TONY BLAIR INSTITUTE FOR GLOBAL CHANGE

Restoring Confidence in the Workhorse Covid-19 Vaccines

RYAN WAIN
BRIANNA MILLER

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Foreword by Tony Blair

The global community has an interest in the world getting vaccinated, and fast. Otherwise, we risk mutations of a serious nature that require new vaccines. Therefore we are chasing after each new strain, trying to eliminate it before the next one arises.

In the next weeks my Institute will publish a plan for how the world could be vaccinated by the end of 2021.

But there is no possibility of such a global vaccination programme succeeding if vaccines such as the one developed by Oxford University/AstraZeneca are discredited based on unjustified anxieties about safety or efficacy.

Because if this is true of AstraZeneca's vaccine, it could equally apply to other adenovirus vaccines, such as Johnson & Johnson's vaccine, and the consequence will be that the world is deprived wholly unnecessarily of the workhorse vaccines vital for global vaccination.

In this paper, we set out why the reluctance – particularly around the AstraZeneca vaccine – is completely wrong and unjustified, why regulators in different countries are taking decisions based on a narrow and unbalanced view of risk, and why the policymakers in government need to grip this situation urgently and bring some coherence and logic to the issue of vaccine assessment. And do it globally.

We combine this with a call for much better publication of the data on vaccine efficacy and safety. The UK government has a particular interest in this because AstraZeneca is a UK-developed vaccine and because it is the vaccine most used in the UK.

There is a vaccine surveillance programme that launched in January, apparently updated in March, which is designed to give comprehensive data on what is happening with Covid-19 and the impact of the vaccines. In addition, there are the reports of Public Health England and the Medicines & Healthcare products Regulatory Agency. All these contain useful data, but they presently fall short of what we believe is necessary for that data to be comprehensive and persuasive in light of the now global anxieties expressed about the AstraZeneca vaccine.

I accept completely that the presentation of data has to be carefully curated so that it does not mislead but accurately informs.

However, we are in a situation where, in my judgement, only the release of the total data set for the UK vaccination programme will carry the global credibility AstraZeneca needs.

We need to see – as Israel has done with the Pfizer-BioNTech vaccine – the following information:

1. The number of people vaccinated, then broken down by first dose and second dose and by age group
2. After vaccination, how many people contracted Covid-19
3. How many of those people were hospitalised
4. How many of those people died

We can then also compare AstraZeneca and Pfizer to see the results. The UK is in a unique position to do this because it is the only country that, at scale, has deployed both vaccines in similar amounts.

But this needs to be done now.

Then, at a global level, possibly beginning with the G7 countries – though China and India have a big interest in this also – there should be a global group of experts established who can pronounce on vaccine assessments and bring some order to the present fragmented disorder, which will have serious adverse effects on our ability to vaccinate the world and return to something approaching normal.

Tony Blair
Executive Chairman

Executive Summary

Vaccines are working and we must continue with their rollout to reach herd immunity. This is true globally as much as in the UK because the threat of new strains means that virus anywhere is potentially virus everywhere. The world must be ambitious: global vaccination in 2021 should be a global mission.

Key to this mission is a low-cost, easy-to-store and widely available vaccine. We already have this in the form of the Oxford/AstraZeneca vaccine: an effective and safe vaccine that is being sold on a non-profit basis. This could be the workhorse of the global vaccination effort, but its uptake is under threat. Indeed, every time the risk-to-benefit ratio of the AstraZeneca vaccine is overstated or its positive impact goes unrecognised, damage is done to the category of adenovirus vaccines that make up the additional workhorse vaccines in the global vaccine effort – including accounting for more than 90 per cent of COVAX supplies. Around the world, we have already seen the rollout of AstraZeneca restricted by different regulators for different reasons. They include:

- South Africa: Halted rollout plans of the AstraZeneca vaccine in February after small-scale studies suggested the jab provided only minimal protection against mild and moderate illness caused by the variant circulating there, despite the same data showing a strong T-cell response and zero cases of death or hospitalisations. [1] The Johnson & Johnson/Janssen (J&J) vaccine is likely to have the same response.
- Germany: Health regulators initially approved the AstraZeneca vaccine exclusively for individuals under the age of 65, citing insufficient efficacy data among older age groups. Since then, the country has reversed that decision and now only recommends the use of the vaccine for those over the age of 65, citing incidents of blood clots among younger people.
- France: Restricted the use of the AstraZeneca vaccine to over-55s because of reports of blood clots. In addition, individuals under 55 who received an AstraZeneca jab prior to this decision will not receive a second dose of AstraZeneca. Instead, more than 530,000 individuals will now receive their second dose of either Pfizer-BioNTech or Moderna as part of a 'mix-and-match strategy', an approach to vaccination not yet recommended by the World Health Organisation. [2]
- Denmark: Denmark became the first country in the world to permanently discontinue the use of the AstraZeneca vaccine on 14 April. Danish health authorities said they would stop using the jab because of the possible link between the vaccine and cerebral venous sinus thrombosis (CVST), a blood clot in the brain. [3]
- UK: Restricted the use of AstraZeneca for under-30s because data shows a temporary skew in the risk-to-benefit calculation of the vaccine for under-30s when case numbers are low. However, when cases increase, restricting the use of AstraZeneca to over-30s is a disproportionate response based on the adjusted risk-to-benefit calculation.

These decisions disguise the fact that the vaccine works [4] and immeasurably improves health outcomes. But they go even further: they actually turn people off from a vaccine that is central to reaching herd immunity. This growing hesitancy is evident in certain countries such as France, Germany and Italy, and among certain demographics – including those from black and Asian communities in the UK. If hesitancy is not addressed, we will not reach herd immunity and more people will die from Covid-19.

Much of the hesitancy surrounding the AstraZeneca vaccine can at least in part be attributed to the presentation of the data looking at potential causal links between the jab and blood clots. For data to be the most effective, it needs to be contextualised. For example, the likelihood of developing a blood clot from the AstraZeneca vaccine is around 1 in 250,000 [5], whereas the likelihood of developing a blood clot from oral contraceptives is estimated to be around 1 in 2,000 [6] and some studies even suggest 1 in 1,000. [7]

Data, and the way we present it, is the most important tool we have. Without it, we are fighting blind and when we choose not to publish it, we are creating vacuums where misinformation, fear and confusion thrive. We need better, clearer data that sets out the health outcomes for those who have the vaccine versus those who don't. This could be in the form of raw numbers, updated daily, where we see the number of Covid cases, hospitalisations and deaths, broken down by age, vaccine status and vaccine type. The data should be comparable wherever possible, with clear indications when data is not comparable. Ideally, it should be contextualised and translated into meaningful and objective insights.

The UK is uniquely positioned to lead on this. Thanks to an excellent vaccine rollout programme, we have seen both Pfizer and AstraZeneca jabs – mRNA and adenovirus vaccines respectively – administered at scale and in similar numbers. This gives rise to data that can show the comparative benefit of taking either vaccine. We know this benefit to be similar from Public Health Scotland data. [8] This will restore confidence in the workhorse vaccine. To date, more than 21.6 million doses of AstraZeneca have been administered – more than anywhere else in the world – essentially creating the largest study group in the history of vaccination programmes. We believe for reasons we set out in this paper that more vaccination data needs to be published as soon as possible.

We have approached Public Health England (PHE) about publishing such data but, so far, they have been hesitant. We understand why they are adopting this position. All new data must be treated with proper scrutiny and mined for unintended consequences. When it comes to raw numbers of cases, hospitalisations and deaths, broken down by vaccine status, type and age, this cannot be underestimated. We appreciate that data may not be comparable and could be incomplete. For example, it's likely that different types of vaccine have been administered to different age groups and that older age groups, for whom vaccination started earlier, are likely to have had their two doses already (and therefore enhanced protection). Furthermore, these two doses are likely to have been Pfizer because it was approved earlier. There will be many more examples of why this data can't be shared and made comparable yet.

However, we believe we are at a crisis point for adenovirus-based vaccines – including AstraZeneca – and so the benefits of immediately showing how these vaccines save lives in an easy-to-understand way far outweigh the risks. Our respect for PHE remains. They have done exceptional work throughout the pandemic and continue to do so. But, for reasons set out in this paper and for the sake of the global vaccine effort, these numbers should be published as soon as possible.

There is precedent. The UK's Yellow Card scheme is a tool for self-reporting side effects post-vaccination, but it has also been used by some patients (or their doctors) to report contracting Covid-19. These reports are broken down by vaccine manufacturer and published bi-weekly. Incomplete and not accounting for age, the data shows that the AstraZeneca vaccine is far from the poorer cousin of Pfizer:

	AstraZeneca	**Pfizer**
First doses	20,600,000	11,000,000
Second doses	1,000,000	4,400,000
Total doses	21,600,000	15,400,000
Yellow Card reports of contracting Covid-19 after receiving a dose	321	626
Yellow Card reports of death from Covid-19 after receiving a dose	22	40
Yellow Card reported cases per 100,000 doses	1.49	4.07
Yellow Card reported deaths per 100,000 doses	0.10	0.26

This Yellow Card data was buried on pages 23 and 27 of two large documents released bi-weekly. The government should be more proactive in communicating and sharing this data, while also ensuring access to data sets for academics and other bodies.

Complete data sets, broken down by age and level of vaccination, will allow for a fuller comparison of health outcomes between vaccine types and, more importantly, between the vaccinated and unvaccinated. This data is available for the Pfizer vaccine in Israel and it is hugely impressive (see Chapter entitled *Improve Data, Improve Confidence*). Not doing the same in a country where AstraZeneca is being widely rolled out risks further skewing the risk-to-benefit ratio, leading to rising hesitancy and a drop in vaccination rates at home and around the world.

For the same reason, more must be done to properly contextualise and communicate suspected side effects. In this paper, we welcome the Centres for Disease Control and Prevention's (CDC) V-safe initiative in the US and recommend its adoption in the UK. Today the UK elicits reports of side effects through its Yellow Card scheme, inviting anyone with suspected side effects to report them – meaning the many more who don't get side effects aren't being recorded. V-safe is different, inviting all vaccine recipients to submit data whether they have had side effects or not.

The benefits of the V-safe approach are exemplified when it comes to pregnant women. In this case, the lack of reported side effects among pregnant women who received the vaccine meant that it was a straightforward, evidence-based decision to extend vaccine eligibility to expectant mothers. For the UK, this decision took three weeks longer, despite clear evidence that shows antibodies are passed to babies through the umbilical cord and breast milk.

This paper sets out why the UK should share more data domestically and internationally, including daily raw numbers on the health outcomes of those vaccinated versus those unvaccinated. This information alone will significantly improve reporting and decision-making and will enable individuals to see the stark reality of vaccination as a huge benefit to them and their communities.

We recommend the UK shares this data daily and immediately.

The world depends on it.

Recommendations

1. Publish clear data on all vaccines in use consisting of absolute numbers for Covid-19 cases, hospitalisations and deaths, broken down by age, vaccine status (not vaccinated, partially vaccinated, fully vaccinated) and vaccine type. This should build on the existing post-vaccination surveillance strategy from Public Health England by publishing data more regularly than quarterly,

as currently planned, and in as clear a way as possible.

2. Introduce follow-up active monitoring akin to the CDC's V-safe to everyone who has been inoculated. This would show that serious side effects don't occur in the vast majority of the population and inform better decision-making – as evidenced by the gap between the US and UK's respective decisions to extend vaccine eligibility to pregnant women.

3. Establish a high-level group of experts who can provide clear and consistent guidance to various national regulatory bodies, allowing for more consistent and clearer decisions regarding the safety of Covid-19 vaccines. This group, led by the G7, should facilitate global data sharing on vaccine side effects and the impact that vaccinations are having on cases, hospitalisations and deaths to support better decision-making and provide a bigger sample base for drawing insight. This would also ensure that different regulators aren't taking different and often confusing decisions on vaccine rollout.

4. Do not pause the rollout of vaccinations when a *suspected* side effect is emerging but has not yet been fully investigated and instead conduct investigations alongside rollout. Pausing to investigate is normal and correct practice in *normal* times. We are not in normal times. The risk from halting vaccines is further hesitancy around the workhorse vaccines and this should be a last resort, rather than the go-to option.

5. Assemble the right containment infrastructure, including testing, therapeutics and antivirals, which, when combined with vaccines, will transform Covid-19, making it flu-like and endemic.

Vaccinating the World: Supply but Also Confidence

We can only suppress Covid-19 through widespread vaccination and, even then, the virus is likely to be with us for the long term. In a world of variants that are more transmissible and potentially more deadly, a case of Covid anywhere can be a case of Covid everywhere. This applies on a global level as well as domestically. We need to ensure widespread vaccine uptake across multiple groups in society and across every country. This is a question of supply and confidence – and the measure of both varies across different types of vaccines.

- **We have supply and confidence in mRNA vaccines but cost is a significant limiting factor.** This applies to new mRNA vaccines such as Pfizer and Moderna. Owing to the extensive, well-documented and widely shared rollout of the Pfizer vaccine in Israel, the positive impact of these vaccines has been made available in near real-time data. Of the 1,849,101 people fully vaccinated to 15 March, 79 died from Covid-19 – a rate of just 0.004 per cent compared to Israel's 0.7 per cent fatality rate since the pandemic began. [9] Furthermore, updated data is published daily.

Unfortunately, mRNA vaccines aren't a viable option for vaccinating the world – simply because they're beyond the price point for a number of countries outside of COVAX, as Figure 1 shows, or when it comes to COVAX, there aren't the supplies available.

Figure 1 – Comparing the costs of mRNA to adenovirus-based vaccines

Type	Vaccine	Cost per dose
mRNA	**Pfizer**	EU – $14.70 US – $19.50 Israel – $23.50
	Moderna	EU – $18.00 US – $15.00 Israel – $23.50
Adenovirus	**AstraZeneca**	EU – $4 US – $4
	Johnson & Johnson	EU – $8.50 (only one dose)

Source: BMJ

- **We have supply but increasing hesitancy in adenovirus vaccines – the workhorses of the global vaccination effort**. This is especially true with the AstraZeneca vaccine. We have seen hesitancy rising around the world, including across Europe, and regulators restricting the rollout of the vaccine for certain age groups based on suspected side effects – thereby fuelling hesitancy. In almost every circumstance, the benefits continue to outweigh the risks and, as trial data has shown, the approved vaccines are highly effective. Not only are they equally as effective, adenovirus vaccines are more affordable and can be stored at more manageable temperatures than mRNA vaccines, removing

barriers to transportation and storage for countries that lack cold chain infrastructure. Rolled out at scale, they will get us to herd immunity. These will also be the vaccines that largely make up COVAX's contribution to global vaccine efforts. To date, Pfizer has committed 40 million doses to COVAX and AstraZeneca and Johnson & Johnson have collectively pledged almost 700 million doses. We know that these vaccines are as effective as other types, as shown, from a Public Health Scotland study, and they will likely be responsible for vaccinating a large proportion of the world. [10]

The task at hand is to restore confidence in vaccines that will supply the global vaccination effort. This requires complete data that is clear and easy to understand, and for what we know to be true – that both mRNA and adenovirus vaccines save lives – to be made clear.

Barring a dramatic price reduction in mRNA vaccines, the adenovirus vaccines will be the workhorses of the global vaccination effort and it's important that we make it as easy as possible for the lay person to understand the positive impact of having the vaccine. Currently, effectiveness of vaccines is presented through percentage risk reduction: these are difficult to understand and lead to false comparisons between different vaccine types. Instead, complete raw numbers should be collated and shared daily – showing the number of new Covid-19 cases, hospitalisations and deaths, broken down by vaccination type and status. This happens for mRNA vaccines in Israel and should happen in the UK. As the only country to have rolled out both types of vaccines at scale, administering roughly 15 million doses of each, the UK is well placed to offer this data and show the likely similar benefit conferred by either type of vaccine.

When Restrictions Are Added, Confidence Is Taken Away

Over the past three months, there have been a number of restrictions placed on the AstraZeneca vaccine, which have significantly dampened confidence. Lost in this is the simple fact that the vaccine is good.

Figure 2 – Restrictions applied to the AstraZeneca vaccine in 2021 to date

Date	Country	Restrictions applied to	Reason for restriction
January	Germany	Over-65s	Insufficient trial data for 65-plus age group

February	France	Over-65s	Incomplete trial data
February	Finland	Over-70s	Insufficient data for 70-plus age group
February	South Africa	Everyone	Data from one trial suggested the vaccine was as little as 10.4 per cent effective at preventing mild to moderate infections
March	Canada	Under-55s	Concerns of link to blood clots
March	Denmark	Everyone	Concerns of link to blood clots
March	Finland	Under-65s	Concerns of link to blood clots
March	Germany	Under-60s	Concerns of link to blood clots
March	Sweden	Under-65s	Concerns of link to blood clots

April	France	Under-55s	Concerns of link to blood clots
April	UK	Under-30s	Concerns of link to blood clots

Source: Various media and health authority resources

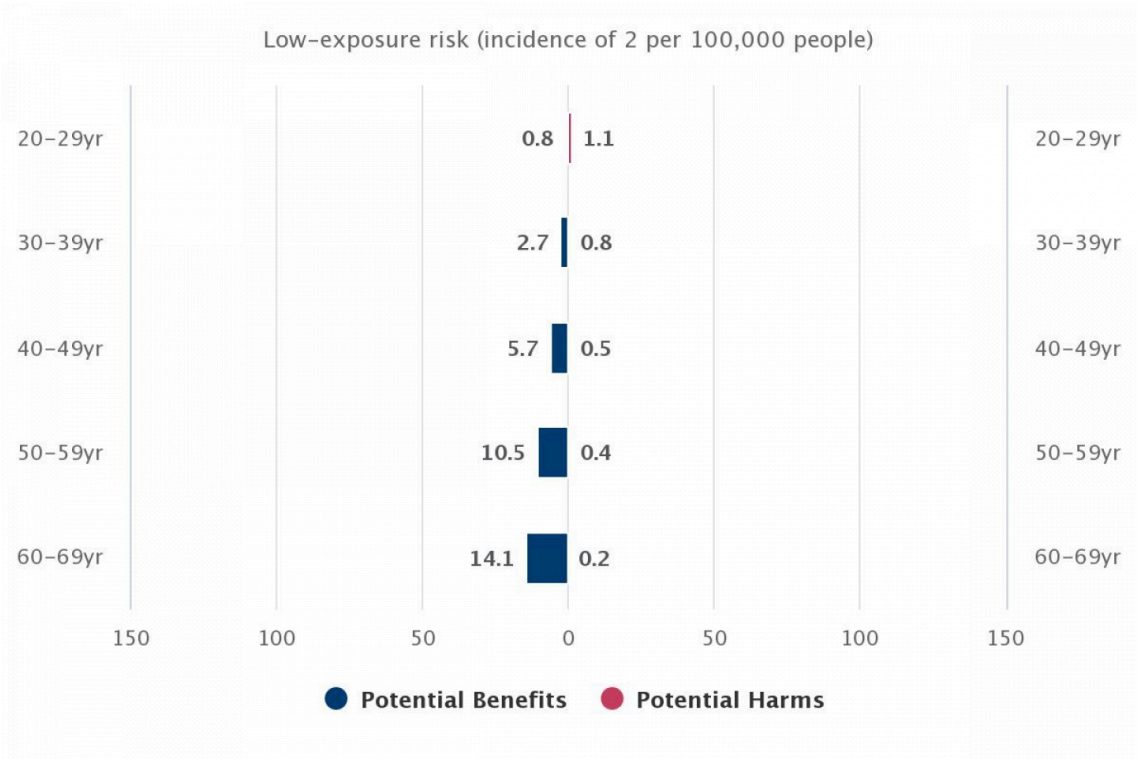
The UK's Decision to Restrict the Use of AstraZeneca for Under-30s

Following reports of blood clots in vaccinated individuals in the UK and 38 fatalities, the Medicines & Healthcare products Regulatory Agency (MHRA) decided to suspend the use of the AstraZeneca for those under the age of 30 on 7 April. The cautionary decision to suspend the vaccine's usage among this age group is likely because the individuals who died were aged between 18 and 79, with three of them aged under 30. [11]

No treatment or vaccine is ever entirely risk-free, so the key question to ask when considering this decision is whether it does more good than harm. As the figures set out below, the risk-to-benefit ratio depends heavily on the prevalence of the virus in society.

For under-30s, when the prevalence of the virus is relatively low – as it is now following a prolonged national lockdown – the risk-to-benefit ratio for under-30s is slightly out of kilter. Operating on a principle of extreme caution, based on this data, the MHRA was right to restrict the usage of this specific vaccine for this age group during this time. During a period where case numbers are low, [12] for every 100,000 people aged 20 to 29 the vaccine prevented 0.8 ICU admissions, however 1.1 out of every 100,000 people aged 20 to 29 would be caused "serious harm" by the vaccine. [13]

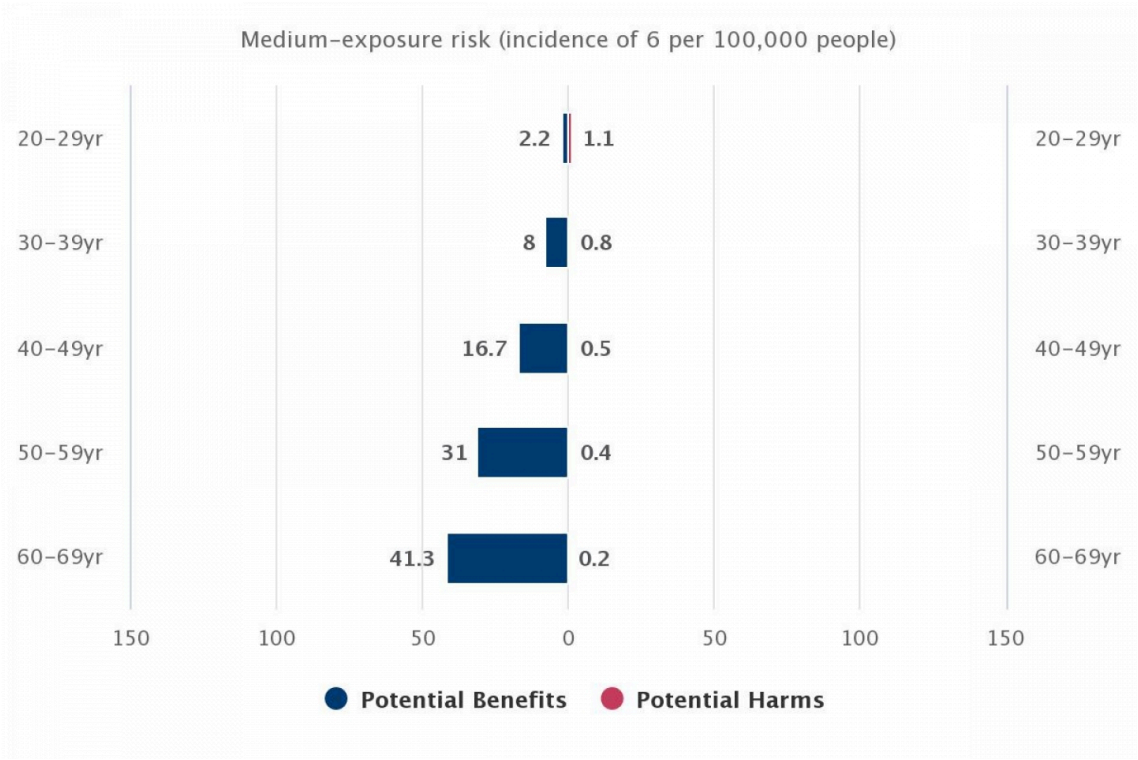
Figure 3 – Potential benefits (ICU admissions prevented) versus harms (blood clots) of the AstraZeneca jab during low-risk period



Source: https://wintoncentre.maths.cam.ac.uk/news/communicating-potential-benefits-and-harms-astra-zeneca-covid-19-vaccine/

If the case numbers were to grow to the rates the UK saw at the peak of the second wave (an incidence rate of about 20 in 10,000), there is much greater risk of severe Covid-19 than there is of blood clots, again across all age groups.

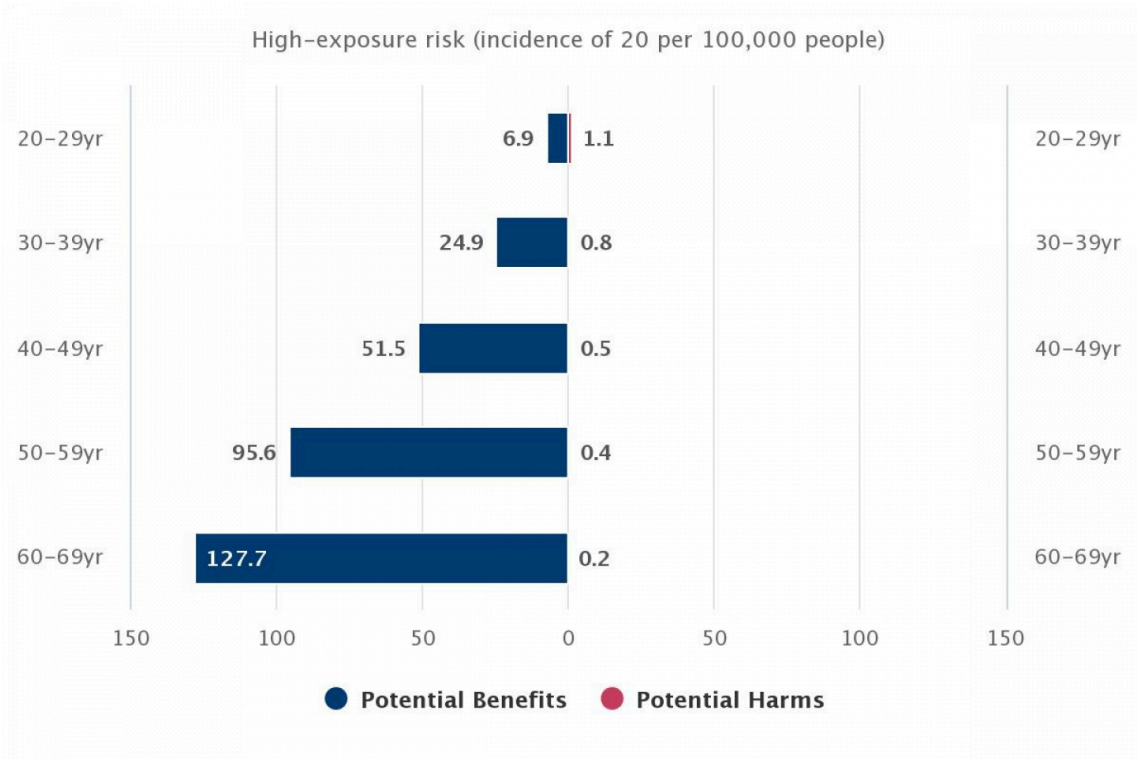
Figure 4 – Potential benefits (ICU admissions prevented) versus harms (blood clots) of the AstraZeneca jab during medium-risk period



Source: https://wintoncentre.maths.cam.ac.uk/news/communicating-potential-benefits-and-harms-astra-zeneca-covid-19-vaccine/

If the case numbers were to grow to the rates the UK saw at the peak of the second wave (an incidence rate of about 20 in 10,000), there is much greater risk of severe Covid-19 than there is of blood clots, again across all age groups.

Figure 5 – Potential benefits (ICU admissions prevented) versus harms (blood clots) of the AstraZeneca jab during high-risk period



Source: https://wintoncentre.maths.cam.ac.uk/news/communicating-potential-benefits-and-harms-astra-zeneca-covid-19-vaccine/

This data supports the MHRA's decision to suspend the use of AstraZeneca for under-30s based on: 1) the current state of the virus in the UK; and 2) the fact that alternative vaccines are available. However, this decision needs to be kept under constant review, especially if/when cases begin to rise again. As the data clearly shows, the risk-to-benefit ratio is heavily dependent on the circumstances. In this instance, the decision is based on low exposure and at higher levels even young people have a greater risk through not being vaccinated.

There are several other benefits of vaccination that these models do not capture. First, a vaccinated person will keep accruing the benefits of vaccination over the lifetime of the vaccine's protection. The risk from vaccination generally occurs at the point of vaccination, and data from the European Medicines Agency (EMA) shows that several of the reported blood clots occurred within seven to 14 days. [14] This means that over time, the benefits will increase but the risks will not. Second, while the three figures above focus on reduced ICU admissions, they do not take into consideration that for every one person shown as being saved from ICU admission, there are many more who might be saved from being admitted to hospital or suffering from Long Covid. The models also do not account for the positive impact vaccination has on transmission. [15]

A decision taken anywhere is a decision that impacts everywhere. We know that Covid anywhere is potentially Covid everywhere. The same mantra can be applied to decisions: a decision taken anywhere can be a decision that impacts everywhere. This means the normal process of pausing the rollout of the vaccine based on a small number of reports should be avoided and, instead, where reports are low in number, investigations should run in parallel to vaccines been rolled out. Likewise, decisions to suspend rollout should be kept under constant review because the risk-to-benefit calculation may be subject to temporal considerations and become unbalanced when cases are extremely low, for example during national lockdowns (this is true for rare blood clots – see above). In these situations, were cases to rise again, then the decision to restrict the AstraZeneca vaccine from being administered to under-30s is preventing more benefit than it is harm.

The Facts on Blood Clots

Small numbers of reports of blood clots arising in relation to the AstraZeneca vaccine, coupled with unclear data on the benefits of the vaccine, clouded the risk-to-benefit ratio and led to unnecessary suspension of vaccine rollout in a number of countries between 10 March and 18 March. This was reversed by an EMA investigation and subsequent announcement that the vaccine did not pose a risk. Germany, France, Italy and Sweden moved ahead with AstraZeneca – although some added restrictions barring use for those under the age of 55 or 65. Norway [16] and Denmark [17] have kept use of the vaccine on hold, while Canada's regulator has advised against the vaccine being administered to under-55s.

The EMA has since released a statement clarifying that although the vaccine may be associated with very rare cases of blood clots in a very small number of people, the benefits of the vaccine in combatting the threat of Covid-19 (which itself results in clotting problems and may be fatal) continue to outweigh the risk of side effects. [18]

As absolute numbers taken from reported side effects of the AstraZeneca vaccine in the UK up to and including the week of suspension demonstrate, the risk of blood clots from the vaccine is minor and proportionate to a real-world risk (see Figures 6 and 7 below). Furthermore, Covid-19 itself increases the risk of blood clots forming. Around one in four patients admitted to ICU with Covid-19 will develop a pulmonary embolism. [19] These rates are much higher than in patients requiring admission to ICU for reasons other than Covid-19.

The Oral Contraceptive Pill Risk

Based on the current data from the UK's rollout of the AstraZeneca vaccine, approximately four people for every 1 million that receive the vaccine develop a blood clot. That equates to about one person in every 250,000 (0.0004 per cent). [20]

An article published in the *Lancet* journal last year estimated the incidence of a blood clot with the combined oral contraceptive pill is about one in 2,000 (0.05 per cent) women per year. [21] In the US, such estimates put the likelihood even higher, with the National Blood Clot Alliance reporting that one in 1,000 women per year who are taking birth control pills will develop a clot, bringing the risk up to 0.1 per cent. [22]

Risk of Blood Clots From Covid-19 Versus Vaccine

The risk of blood clots from the vaccine also needs to be weighed against the risk of getting a blood clot from Covid-19 itself. According to *Sky News*, Professor Sir Munir Pirmohamed, chair of the Commission on Human Medicines, set out the following prevalence rates based on several studies, including one from France and one from the Netherlands: [23]

- Pulmonary embolism occurs in 7.8 per cent of people who have Covid-19.
- Deep vein thrombosis (DVT), or clotting (usually) in the legs, occurs in 11.2 per cent of people who have Covid-19.
- Of those who have Covid-19 and end up in an intensive therapy unit (ITU), 23 per cent will have some form of clot.
- Covid-19 causes strokes in 1.6 per cent of people.
- Up to 30 per cent of people who have Covid-19 will get thrombocytopenia, which is a lowering of the platelet count.

A Role for Aspirin?

Aspirin, a blood-thinning medication, has been used for decades as a preventative measure against recurring blood clots. [24] Long-term treatment with low doses of aspirin can have an anti-platelet effect, which means it makes the blood less sticky and can stop blood clots from developing. [25] However, some believe that the rare cases of blood clots potentially linked to the AstraZeneca vaccine are caused by an immune response, making it unlikely that taking aspirin would impact this type of clotting. [26] More research is needed to determine if/how aspirin could be used to reduce the likelihood of developing a blood clot after receiving a jab.

Suspension of AstraZeneca Vaccine Due to CVST in Germany

On 30 March, the German regulators restricted the AstraZeneca vaccine to over-60s because of a presumed link to 31 cases of cerebral venous sinus thrombosis (CVST) in which clots obstruct the

channels that carry blood away from the brain. All but two of the cases were in women between the ages of 20 and 63. Nine of these patients have so far died.

These 31 cases occurred from among 2,697,479 vaccines and remain incredibly rare. Across the 14-day window following 2.7 million AstraZeneca vaccinations, about 1.7 cases would have been expected. While the EMA confirmed a possible link to very rare cases of blood clotting on 7 April, they did not conclude that the usage of the AstraZeneca vaccine should be halted. [27]

Clearly, this issue merits investigation but it should not lead to the suspension of vaccine rollout, especially when the same vaccine led to just six cases of CVST in the UK among more than 14 million doses of the AstraZeneca vaccine.

The decision to suspend AstraZeneca for under-60s will cause reputational damage to the vaccine – a workhorse of the global inoculation effort – and further exacerbate hesitancy in Germany, with likely spillover to the EU.

Investigations into potential side effects should not necessitate the suspension of vaccine rollout when the international data combined shows that the risk is minor relative to the benefits of a vaccine.

As can be seen from the figures below, which set out reported suspected side effects up to 8 March and then up to 28 March in the UK, there was a significant increase in reporting of blood clots among recipients of the AstraZeneca vaccine. In the first tranche of data, crucially compiled *before* many European regulators had halted the AstraZeneca rollout, the number of reports between different vaccine types was broadly similar. But there has been an increase in reports of blood clots, especially since the initial decision of EU countries to halt rollout of the AstraZeneca vaccine, which could suggest that publicity on the subsequently reversed decision instigated more reports than actual cases.

Figure 6 – Reported blood clots during UK Covid-19 vaccine rollout to 8 March, versus annual expected cases

	Overall		AstraZeneca		Pfizer		
Condition	**Reports** out of 22 million vaccinated	**Fatalities** out of 22 million vaccinated	**Reports**	**Fatalities**	**Reports**	**Fatalities**	**Expected cases in UK population of 66.6**

							million per year
Deep vein thrombosis	22	0	14	0	8	0	54,100 [28]
Pulmonary embolism	28	2	13	1	15	1	45,000 [29]
Cerebral venous sinus thrombosis	4	0	3	0	1	0	270 [30]

Source: Covid-19 AstraZeneca vaccine analysis and Pfizer-BioNTech vaccine analysis

Figure 7 – Reported blood clots during UK Covid-19 vaccine rollout to 28 March, versus annual expected cases

	Overall		**AstraZeneca**		**Pfizer**		
Condition	**Reports** out of 28 million vaccinated	**Fatalities** out of 28 million vaccinated	**Reports**	**Fatalities**	**Reports**	**Fatalities**	**Expected cases in UK population of 66.6 million per year**

Deep vein thrombosis	290	3	240	3	50	0	54,100 [31]
Pulmonary embolism	352	44	287	37	65	7	45,000 [32]
Cerebral venous sinus thrombosis	49	5	46	5	3	0	270 [33]

Source: Covid-19 AstraZeneca vaccine analysis and Pfizer-BioNTech vaccine analysis

As the figures above show, the number of thrombotic events reported up to 28 March is higher than the number reported up to 8 March. This could be because the publicity surrounding blood clot incidents across Europe instigated more reporting in the UK or it could also be that, during this period, thousands of people across the EU and UK would naturally have suffered from blood clots, regardless of whether they were vaccinated. In addition, thousands more people over the few weeks between the dates in these charts were vaccinated, so statistically speaking we would expect an increase based on the additional people getting vaccinated.

After convening a committee of experts, including experts in blood disorders, the EMA concluded that the total number of cases of embolic and thrombotic events after vaccination reported to EudraVigilance (the EMA's system for processing information on suspected adverse reactions to medicines), in relation to the number of people vaccinated was lower than the rate of such events in the general population. [34]

Neither the EMA nor the MHRA have found evidence that Covid-19 vaccinations pose a significant risk to people, and the benefits of being vaccinated still outweigh the risks of getting the virus.

Across all vaccine types there will be recipients who develop blood clots. For example, the below data from the US's VAERS database – an equivalent of the UK's Yellow Card scheme - shows a substantial number of reports across mRNA vaccines.

Figure 8 – Thrombocytopenic, thromboembolic and haemorrhagic events reported after vaccination, up to 9 April

Adverse event	J&J	Pfizer	Moderna
Thromboembolism	55	627	550
Thrombocytopenia and platelet count decreased	10	117	115
Thromboembolism and thrombocytopenia	4	12	14
Immune thrombocytopenia	2	27	26
Cerebral venous sinus thrombosis	2	0	3
Haemorrhagic disorders	95	662	600
Haemorrhage with thrombocytopenia	7	60	59

Haemorrhage with immune thrombocytopenia	2	27	26
Disseminated intravascular coagulation	3	3	5
Thrombotic thrombocytopenic purpura	0	5	0
Total doses administered	4,917,225	90,256,586	79,551,820
Individuals vaccinated	4,917,225	57,447,938	51,079,761

Source: CDC's Vaccine Adverse Reporting System (VAERS)

Data Contextualisation: Covid-19 and the Flu

The flu vaccine is designed to minimise the risk of developing severe infections and the likelihood of being admitted to hospital. Receiving a vaccination does not mean an individual has no chance of catching the virus.

A study published in 2018 found that the inactivated flu vaccine between 2012 and 2015 was effective in reducing deaths and severe cases of infection in both ICU patients and general ward patients. However, some still caught the virus.

- Of the 101 individuals enrolled in the study, with an acute respiratory illness in the ICU, 41

tested positive for the flu, only 16 of whom had received the flu jab.

- There were 3,034 general ward patients enrolled who had acute respiratory illness; 849 patients tested positive for the flu and 475 of those patients had received the flu jab. [35]

Similar to Covid-19, adults aged 65 and older suffer the most severe health effects of seasonal influenza, with one study concluding that approximately 90 per cent of influenza-related deaths and between 50 and 70 per cent of influenza-related hospitalisations occur in this age group. [36] For the 2019–2020 flu season in the US, there were 22,000 flu-related deaths, which would mean that approximately 19,800 (90 per cent) of deaths occurred in the over-65s. In the same 2019–2020 flu season, the CDC estimated that the flu was associated with 38 million illnesses, 18 million medical visits and 405,000 hospitalisations. [37] For the same year, approximately 101 million flu vaccinations [38] were given in the US, and the CDC reported that vaccination prevented an estimated 7.5 million influenza illnesses, 3.7 million influenza-associated medical visits, 105,000 influenza-associated hospitalisations and 6,300 influenza-associated deaths. [39]

As Confidence Fades, Vaccine Hesitancy Builds

A side effect of the decision to temporarily suspend the AstraZeneca vaccine rollout was that it drove up hesitancy in European countries. YouGov polling shows how hesitancy has increased in response to reporting of blood clots, [40] for example:

- 55 per cent of Germans believe the AstraZeneca vaccine is unsafe, up from 40 per cent in February.
- 61 per cent of people in France believe the AstraZeneca vaccine is unsafe, up from 43 per cent in February.
- 43 per cent of Italians believe the AstraZeneca vaccine is unsafe, up from 16 per cent in February.

There is a clear correlation between individuals who are well informed about vaccines and those who are willing to take it. One study found that among respondents stating they are “very well” or “well” informed, 65 per cent would be willing to get a Covid-19 vaccine, while only 32 per cent of those indicating they are “not informed” or “poorly informed” said they would do the same. Among the people who said they were “not willing” or “not fully willing” to get vaccinated, the main reason for this reluctance is the concern about possible side effects (55 per cent), followed by a lack of trust in certain Covid-19 vaccines (36 per cent). [41] This is one reason why clear, complete data can have a positive impact on hesitancy – the more data people see and understand, the more likely they are to choose vaccination.

Figure 9 – Sharp drop in vaccination rates following suspension of AstraZeneca vaccine rollout

Source: https://ourworldindata.org/grapher/daily-covid-19-vaccination-doses?time=2021-02-10..latest&country=DEU~FRA~ITA

Pausing the use of the AstraZeneca vaccine adversely affected the speed and efficiency of various rollout programmes across the continent, further impeding efforts to reach herd immunity. The scale of the issue can be seen when comparing usage of AstraZeneca to different vaccines. Italy, Germany and France used 53 to 60 per cent of their AstraZeneca doses following the suspension while utilisation rates for the Pfizer vaccine exceed 90 per cent. At a German vaccination centre in Berlin, a site that only distributes the AstraZeneca vaccine, fewer than 200 people are turning up for the 3,800 daily appointments that are available. [42] This scale of hesitancy is worrying and can be addressed in part by publishing clearer data.

This hesitancy is also apparent when looking at data from the Johnson & Johnson vaccine in the US. The CDC has recommended pausing rollout of the vaccine while it investigates six cases of blood clots discovered in women who had been vaccinated. Comparing the results from those who took the YouGov survey before the announcement with those who took the survey afterwards illustrates the huge impact the CDC's decision has had on the perceived safety of the Johnson & Johnson vaccine. [43] The results are below.

Results from before the CDC's recommendation to pause the rollout of the Johnson & Johnson vaccine:

- 52 per cent of respondents thought the vaccine was safe
- 26 per cent of respondents thought the vaccine was unsafe
- 22 per cent of respondents didn't know

Results from after the CDC's recommendation to pause the rollout of the Johnson & Johnson vaccine:

- 37 per cent of respondents thought the vaccine was safe
- 39 per cent of respondents thought the vaccine was unsafe
- 24 per cent of respondents didn't know

Another study found that just 55 per cent of the US population is either vaccinated, scheduled to be vaccinated, or would "definitely" or "likely" get the vaccine. That could indicate that once the US reaches this threshold, the uptake of vaccinations will begin to slow and reaching higher levels of immunity among the population will be difficult if this hesitancy is not addressed. [44]

Hesitancy Among Young People and Underrepresented Communities

Data from the Office for National Statistics (ONS) showed that vaccine doubts were reported among young adults, black and black British people [45], low earners, those living in rented accommodation and people living in the most deprived areas of the UK. Those aged between 16 and 29 reported the highest level of hesitancy at 17 per cent compared to 1 per cent of people aged 80 and over, while more than four in 10 (44 per cent) of black or black British adults reported vaccine hesitancy – the highest level in all ethnic groups.

Worries about side effects and long-term health were among the common reasons for hesitancy, along with waiting to see the effectiveness of vaccines. Over half of Britons from a BAME background feel they need more information on the Covid-19 vaccine to make their decision about whether to take it compared with just 24 per cent of white Britons.

Clearer data highlighting the benefits of the vaccine and the very low risks will be important in addressing hesitancy. It will support better reporting and information-sharing within communities and combat misinformation.

Improve Data, Improve Confidence

A percentage reduction in an individual's likelihood of contracting symptomatic Covid-19 is more confusing than, say, looking at the numbers on how many people have had the vaccine and how many of those have since gone on to contract the virus. Publication of the data in a form that is easily understood, using absolute figures (not just percentages) would be easier to follow and become an important tool in driving vaccine uptake. It would more clearly show the benefit-to-risk ratio of being vaccinated.

Access to Data

In this paper, we have been unable to access absolute numbers from the UK's vaccine rollout. This is imperative to restoring confidence globally because it provides a direct comparison between mRNA and adenovirus vaccines – or Pfizer and AstraZeneca respectively – showing comparable health outcomes between each.

Israel – a country with a robust data structure – does provide this data and a snapshot can be seen in Figure 10. Raw numbers are published daily, and the information in Figure 9 is taken from 16 March to 22 March and shows quite clearly what taking a vaccine means for an individual.

Figure 10 – Covid-19 cases, hospitalisations and deaths in Israel as of 15 March among 1.8 million people fully vaccinated before 31 January

Total vaccinated	1,849,101	Percentage
Positive cases (from 7 days after second dose to 15 March)	2,381	0.13%
Hospitalised to 15 March	263	0.014%

Serious condition to 15 March	194	0.01%
Deaths to 15 March	79	0.004%

Source: Israeli Ministry of Health

This data would be further improved by setting out the age ranges, sexes and comorbidities of the 79 who died. However, given that the Covid-19 fatality rate in Israel during the past year was 0.7 per cent and a total of 6,197 [46] people have died from the disease, the difference a vaccine makes is clear.

Figure 11 – Number of severe and critical Covid-19 cases in Israel between 16 and 22 March by vaccination status

Date in March	Total number of severe and critical patients with Covid-19	Of these … how many were not vaccinated?	Of these … how many were partially vaccinated?	Of these … how many were fully vaccinated (both doses given and 7 days passed)
16	57	46	9	2
17	35	27	6	2
18	55	42	6	7
19	43	27	12	4

20	34	30	2	2
21	40	29	5	6
22	18	11	4	3

Source: Israeli Ministry of Health

This data would benefit from further breakdowns – for example, by setting out the ages and any comorbidities of those who have died – but it is an effective way to see the positive impact of vaccination.

It is worth noting that Israel began to ease lockdown restrictions on 11 February, with the reopening of kindergartens and grades 1 to 4. The second tranche of easing measures came into effect on 21 February and the third on 7 March. So far, the lockdown easing measures have had no adverse impact on the rate of hospitalisation or rate of infection, but further disaggregation will be needed to differentiate if the reduction in cases, deaths and hospitalisations is a result of the impact of lockdown or from the impact of the vaccine on its own. However, the above data shows – quite clearly – that the severity of cases is disproportionately skewed to the unvaccinated.

Alongside near real-time updates, the data is also useful when it is amalgamated, providing a holistic picture of vaccine rollout. Figure 10 shows the absolute numbers of incidents among those who had received two doses of the vaccine before 31 January. This is from a total of 1,849,101 people.

On 15 April the CDC in the US published its first iteration of what is being referred to there as 'breakthrough cases' – the number of people who become infected with Covid-19 after receiving both doses of a vaccine. This data was further broken down in absolute numbers into the number of cases, number of individuals who ended up in hospital, and the number of people who died. Of the 77 million Americans that had been fully vaccinated up until the point data was collected about 5,800 people tested positive for Covid-19, 396 of those cases required hospitalisation, and 74 people died. [47] Of the 5,800 cases, 1,682 infections [48] were reported as asymptomatic, indicating the impact the vaccines have on reducing the severity of infection.

Figure 12 – Covid-19 cases, hospitalisations and deaths in the US among 77 million fully vaccinated individuals, published 15 April

Total fully vaccinated	77,000,000	Percentage
Positive cases	5,800	0.008%
Hospitalisations	396	0.0005%
Deaths	74	0.000096%

Source: CDC

The CDC is searching for patterns based on patient age and gender, location, type of vaccine, variants and other factors, but told CNN that thus far, no unexpected patterns have been identified in case demographics or vaccine characteristics. [49] No vaccination is 100% effective so breakthrough cases are expected, however they still represent a very small proportion of those who have been vaccinated.

Absolute Numbers in the UK

There should be no barrier to this data being published and updated in near real-time. As Figure 13 sets out below, absolute numbers on deaths and hospitalisations can be amalgamated through different sources that are updated daily. The next step would be to connect this data to patient records and set out how many of each had been vaccinated.

Figure 13 – Absolute numbers on UK Covid-19 cases, hospitalisations and deaths

Date	Total hospitalised patients	Daily hospital admissions	Daily deaths (within 28 days of a positive test)
06/04/2021	3133	221	21
05/04/2021	3246	233	15
04/04/2021	3220	194	22
03/04/2021	3237	222	28
02/04/2021	3369	236	25
01/04/2021	3552	232	28
31/03/2021	3737	268	37
30/03/2021	3971	257	37
29/03/2021	4193	251	34

28/03/2021	4181	271	32
27/03/2021	4433	270	36

Source: https://coronavirus.data.gov.uk/details/download

Yellow Card Data – AstraZeneca Compared to Pfizer

The UK's Yellow Card scheme (see the Chapter below on *Data and Side Effects*) is used by patients receiving a vaccine – or their doctor – to submit reports, or 'Yellow Cards', reporting any suspected adverse effects from vaccination. These reports are broken down by vaccine manufacturer and published bi-weekly. Among the many different Yellow Cards raised, some patients or their doctors have self-reported that, following inoculation, they've contracted or died from Covid-19.

This data is not complete and does not account for age, which matters particularly in the UK as the Pfizer vaccine was given earlier to older people who may be more likely to die from Covid-19. The Yellow Card data shows:

As of 5 April, the following have been administered:

- First doses: 11 million of Pfizer/20.6 million of AstraZeneca
- Second doses: 4.4 million of Pfizer/1 million of AstraZeneca
- Total doses: 15.4million Pfizer/21.6million AstraZeneca

As of 5 April, following the 21.6 million doses of AstraZeneca given in the UK, there were reports of 321 cases of Covid-19 and 22 fatalities. [50]

In the same period, following the 15.4 million doses of Pfizer given in the UK, there were reports of 626 cases of Covid-19 and 40 fatalities: [51]

	AstraZeneca	Pfizer
First doses	20,600,000	11,000,000
Second doses	1,000,000	4,400,000
Total doses	21,600,000	15,400,000
Yellow Card reports of contracting Covid-19 after receiving a dose	321	626
Yellow Card reports of death from Covid-19 after receiving a dose	22	40
Yellow Card reported cases per 100,000 doses	1.49	4.07
Yellow Card reported deaths per 100,000 doses	0.10	0.26

This data was buried deep in two voluminous documents. It is a classic example of government needing to get a hold on data and specifically the communication of it. Here is a very telling comparison between two types of vaccines and yet it is neither highlighted nor easily accessible.

This Yellow Card data was relied on to show to the potential side effects of AstraZeneca's vaccine when it came to blood clots. It is not complete, but it serves as useful illustration for the main recommendation of this paper, namely that regular data be shared showing the health outcomes of those vaccinated, broken down by vaccine type and vaccine manufacturer. As the above table demonstrates, this is likely to

provide reassurance around the benefits of vaccines in general and, when it comes to the AstraZeneca vaccine, play a big role in rebuilding confidence in what will be the workhorse vaccine.

The Data the UK Should Be Publishing

Our understanding is that there is no real-time hospitalisation data available in the UK as hospitals only submit data after a patient has been discharged. However, real-time data on cases and deaths, cross-referenced with vaccine status, is possible. We believe that the absolute numbers would be more comprehensible and show a significant difference between health outcomes for vaccinated versus unvaccinated, especially in older age groups. The data should be further broken down by the number of doses received, differentiating between those who are partially vaccinated and those who are fully vaccinated.

Below are four data tables (Figures 14–17) that the UK should be publishing daily – one table for the unvaccinated population and one table for each type of vaccine that is in use. As more vaccines come online, additional data for those specific vaccines should be published.

Figure 14 – Absolute numbers among the unvaccinated population

Date	New cases	Hospitalisations	Deaths
10 April			
11 April			
12 April			
13 April			

14 April
15 April
16 April

Figure 15 – Absolute numbers among Pfizer vaccine recipients

Date	New cases		Hospitalisations		Deaths	
Vaccination Status	Partially vaccinated	Fully vaccinated	Partially vaccinated	Fully vaccinated	Partially vaccinated	Fully vaccinated
10 April						
11 April						
12 April						
13 April						

14 April
15 April
16 April

Figure 16 – Absolute numbers among AstraZeneca vaccine recipients

Date	New cases		Hospitalisations		Deaths	
Vaccination status	Partially vaccinated	Fully vaccinated	Partially vaccinated	Fully vaccinated	Partially vaccinated	Fully vaccinated
10 April						
11 April						
12 April						
13 April						

14 April
15 April
16 April

Figure 17 – Absolute numbers among Moderna vaccine recipients

Date	New cases		Hospitalisations		Deaths	
Vaccination status	Partially vaccinated	Fully vaccinated	Partially vaccinated	Fully vaccinated	Partially vaccinated	Fully vaccinated
10 April						
11 April						
12 April						
13 April						

14 April

15 April

16 April

Real-Time Advantage

Updating numbers in as close to real-time as possible is critical because it would allow decisions to be made (or challenged) in real-time, rather than allowing for the delay that is required to interpret data in risk-based studies. This is especially important for mitigating challenges like those seen with AstraZeneca across Europe.

The raw data behind this chart shows the performance of the vaccines against hospitalisation very clearly and in a way that will be more meaningful to the public than percentages. We can illustrate this by returning to the latest full week of data (referenced above).

Existing Approach to Vaccination Data

PHE has set out its plan for post-vaccination monitoring in a comprehensive document, "COVID-19 Vaccine Surveillance Strategy" in March 2021. This includes an approach to vaccine efficacy and reporting on the vaccines' impact on transmission, infection, hospitalisation and death. The strategy states it will report on "the comparative effectiveness of different vaccines in the real world" suggesting that outcomes by vaccine type are being recorded. This data set and the raw numbers behind it should be made available in an easily accessible way, as proposed in this paper.

Currently, the proposal is for analyses to be "stratified into 3 month follow-up periods for the first year, 6 month periods, for the following year and annually thereafter." We would propose that data on health outcomes is published sooner and more regularly, given the urgency of the situation and the need to demonstrate effectiveness of all vaccines.

The strategy should also ensure completeness of data. It is unclear whether data sets will include every patient, stating that it will be drawn from multiple sources:

- National Immunisation Management Service (NIMS): This holds vaccination records
- The Second Generation Surveillance System (SGSS): The national laboratory reporting system used in England to capture routine laboratory data, including on Covid-19
- Questionnaires following GP or hospitalisation visits
- Tests at GP or hospitals following visits
- GP health records (with a feed in from NIMS)

It is reassuring that this data is available but it is imperative that it:

1. is shared regularly, certainly more than quarterly
2. it is as complete as possible, especially when it comes to hospitalisation or deaths, where there should be a straightforward link to patient records upon record either event
3. It is not published solely as risk-based percentages, but in an easy-to-understand format, such "cases, hospitalisations or deaths per 100k".

We appreciate the challenges in detecting infection among vaccinated patients. This can be drawn from linking testing data to vaccination record and, where asymptomatic testing occurs, through existing surveillance efforts that stratify data.

Data and Side Effects

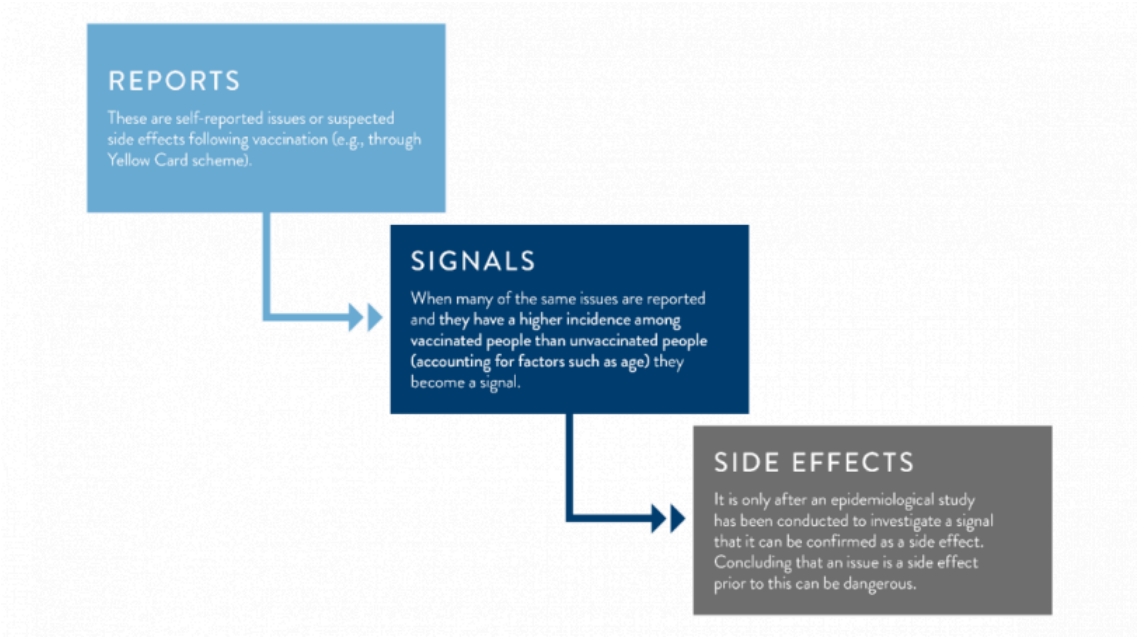
As the issues surrounding blood clots demonstrate, the importance of clear data is particularly acute when it comes to calculating the risk of taking the vaccine itself. It must be proportionate and ensure that correlation is not confused for causation.

When does a *report* of a side effect become an actual side effect? This may seem like an unusual question but it is hugely important. Failure to understand it, particularly when it comes to the significant steps required to confirm a side effect, has already led to vaccine rollout being held up.

From Report to Side Effect

Before confirming a side effect, issues are self-reported by those receiving the vaccine. Many reports of the same suspected side effect will become 'signals' – leading to further investigation and possible confirmation. Crucially, data collected by health regulators including the MHRA **cannot confirm a side effect**; instead it simply contributes to a body of data that should then be investigated by a formal epidemiological study.

Figure 17 – Passive reporting on side effects via the Yellow Card scheme



Source: https://www.gov.uk/government/publications/coronavirus-covid-19-vaccine-adverse-reactions

When someone receives any approved vaccine, they are encouraged to report suspected side effects via the Yellow Card vaccine monitoring scheme run by MHRA. Through this scheme, members of the public and health-care professionals voluntarily submit reports of suspected side effects to the MHRA. Drug companies also submit such reports as part of their legal requirements. Safety scientists at the MHRA continuously evaluate Yellow Card reports to generate signals of potential safety issues.

Everyone is encouraged to report any suspicion or concern they have, even if in doubt, and they do not need to be sure of a link between a medicine or a vaccine and a suspected side effect.

Data and Reporting in the US

In addition to the recently published data on breakthrough cases among the fully vaccinated, the CDC uses both new and existing information technology (IT) systems to rapidly collect reliable data regarding vaccine rollout and take up in the US. While the US publishes more data than the UK, it is still not enough to clearly lay out the benefits of vaccines compared to the risk of getting Covid-19.

Data published regarding Covid-19 vaccines:

- Total doses delivered to the US, broken down by vaccine manufacturer.
- Total doses administered in the US, broken down by vaccine manufacturer.
- Total doses administered to those aged 65 and older, in absolute numbers.
- Total doses administered to those aged 18 and older, in absolute numbers.
- VaccineFinder is a platform where providers report their available Covid-19 vaccine inventory each day.

Data collected regarding Covid-19 vaccines:

- Vaccine waste: the CDC tracks the number of manufactured vaccine doses that are not administered, but this information is not currently publicly available through its Covid Data Tracker.

Data published regarding Covid-19 vaccine side effects through the Vaccine Adverse Event Reporting System (VAERS):

- The type of vaccine received.
- The timing of the vaccination.
- The onset of the adverse event.
- Current illnesses or medication.
- Past history of adverse events following vaccination.

- Demographic information.

V-safe After Vaccination Health Checker

V-safe is a safety monitoring system in the US established by the CDC specifically for the Covid-19 vaccination programme, for use alongside VAERS. It was rolled out during the first month of US vaccinations. V-safe participants voluntarily self-enrol to receive smartphone text messages providing hyperlinks to web surveys about their post-vaccination symptoms.

Individuals who sign up to V-safe receive daily health check-ins via smartphone text messages that include a link to web-based surveys for the first seven days post-vaccination. Check-ins are then sent weekly for the following six weeks, and then once at three, six and 12 months. The health check-in process resets when a person receives a second dose of vaccine.

Active Reporting in the UK

The UK system relies on someone "making a connection" between the vaccine and a suspected side effect. Significantly, it also does not collect data from those who experience no side effects. This risks disproportionate reporting on potential side effects. It would be more useful if individuals could see how many people didn't report side effects, along with the nature and number of those reported.

The MHRA does engage in some active monitoring, with proposals to analyse anonymised patient records from approximately 20 per cent of GP practices in England, including 13 million registered patients.

The UK would benefit from a system similar to V-safe, which has widespread adoption. Those already vaccinated could be encouraged to enter their data immediately while the newly inoculated would be encouraged to sign up and report suspected side effects or confirm they have none. This would build reassurance, particularly among the younger age groups who over-index on vaccine hesitancy.

Recommendation

Introduce follow-up active monitoring akin to CDC's V-safe to all of those who have been inoculated. This would encourage greater engagement with the Yellow Card process and result in quicker identification of signals. Prompted reminders for individuals to engage in safety monitoring will help identify signals where they exist but, equally as important, will collect data from individuals who report no adverse reactions and therefore facilitate a better appreciation of risk.

Active Reporting: Vaccine Uptake Among Pregnant Women

A US CDC presentation given 1 March 2021 reported that V-safe data as of mid-February "did not indicate any safety problem" among pregnant women. As of 29 March, an additional 69,000 pregnant women received a Covid-19 vaccination and signed up to report any side effects or lack thereof to V-safe. Until just last week, 16 April, the MHRA in the UK advised against vaccinating pregnant women, stating "...the vaccines have not yet been tested in pregnancy, so until more information is available, those who are pregnant should not routinely have this vaccine." [52] Although the UK eventually reached the conclusion that vaccination should be expanded to pregnant women, it took much longer than it did in the US because of the active reporting being collected there through V-safe.

When we look at data from elsewhere, though, particularly from the US, it highlights the potential positive benefits of vaccination especially after the first trimester. In the US, the latest report on side effects dedicates an entire chapter to pregnant women. [53] It shows no disproportionate health outcomes among pregnant women receiving a Covid-19 vaccine compared to normal health outcomes for the same group. This is an advantage of the V-safe platform, which captures outcomes of all those vaccinated, rather than the UK's system that only encourages reporting of suspected side effects.

Pregnant women with the virus are at increased risk of severe Covid-19, particularly if they are from ethnic minority backgrounds, or if they have pre-existing conditions such as obesity, high blood pressure and diabetes, according to research led by the University of Birmingham and the World Health Organisation (WHO). Pregnant women with severe cases of Covid-19 are also at higher risk of preterm birth. The review found that one in ten pregnant and recently pregnant women attending or admitted to hospital for any reason were diagnosed with confirmed Covid-19. Overall, 339 pregnant women with confirmed Covid-19 died from any cause (0.02 per cent of a total 41,664 women involved in 59 studies). [54]

With every study it is becoming clearer that Covid-19 during pregnancy can be associated with adverse outcomes for both mother and child. To mitigate this risk, it then becomes essential to determine any risks associated with pregnancy and vaccination. So far, none have been reported. While data is currently limited for Covid-19 vaccines, previous research shows that the use of adenovirus-based vaccines for other diseases was not associated with adverse pregnancy-related outcomes. Although specific studies have not been done with mRNA vaccines because women were not included in those clinical trials, observational data from vaccinated pregnant individuals is currently being collected both by the companies and by the CDC. No specific safety signals have been observed thus far among pregnant vaccine recipients. [55]

Not only have there been no safety signals reported, some studies show that vaccination during pregnancy can provide benefits to the infant. At least three studies of pregnant women who had received

the Pfizer or Moderna vaccines during their pregnancy reported finding antibodies in the women's umbilical-cord blood, indicating the women's babies received antibodies as well. Although the studies did not look specifically at vaccine safety, none of the vaccinated pregnant women reported any more side effects than the women who were not pregnant. Recent studies have suggested that new mothers who were vaccinated could pass along antibodies to their infants through breast feeding. [56]

Figure 18 – Outcomes for pregnant women who have received a Covid-19 vaccine versus normal outcomes

Outcomes	Background rates	V-safe pregnancy registry overall
Pregnancy outcome		
Miscarriage (<20 weeks)	26%	15%
Stillbirth (>20 weeks)	0.6%	1%
Pregnancy complications		
Gestational diabetes	7–14%	10%
Pre-eclampsia or gestational hypertension	10–15%	15%

Eclampsia	0.27%	0%
Intrauterine growth restriction	3–7%	1%
Neonatal		
Preterm birth	10.1%	10%
Congenital anomalies	3%	4%
Small for gestational age	3–7%	4%
Neonatal death	0.38%	0%

Source: V-safe Covid-19 Vaccine Pregnancy Registry

Health authorities in many countries have not given definitive guidance for pregnant women or clearly presented the risks posed by a Covid-19 infection during pregnancy compared to the potential risks of receiving a Covid-19 vaccine. However, the gap in data regarding pregnant women and whether they can receive Covid-19 vaccines is shrinking.

Data from the CDC's V-safe Vaccine Pregnancy Registry in the US has contributed to this growing body of research. The advantage of the V-safe model of data collection is that it collects data from all pregnant women – not just those reporting side effects. Based on this comprehensive data and other studies conducted around the world, it is becoming increasingly clear that it is safe to receive a jab during pregnancy.

At a White House press conference on 5 April, Dr Anthony Fauci emphasised the recommendation put out by the American College of Obstetricians and Gynecologists that although it didn't directly recommend vaccination in pregnant women, importantly, all pregnant individuals who choose to receive the vaccine must be allowed to do so in alignment with state and local vaccination allocation plans. [57]

It is important to continue to collect data regarding pregnant women and vaccines, ideally in a V-safe type of model that logs reports of symptoms as well as the absence of symptoms. Consideration should also be given to the recent research showing that antibodies can be passed along to infants, as well as the data that indicates pregnant women do not report any more side effects than non-pregnant women who received a vaccine. This is one example of how data collection and reporting in V-safe style can lead to improved data that is ready for analysis much more quickly.

Global Coordination of Data Collection

The UK should recognise the importance of sharing data across borders to inform decision-making. Work should be done to share close to real-time data as vaccines are rolled out across different geographies. This will support better decision-making and provide a bigger sample base for drawing insight.

The G7 should establish a high-level group of experts who can provide clear and consistent guidance to various national regulatory bodies allowing for more consistent and clear decisions regarding the safety of Covid-19 vaccines. Sharing data and coordinating communication of it, as well as aiming for more uniform, cross-border decision-making, is essential to restoring public confidence in the workhorse vaccines.

As well as publishing data on the comparative benefits of each vaccine, the UK should lead this global sharing of data through its presidency of the G7.

Conclusion

We need greater confidence in those vaccines that are in plentiful supply. They work perfectly well for the mission ahead domestically and globally: the aim that we should all have to vaccinate the world in 2021.

The reality is that a certain proportion of the population will still get Covid-19, some will be hospitalised and some will die. However, vaccines significantly reduce the prevalence in all three of these categories – cases, hospitalisations and deaths. Even with vaccinations being administered at speed, it is still not possible to eliminate the need for effective containment infrastructure: testing, therapeutics and antivirals.

With vaccines and containment infrastructure combined, Covid-19 can eventually be treated and viewed in the same way as the seasonal flu. This is a realistic end goal for the pandemic. History tells us that only one human virus – smallpox – has ever been eradicated. The reality is that Covid-19 will not disappear and the pursuit of 'zero Covid' is a fantasy.

Clearer data will better prepare us for an endemic state, in which we tolerate an acceptable level of risk and some Covid-19 cases, hospitalisations and deaths. In addition, with advancements in vaccine development, we could see a single jab being used to protect against both seasonal flu strains and Covid-19. This research is already underway as indicated by Moderna's CEO Stéphane Bancel who explained that the company is developing a vaccine targeting both seasonal flu and Covid-19, which, if successful, would protect recipients from both illnesses. [58]

The end goal for Covid-19 is to live safely and freely alongside the virus as it reaches an endemic state. Improved, clearer data is critical to guiding us towards that destination. If we combat rising vaccine hesitancy, eventually the virus will be reduced to seasonal outbreaks, just as we have for the flu. Data will show mortality coming down as better therapeutics come online, and case numbers reducing in parallel to vaccines being rolled out.

1. Publish clear data on all vaccines in use consisting of absolute numbers for Covid-19 cases, hospitalisations and deaths, broken down by age, vaccine status (not vaccinated, partially vaccinated, fully vaccinated) and vaccine type. This should build on the existing post-vaccination surveillance strategy from Public Health England by publishing data more regularly than quarterly, as currently planned, and in as clear a way as possible.

2. Introduce follow-up active monitoring akin to the CDC's V-safe to everyone who has been inoculated. This would show that serious side effects don't occur in the vast majority of the population and inform better decision-making – as evidenced by the gap between the US and UK's

respective decisions to extend vaccine eligibility to pregnant women.

3. Establish a high-level group of experts who can provide clear and consistent guidance to various national regulatory bodies allowing for more consistent and clear decisions regarding the safety of Covid-19 vaccines. This group, led by the G7, should facilitate global data sharing on vaccine side effects and the impact that vaccinations are having on cases, hospitalisations and deaths to support better decision-making and provide a bigger sample base for drawing insight. This would also ensure that different regulators aren't taking different and often confusing decisions on vaccine rollout.

4. Do not pause the rollout of vaccinations when a *suspected* side effect is emerging but has not yet been fully investigated and instead conduct investigations alongside rollout. Pausing to investigate is normal and correct practice in *normal* times. We are not in normal times. The risk from halting vaccines is further hesitancy around the workhorse vaccines and this should be a last resort, rather than the go-to option.

5. Assemble the right containment infrastructure, including testing, therapeutics and antivirals, which, when combined with vaccines, will transform Covid-19, making it flu-like and endemic.

Charts created with Highcharts unless otherwise credited.

Footnotes

1. ^ https://www.forbes.com/sites/williamhaseltine/2021/03/17/astrazeneca-vaccine-fails-to-protect-against-the-south-african-variant/?sh=4520682a6526
2. ^ https://www.telegraph.co.uk/news/2021/04/09/france-drops-astrazeneca-second-dose-under-55s/
3. ^ https://www.telegraph.co.uk/news/2021/04/14/denmark-permanently-stops-using-astrazeneca-vaccine/
4. ^ https://publichealthscotland.scot/news/2021/february/vaccine-linked-to-reduction-in-risk-of-covid-19-admissions-to-hospitals/
5. ^ https://news.sky.com/story/covid-19-what-is-the-blood-clot-risk-from-the-oxford-astrazeneca-vaccine-and-how-does-it-compare-12268572#:~:text=In%20the%20US%2C%20the%20National,putting%20the%20risk%20at%200.1%25
6. ^ https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30756-X/fulltext
7. ^ https://www.stoptheclot.org/about-clots/webinar_contra/birth_control_clots/
8. ^ https://publichealthscotland.scot/news/2021/february/vaccine-linked-to-reduction-in-risk-of-covid-19-admissions-to-hospitals/
9. ^ Israel COVID-19 Corona Tracker
10. ^ https://publichealthscotland.scot/news/2021/february/vaccine-linked-to-reduction-in-risk-of-covid-19-admissions-to-hospitals/
11. ^ https://www.bbc.co.uk/news/health-56665517
12. ^ (I.E. Incidence of 2 in 10,000 per day - roughly equivalent to the number of daily cases in the UK in March 2021)
13. ^ https://wintoncentre.maths.cam.ac.uk/news/communicating-potential-benefits-and-harms-astra-zeneca-covid-19-vaccine/
14. ^ https://www.theguardian.com/world/live/2021/mar/18/coronavirus-live-news-uk-says-eu-vaccine-threat-needs-explaining-tanzania-president-dies?page=with:block-605378d68f083d3e63c4c4d2
15. ^ https://wintoncentre.maths.cam.ac.uk/news/communicating-potential-benefits-and-harms-astra-zeneca-covid-19-vaccine/
16. ^ https://www.ft.com/content/40943f39-a9de-44ea-a7b3-2d45199d6ae1

17. ^ https://www.voanews.com/covid-19-pandemic/denmark-extends-astrazeneca-suspension-three-weeks
18. ^ https://www.ema.europa.eu/en/news/covid-19-vaccine-astrazeneca-benefits-still-outweigh-risks-despite-possible-link-rare-blood-clots
19. ^ https://onlinelibrary.wiley.com/doi/epdf/10.1111/jth.14869
20. ^ https://news.sky.com/story/covid-19-what-is-the-blood-clot-risk-from-the-oxford-astrazeneca-vaccine-and-how-does-it-compare-12268572#:~:text=In%20the%20US%2C%20the%20National,putting%20the%20risk%20at%200.1%25
21. ^ https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30756-X/fulltext
22. ^ https://www.stoptheclot.org/about-clots/webinar_contra/birth_control_clots/
23. ^ https://news.sky.com/story/covid-19-what-is-the-blood-clot-risk-from-the-oxford-astrazeneca-vaccine-and-how-does-it-compare-12268572#:~:text=In%20the%20US%2C%20the%20National,putting%20the%20risk%20at%200.1%25
24. ^ https://www.huffingtonpost.co.uk/entry/taking-aspirin-before-the-astrazeneca-covid-vaccine_uk_60701930c5b6616dcd761f36
25. ^ https://www.nhsinform.scot/tests-and-treatments/medicines-and-medical-aids/types-of-medicine/aspirin
26. ^ https://www.ema.europa.eu/en/news/astrazenecas-covid-19-vaccine-ema-finds-possible-link-very-rare-cases-unusual-blood-clots-low-blood
27. ^ https://www.politico.eu/article/eu-regulator-backs-oxford-astrazeneca-vaccine-confirms-link-to-very-rare-blood-clot/?utm_source=dailybrief&utm_medium=email&utm_campaign=DailyBrief2021Apr8&utm_term=DailyNewsBrie
28. ^ Based on the estimated rate of 1 in 1,000 per year[28] for the UK population age 16+
29. ^ based on the estimated rate of 1 in 1,200 per year[29] for the UK population age 16+
30. ^ based on the estimated rate of 5 in 1,000,000 per year[30] for the UK population age 16+
31. ^ Based on the estimated rate of 1 in 1,000 per year[31] for the UK population age 16+
32. ^ based on the estimated rate of 1 in 1,200 per year[32] for the UK population age 16+
33. ^ based on the estimated rate of 5 in 1,000,000 per year[33] for the UK population age 16+
34. ^ https://www.ema.europa.eu/en/documents/covid-19-vaccine-safety-update/

covid-19-vaccine-safety-update-vaxzevria-previously-covid-19-vaccine-astrazeneca-29-march-2021_en.pdf

35. ^ https://www.sciencedirect.com/science/article/pii/S0264410X18309976?via%3Dihub
36. ^ https://www.cdc.gov/flu/spotlights/2018-2019/hopitalization-rates-older.html
37. ^ https://www.cdc.gov/flu/about/burden/2019-2020.html#:~:text=During%20the%202019%2D2020%20influenza,405%2C000%20hospitalizations%2C
38. ^ 48.4% of US Adult Population received the vaccine in 2019/20 - https://www.cdc.gov/flu/fluvaxview/coverage-1920estimates.htm
39. ^ https://www.cdc.gov/flu/vaccines-work/vaccineeffect.htm
40. ^ https://yougov.co.uk/topics/international/articles-reports/2021/03/22/europeans-now-see-astrazeneca-vaccine-unsafe-follo
41. ^ https://s3.eu-central-1.amazonaws.com/euobs-media/107197e5f2ddfde1654d9f30c4be9418.pdf
42. ^ https://www.tortoisemedia.com/2021/04/07/sensemaker-210407/
43. ^ https://today.yougov.com/topics/politics/articles-reports/2021/04/15/johnson-johnson-vaccine-confidence?utm_source=twitter&utm_medium=website_article&utm_campaign=johnson_johnson_vaccine_confidenc
44. ^ https://www.bcg.com/en-us/publications/2021/covid-19-us-vaccine-sentiment-series
45. ^ https://inews.co.uk/news/black-half-likely-covid-19-vaccine-white-861656
46. ^ https://www.worldometers.info/coronavirus/country/israel/
47. ^ https://edition.cnn.com/2021/04/14/health/breakthrough-infections-covid-vaccines-cdc/index.html
48. ^ https://uk.news.yahoo.com/cdc-breakthrough-cases-explained-173107351.html
49. ^ https://edition.cnn.com/2021/04/14/health/breakthrough-infections-covid-vaccines-cdc/index.html
50. ^ https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/978315/050421_AZ_DAP.pdf
51. ^ https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/978316/050421_PF_DAP.pdf

52. ^ COVID-19 vaccination: a guide for all women of childbearing age, pregnant or breastfeeding - GOV.UK (www.gov.uk)

53. ^ https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-02/28-03-01/05-covid-Shimabukuro.pdf

54. ^ https://www.birmingham.ac.uk/news/latest/2021/03/covid-pregnant-women-babies-risk.aspx

55. ^ https://www.whitehouse.gov/briefing-room/press-briefings/2021/04/05/press-briefing-by-white-house-covid-19-response-team-and-public-health-officials-24/

56. ^ https://www.wsj.com/articles/covid-19-vaccinations-of-pregnant-mothers-also-protect-newborns-studies-suggest-11617183001

57. ^ https://www.whitehouse.gov/wp-content/uploads/2021/04/COVID-Press-Briefing_5April2021_for-transcript.pdf

58. ^ https://www.wsj.com/livecoverage/covid-2021-03-23/card/qVE01KdPTaZWp3oBX9yb

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