these queries. General practices were therefore faced dealing with large numbers of questions from patients about data and vaccine passport issues; and also about eligibility for additional vaccinations in immunocompromised people. A key lesson for

the future is to have well-functioning IT systems and also clear processes for recording vaccines in people who were vaccinated outside the UK's official programme.

Addressing vaccine hesitancy

Concerns about Covid-19 vaccination and the resulting vaccine hesitancy are important issues globally.[14] Early survey data showed that the UK had lower overall levels of vaccine hesitancy than many other countries; however, people in the youngest age groups and those from ethnic minority groups were more likely to report they would decline covid-19 vaccination. Once vaccination started in the UK, vaccination rates were lowest in these groups, leaving around 8% of people aged 12 and over currently unvaccinated across the UK; with vaccination rates lowest in large urban areas such as London. One key lesson for the future is therefore to have clear plans in place to improve confidence in vaccines and improve vaccine uptake; particularly among younger people, those from ethnic minority groups, and people living in deprived areas. Local community engagement is essential for this and there are numerous examples from around the UK of local initiatives that helped to improve vaccine uptake.

Infrastructure for vaccine delivery

The NHS has used a range of sites to deliver vaccines. These included sites run by hospitals as well as GP-led and community pharmacy sites. In the first phase of the vaccination programme (for people aged 18 and over), the majority of vaccines were delivered by GP-led sites. In the longer term, the NHS needs to decide how covid-19 vaccines will be delivered. A GP-led programme for delivery – supported by pharmacies and hospital sites – offers many potential benefits. This includes the easier access to GP and pharmacy sites for patients than hospitals; and on the ongoing relationships that primary care teams have with their patients that can help improve vaccination rates in people who are vaccine hesitant or who are not concerned by the possible impacts of covid-19 on their health. The greater frequency of contact between NHS primary care staff and patients also offers opportunities to increase uptake through raising vaccination during other clinical encounters, as well as providing the opportunity for health promotion activities, including co-administration of other vaccines such as for influenza during vaccination appointments.

Monitoring vaccine uptake, safety and efficacy

One area in which the UK excelled internationally was in using data from the NHS, covid-19 testing, and national mortality records to monitor vaccine uptake, safety and effectiveness. Using data from the four UK nations, Public Health England established a dashboard that allowed daily vaccine delivery data to be viewed (this work later transferred to the Health

Security Agency).[15] Other outputs included weekly vaccination publications with more detailed data on vaccine uptake by age group. Some vaccine efficacy data was also included in these publications.[16]

Additional data on vaccine safety and efficacy came from information from electronic GP records linked to other data, and the yellow card scheme that allows reports of side effects from both professionals and patients.[8] This allowed research on the effectiveness of vaccines; for example, in preventing hospitalisations and deaths; as well as research on the side-effects of vaccination. Because randomised controlled are generally too small to identify rare but serious side effects, large clinical databases are needed to provide these data. In the UK, this includes databases such as OpenSAFELY and QResearch (58 million and 12 million patients respectively). [17, 18] Real-world data has also informed vaccination policy in groups for whom data was lacking in clinical trials – for example, in pregnant women and in young people.

In the longer term, the large clinical databases established in the UK will provide information for public health planning globally. This would include, for example, information on how quickly vaccine efficacy weakens in different groups of people and the effectiveness of booster doses; which will guide policies on the necessity and frequency of additional vaccinations. The databases will also allow the detection of rare but serious side effects from vaccination. It will also be possible to compare the safety and efficacy of different vaccines; and the effectiveness of vaccines against any new variants of SARS-CoV-2 that emerge.[8]

Ensuring vaccine supply for the UK

Early on in its vaccination programme, the UK government found itself in a dispute with the European Commission, related to the failure of AstraZeneca to supply the contracted volumes of its vaccines to member states of the European Union.[19] The European Commission then threatened to reduce exports of Pfizer vaccines to the UK. In the final event, no restrictions were imposed and the UK continued to received its due amounts of Pfizer vaccines. The episode does illustrate, however, that the UK is currently very reliant on overseas-manufactured vaccines (principally, Pfizer vaccines from the European Union). With the USA also prioritising its own citizens for vaccines, the UK government will need to consider how it works with the pharmaceutical industry, biotechnology companies and universities to ensure that the UK can develop, test and manufacture vaccines for the current and any future pandemic at the speed and quantity needed.

Lessons for the future

Overall, there were many successes in the UK's Covid-19 vaccination programme - such as the excellent data on vaccine uptake and effectiveness - but also issues that need to be addressed. One key lesson for the future is that investment in the UK's scientific infrastructure is essential so that the UK is prepared for any future pandemic. Sharing of scientific information and data between countries is also needed.[20] It is also essential to have rapid systems for approving vaccines for use in the UK, and data for monitoring safety and effectiveness, which are needed for the detection of rare but potentially serious side effects and generating data on the risk-benefit equation on the use of vaccines in groups such as children and pregnant women. Good IT systems are also essential for identifying patients in priority groups for vaccination; and for establishing vaccine booking and recording systems that are easy for the public to use and which seamlessly transfer data to primary care medical records and the NHS App.

A sustainable infrastructure for vaccine delivery is also needed that allows high uptake of vaccines to be achieved rapidly in all population groups, including those that are vaccine hesitant or who are less concerned about the risks of infection. Finally, an effective public and professional dialogue is needed on all decisions about the approval of vaccines so that there is full confidence in decisions taken by bodies such as the JCVI, particularly where the UK veers away from the international consensus; for example, in the use of vaccines in children and adolescents, and in modifying dosing schedules. This might require, for example, the JCVI holding meetings in public and having much more rigorous press conferences after its meetings; and also responding to written questions from the public and from professional organisations about its recommendations.

References

1. Fauci AS. The story behind COVID-19 vaccines. Science. 2021 Apr 9;372(6538):109.
2. Baraniuk C. Covid-19: How the UK vaccine rollout delivered success, so far BMJ 2021; 372 :n421 doi:10.1136/bmj.n421
3. Majeed A, Molokhia M. Vaccinating the UK against covid-19. BMJ. 2020 Nov 30;371:m4654. doi: 10.1136/bmj.m4654.
4. Polack FP, Thomas SJ, Kitchin N, et al., C4591001 Clinical Trial Group. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. N Engl J Med 2020;383:2603-15. doi:10.1056/NEJMoa2034577.
5. Voysey M, Clemens SAC, Madhi SA, et al., Oxford COVID Vaccine Trial Group. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. Lancet2021;397:99-111.

6. Lopez Bernal J, Andrews N, Gower C, Robertson C, Stowe J, Tessier E et al. Effectiveness of the Pfizer-BioNTech and Oxford-AstraZeneca vaccines on covid-19 related symptoms, hospital admissions, and mortality in older adults in England: test negative case-control study BMJ 2021; 373:n1088.
7. Vasileiou E Simpson CR Shi T et al. Interim findings from first-dose mass COVID-19 vaccination roll-out and COVID-19 hospital admissions in Scotland: a national prospective cohort study. Lancet. 2021; 397: 1646-1657.
8. Majeed A, Papaluca M, Molokhia M. Assessing the long-term safety and efficacy of COVID-19 vaccines. Journal of the Royal Society of Medicine. 2021;114(7):337-340.
9. Osama T, Razai MS, Majeed A. COVID-19 vaccine allocation: addressing the United Kingdom's colour-blind strategy. Journal of the Royal Society of Medicine. 2021;114(5):240-243.
10. Gurdasani D, Bhatt S, Costello A, et al. Vaccinating adolescents against SARS-CoV-2 in England: a risk–benefit analysis. Journal of the Royal Society of Medicine. 2021;114(11):513-524.
11. Ward, J.L., Harwood, R., Smith, C. et al. Risk factors for PICU admission and death among children and young people hospitalized with COVID-19 and PIMS-TS in England during the first pandemic year. Nat Med (2021). https://doi.org/10.1038/s41591-021-01627-9.
12. Wise J. Covid-19: UK will offer third vaccine dose to severely immunosuppressed people BMJ 2021; 374 :n2160 doi:10.1136/bmj.n2160
13. Iacobucci G. Covid-19: How is the UK's vaccine booster programme faring? BMJ 2021; 375 :n2702 doi:10.1136/bmj.n2702
14. Machingaidze, S., Wiysonge, C.S. Understanding COVID-19 vaccine hesitancy. Nat Med 27, 1338–1339 (2021). https://doi.org/10.1038/s41591-021-01459-7
15. About the coronavirus (COVID-19) in the UK dashboard. https://coronavirus.data.gov.uk/about
16. Monitoring reports of the effectiveness of COVID-19 vaccination. https://www.gov.uk/guidance/monitoring-reports-of-the-effectiveness-of-covid-19-vaccination
17. Helen J Curtis, Peter Inglesby, Caroline E Morton, et al. Trends and clinical characteristics of COVID-19 vaccine recipients: a federated analysis of 57.9 million patients' primary care records in situ using OpenSAFELY. British Journal of General Practice 2022; 72 (714): e51-e62. DOI: 10.3399/BJGP.2021.0376
18. Hippisley-Cox J, Coupland C A, Mehta N, Keogh R H, Diaz-Ordaz K, Khunti K et al. Risk prediction of covid-19 related death and hospital admission in adults after covid-19 vaccination: national prospective cohort study BMJ 2021; 374 :n2244 doi:10.1136/bmj.n2244
19. EU demands immediate access to UK-made vaccines in AstraZeneca legal battle. https://www.reuters.com/world/europe/eu-legal-case-against-astrazeneca-begins-brussels-court-2021-04-28/
20. Wouters OJ, Shadlen KC, Salcher-Konrad M, Pollard AJ, Larson HJ, Teerawattananon Y, Jit M. Challenges in ensuring global access to COVID-19 vaccines: production, affordability, allocation, and deployment. The Lancet. 2021 Feb 12.