

# COVID-19: THROMBOTIC ADVERSE EVENTS WITH ADENOVIRUS VACCINES



A Rapid Guidance Summary from the Penn Medicine Center for Evidence-based Practice  
Last updated May 17, 2021. All links rechecked May 17 unless otherwise noted.

*This Rapid Guidance Summary is a description of existing guidance and evidence reviews from a variety of sources that was in effect at the time of publication. It should not be used or interpreted as a clinical practice guideline, but instead can be used in development of local recommendations and policies.*

## Key questions answered in this summary

- What is the risk of thrombosis with thrombocytopenia syndrome (TTS) in patients who are given COVID-19 vaccines made with adenovirus vector technology?
- Which patient groups should not be given adenovirus vaccines?

*CEP NOTE: Several different names have been used for the thrombotic syndromes that are the subject of this report: Authorities in the United States are calling it “thrombosis with thrombocytopenia syndrome” (TTS) while some foreign agencies refer to it as “vaccine-induced thrombotic thrombocytopenia” (VITT) or vaccine-induced prothrombotic immune thrombocytopenia (VIPIT). Please see the separate [CEP Rapid Guidance Summary](#) for information on diagnosis and treatment of TTS.*

## Summary of major recommendations

- Each of the regulatory agencies that have authorized marketing and use of the AstraZeneca and Johnson & Johnson (J&J/Janssen) vaccines have acknowledged a risk of TTS and other thrombotic adverse events with use of the vaccines.
- None of the agencies have withdrawn authorization; all of them conclude that the risk of harm from remaining unvaccinated is greater than the risk of harm from the vaccines.
- The estimated risk is 4 to 10 events per million doses. More recent estimates have been on the higher end of this range. While the majority of reported instances of TTS are in young adult women, there is not a consensus that age and gender are risk factors.
- Some advisory committees have recommended to their respective national health agencies that mRNA vaccines should be preferred over adenovirus vaccines for younger patients, so long as vaccine supplies are such that it will not unduly delay vaccination. Age thresholds in these recommendations range from 30 to 60.
- In response to those advisory statements, some regulatory agencies and national health agencies, along with some professional societies, have reiterated their position that the benefits of adenovirus vaccines outweigh the risks.
- Guideline producers recommend that decision-making concerning the use of these vaccines should take into account local infection and transmission levels, local vaccine availability, and logistical and other challenges in vaccinating patients, to compare risk of hospitalization and death from TTS to the risk of hospitalization and death from COVID-19 disease.
- None of the guidance documents give any information on the comparative risk of these events with the AstraZeneca vaccine versus the J&J vaccine.

## Current regulatory status of adenovirus vaccines

Manufacturer (partner)	AstraZeneca	Johnson & Johnson
Trade name(s)	Vaxzevria, Covishield	COVID-19 Vaccine Janssen (†)

Candidate name(s)	ChAdOx-1S, ADZ-1222	Ad26.COVS-S [recombinant]
<a href="#">USA</a> (FDA)	Not authorized	Feb. 27: Emergency use authorization April 13: FDA recommends <a href="#">pause</a> in use April 23: <a href="#">Pause halted. Recommendation for use reaffirmed, warning added.</a>
<a href="#">Canada</a> (Health Canada)	Feb. 26: Authorized with conditions (‡)	March 5: Authorized with conditions
<a href="#">United Kingdom</a> (MHRA)	Dec. 30: Approved	Not approved
<a href="#">European Union</a> (EMA)	Jan. 29: Conditional marketing authorization March 30: Warning added (§) April 14, May 11: <a href="#">Safety update, but no change in recommendations</a>	March 11: Conditional marketing authorization April 20: Warning added (§) April 22, May 11: <a href="#">Safety update, but no change in recommendations</a>

CEP NOTE: The Sputnik V vaccine (candidate name Gam-COVID-Vac, manufacturer Gamaleya, applicant R-Pharm Germany) is an adenovirus vaccine, but it has not been approved by any of the above agencies. Initial review by EMA began March 4.

†–Janssen Pharmaceuticals is a subsidiary of Johnson & Johnson.

‡–product manufactured by Verity Pharmaceuticals Inc./Serum Institute of India also authorized.

§–EU member countries may make their own decisions regarding use of approved products, and some countries have suspended use of the AstraZeneca and/or J&J/Janssen vaccines.

### Government agency or advisory panel information on incidence of TTS

Source	Recommendations
<a href="#">CDC</a> (USA) May 11	After receiving the J&J/Janssen COVID-19 Vaccine, there is risk for a rare but serious adverse event—blood clots with low platelets (thrombosis with thrombocytopenia syndrome, or TTS). Women younger than 50 years old should especially be aware of their increased risk for this rare adverse event. There are other COVID-19 vaccines available for which this risk has not been seen.  This adverse event is rare, occurring at a rate of about 7 per 1 million vaccinated women between 18 and 49 years old. For women 50 years and older and men of all ages, this adverse event is even more rare.
<a href="#">JCVI</a> (UK) May 7	Up to 28 April 2021, the MHRA had received 242 reports of blood clotting cases in people who also had low levels of platelets in the UK, following the use of Oxford/AstraZeneca vaccine. These numbers are very small compared to the millions of people who have received the vaccine. The overall incidence of case reports of thromboembolic events with low platelets after first or unknown doses was 10.5 per million doses.
<a href="#">NACI</a> (Canada) May 3	The rate of this adverse event has been estimated to be between 1/100,000 and 1/250,000 persons vaccinated with the AstraZeneca COVID-19 vaccine, however this rate is evolving as cases continue to be reported and investigated. The estimate in Canada as of April 28, 2021 is closer to 1/100,000. The case fatality rate typically ranges between 20 and 40%. Other predisposing factors for VITT are unclear.  Evidence of this adverse event after vaccination with the Janssen COVID-19 vaccine is emerging in the United States. As of April 28, 2021, 17 cases have been confirmed after 8 million doses of the Janssen vaccine administered. Most of these cases were in female between 18 and 59 years of age, however additional cases are under investigation. Initial cases of VITT after vaccination with AstraZeneca COVID-19 vaccine were also seen in younger females; however, reports of VITT in older adults and in males have more recently been confirmed. The risk of developing VITT after receipt of the AstraZeneca COVID-19 vaccine does not seem to be related to age or sex.
<a href="#">FDA</a> (USA) April 23	Most cases of thrombosis with thrombocytopenia reported following the Janssen COVID-19 Vaccine have occurred in females ages 18 through 49 years; some have been fatal.  Specific risk factors for thrombosis with thrombocytopenia following the Janssen COVID-19 Vaccine and the level of potential excess risk due to vaccination are under investigation.

Source	Recommendations
<a href="#">ATAGI</a> (Australia) April 23	<p>There is currently uncertainty in, and different reported rates of risk, for this adverse event. Studies have suggested it may occur in approximately 4 - 6 people in every one million people in the 4-20 days after the first dose of vaccine. However, higher rates have been reported in Germany and some Scandinavian countries.</p> <p>Some evidence suggests the risk of this condition occurring may be somewhat higher in people of a younger age, however a small number of cases have been reported in people of different ages (including older adults).</p> <p>While there have been more reports of TTS in women in some settings, this may be because more vaccine doses have been given to women. In one country the reported rate of TTS (number of cases adjusted for the number of men and women vaccinated) was similar in men and women.</p> <p>TTS can cause serious long term disability or death (with death occurring in approximately 25% of reported cases). So far no specific biological risk factors or pre-existing medical conditions have been found to modify (i.e. increase or decrease) the risk of TTS occurring after AstraZeneca vaccine.</p> <p>We do not yet know to what extent earlier recognition of this syndrome and improved treatments will improve patient outcomes. More cases can be expected to occur, albeit rarely.</p>
<a href="#">EMA</a> (EU) April 14	The product information for Vaxzevria should ... specify thrombocytopenia as a new common side effect (occurring in less than 1 in 10 persons) and thrombosis in combination with thrombocytopenia as a new very rare side effect (occurring in less than 1 in 10,000 persons).

## Government agency guidance on use of adenovirus vaccines

Source	Recommendations
<b>USA</b>	
<a href="#">CDC</a> (USA) May 13	The best COVID-19 vaccine is the first one that is available to you. Do not wait for a specific brand. All currently authorized and recommended COVID-19 vaccines are safe, are effective, and reduce your risk of severe illness. CDC does not recommend one vaccine over another.
<a href="#">ACIP</a> (USA) April 30	On April 23, ACIP concluded that the benefits of resuming Janssen COVID-19 vaccination among persons aged ≥18 years outweighed the risks and reaffirmed its interim recommendation under FDA's Emergency Use Authorization, which includes a new warning for rare clotting events among women aged 18–49 years.
<b>UK</b>	
<a href="#">JCVI</a> May 7	<p>The chances of a younger person becoming seriously ill with COVID-19 get smaller as infection rates increasingly come under control in the UK. Considering this alongside the portfolio of vaccines available in the UK in the coming months and taking a precautionary approach in relation to the extremely small risk of thrombosis and thrombocytopenia following the first dose of the Oxford/AstraZeneca vaccine, the JCVI has advised a preference for adults aged 30 to 39 without underlying health conditions to receive an alternative to the Oxford/AstraZeneca vaccine – where available and only if this does not cause substantial delays in being vaccinated.</p> <p>This follows the <a href="#">decision</a> on April 7 to offer a preference for adults aged under 30.</p> <p><i>CEP NOTE: the April 7 guidance stated that it is preferable to offer persons aged under 30 an mRNA vaccine.</i></p>
<a href="#">MHRA</a> May 7	Our position remains that the benefits of the COVID-19 Vaccine AstraZeneca against COVID-19, with its associated risk of hospitalization and death, continue to outweigh the risks for the vast majority of people. The balance of benefits and risks is very favorable for older people but is more finely balanced for younger people and we advise that this evolving evidence should be taken into account when considering the use of the vaccine, <a href="#">as JCVI has done</a> .

Source	Recommendations
<p><a href="#">MHRA</a> April 15</p>	<p>Up to and including 31 March 2021, the MHRA had received 79 UK reports of blood clotting cases alongside low levels of platelets following the use of the COVID-19 Vaccine AstraZeneca:</p> <ul style="list-style-type: none"> <li>• 44 of the 79 cases were of CVST with thrombocytopenia</li> <li>• 35 of the 79 cases were of thrombosis in other major veins with thrombocytopenia</li> <li>• 79 cases occurred in 51 women and 28 men, aged from 18 to 79 years. It should be noted that more women have been vaccinated with COVID-19 Vaccine AstraZeneca than men.</li> <li>• Sadly, 19 people have died out of the 79 cases – 13 females and 6 males. 11 out of the 19 people who died were under the age of 50, 3 of whom were under 30. 14 of these 19 cases were of CVST with thrombocytopenia and 5 were of thrombosis with thrombocytopenia.</li> <li>• All 79 cases occurred after a first dose of the vaccine.</li> </ul> <p>This risk, based on reports up to and including 31 March, is slightly higher than the risk calculated from the reports published up to and including 24 March. However, likelihood of these blood clots occurring is still extremely rare. As a precaution, administration of COVID-19 Vaccine AstraZeneca in people of any age who are at higher risk of blood clots because of their medical condition should be considered only if benefits from the protection from COVID-19 infection outweighs potential risks.</p> <p>Anyone who experienced cerebral or other major blood clots occurring with low levels of platelets after their first vaccine dose of COVID-19 Vaccine AstraZeneca should not have their second dose. Anyone who did not have these side effects should come forward for their second dose when invited.</p> <p>Pregnancy predisposes to thrombosis, therefore women should discuss with their healthcare professional whether the benefits of having the vaccine outweigh the risks for them.</p> <p>The MHRA recently confirmed that the evidence to date does not suggest that the COVID-19 Vaccine AstraZeneca causes venous thromboembolism without a low platelet count.</p> <p>The data suggest there is a slightly higher incidence reported in the younger adult age groups and the MHRA advises that this evolving evidence should be taken into account when considering the use of the vaccine.</p> <p>The MHRA is not recommending age restrictions in COVID-19 Vaccine AstraZeneca vaccine use.</p> <p><i>CEP NOTE: J&amp;J/Janssen vaccine is presently not approved for use in the UK.</i></p>
<b>European Union</b>	
<p><a href="#">EMA</a> April 20</p>	<p>At its meeting of 20 April 2021, EMA's safety committee (PRAC) concluded that a warning about unusual blood clots with low blood platelets should be added to the product information for COVID-19 Vaccine Janssen. PRAC also concluded that these events should be listed as very rare side effects of the vaccine.</p> <p>In reaching its conclusion, the Committee took into consideration all currently available evidence including eight reports from the United States of serious cases of unusual blood clots associated with low levels of blood platelets, one of which had a fatal outcome. As of 13 April 2021, over 7 million people had received Janssen's vaccine in the United States.</p> <p>All cases occurred in people under 60 years of age within three weeks after vaccination, the majority in women. Based on the currently available evidence, specific risk factors have not been confirmed.</p>
<p><a href="#">EMA</a> (EU) April 14</p>	<p><b>Summary:</b> Very rare, potentially serious, events of unusual blood clots in combination with low blood platelet levels have been confirmed as a new side effect of Vaxzevria. There are no recommended changes to the product information regarding how to use this vaccine; Vaxzevria is effective in preventing COVID-19.</p> <p>Taking into account all available evidence and advice, PRAC concluded that a causal relationship between vaccination with Vaxzevria and very rare cases of thrombosis together with thrombocytopenia, sometimes accompanied by bleeding, is plausible. The reported thromboses with thrombocytopenia include venous thrombosis, also in unusual sites such as cerebral venous sinus thrombosis (CVST) (where blood clots in the brain's venous sinuses prevent blood from draining out of the brain) and splanchnic vein thrombosis (which involves one or more veins in the abdomen [belly]), as well as arterial thrombosis. Although such side effects are very rare, the reported case numbers exceeded what is seen in the general population. The majority of these cases occurred within 14 days after vaccination and mostly in women under 60 years of age; some cases had a fatal outcome. Based on the available data, no specific risk factors were identified.</p>

Source	Recommendations
<a href="#">AIFA</a> (Italy) April 24	<p>The EMA has determined that the benefits of the vaccine in preventing COVID-19 disease (which itself causes clotting problems) far outweigh the risks, the vaccine does not increase the overall risk of thromboembolic events, and there are no issues with individual batches. Rare venous thrombotic events at unusual sites have been recognized as possible side effects of Vaxzevria vaccine. No predisposing risk factors have been confirmed; since most cases have occurred in people under the age of 60, the Italian Ministry of Health has recommended preferential use in people over the age of 60 and established that those who have already received a first dose of the Vaxzevria vaccine can complete the vaccination cycle with the same vaccine.</p> <p>On 20 April, the Pharmacovigilance Risk Assessment Committee (PRAC) of EMA concluded the benefits of the Janssen vaccine outweigh the risks and confirmed authorization for the entire population over 18 years. In Italy, the Ministry of Health, after obtaining the opinion of AIFA's Technical Scientific Committee, recommended its use for individuals over 60 years of age.</p>
<a href="#">STIKO</a> (Germany) April 14	<p>STIKO recommends vaccination with AstraZeneca's Vaxzevria only for persons 60 years of age or older. For adults below this age limit, STIKO does not currently recommend vaccination with this vaccine, as serious illnesses have occurred in some rare cases, predominantly in people under 60 years of age. Such illnesses included blood clots (thromboses) in combination with a reduction in the blood platelet count (thrombocytopenia) and were sometimes accompanied by bleeding. Some of these persons have died.</p> <p>For individuals 60 years of age and older, the risk of becoming severely ill with COVID-19 or dying from COVID-19 is significantly higher than for younger individuals. In addition, the complications described above occurred quite predominantly in persons younger than 60 years. Vaccination with Vaxzevria from AstraZeneca is therefore recommended for persons 60 years and older. The vaccine has been shown to have good efficacy in this age group as well.</p> <p>According to the STIKO recommendation, vaccination with Vaxzevria from AstraZeneca is still possible in people under 60 years of age if they make this decision together with their doctor.</p> <p>The second vaccination following the initial vaccination with Vaxzevria from AstraZeneca: For persons 60 years of age and older who received their 1st vaccination with AstraZeneca's Vaxzevria, it is recommended that they also receive their 2nd vaccination with AstraZeneca's Vaxzevria.</p> <p>For individuals under 60 years of age who have already been vaccinated with AstraZeneca's Vaxzevria, STIKO currently recommends that the 2nd vaccination be given 12 weeks after the 1st vaccination with an mRNA vaccine (Comirnaty from BioNTech/Pfizer or Moderna COVID-19 vaccine from Moderna).</p> <p><i>CEP NOTE: a <a href="#">May 10 guidance</a> from STIKO makes similar recommendations regarding the J&amp;J/Janssen vaccine.</i></p>
<a href="#">HAS</a> (France) April 8	<p>Use of the AstraZeneca vaccine in persons aged under 55 was paused in France on March 19. HAS recommends use of MRNA vaccines for the second dose in persons who received a first dose of AstraZeneca vaccine. The recommended interval for the second dose is 12 weeks.</p>
<p><b>Canada</b></p>	
<a href="#">NACI</a> (Canada) May 3	<p>At this time and based on current evidence, NACI recommends a complete series with viral vector COVID-19 vaccine (AstraZeneca, Janssen) may be offered to individuals 30 and older without contraindications if the individual prefers an earlier vaccine rather than wait for an mRNA vaccine and if the following conditions apply:</p> <ul style="list-style-type: none"> <li>• A benefit-risk analysis determines that the benefit of earlier vaccination with the viral vector COVID-19 vaccine outweighs the risk of the individual getting COVID-19 while waiting for an mRNA COVID-19 vaccine;</li> <li>• The individual provides informed consent once the benefits and risks of VITT compared to COVID-19 are clearly outlined, including how long the individual will have to wait for an mRNA vaccine and public health measures the individual is able to take to minimize their exposure to the COVID-19 virus; and</li> <li>• The individual will have to wait in order to receive an mRNA vaccine.</li> </ul> <p>The public health benefit-risk analysis for the use of the vaccine may vary between jurisdictions. Provinces and territories adapt NACI's recommended age threshold based on their unique circumstances, including local COVID-19 epidemiology, local vaccine supply and logistics and equity considerations. Health officials can refer to a Risk Assessment Tool for the use of the Janssen vaccine included in NACI's updated statement.</p> <p>NACI continues to preferentially recommend authorized mRNA COVID-19 vaccines due to the excellent protection they provide and the absence of any safety signals of concern. NACI notes that Canada has procured and is expecting enough mRNA vaccines to fully vaccinate the eligible Canadian population before fall 2021.</p> <p><i>CEP NOTE: NACI did not differentiate between the AstraZeneca and J&amp;J/Janssen vaccines in this guidance.</i></p>



Source	Recommendations
<a href="#">Health Canada</a> May 4	<p>Health Canada's review of the available information concluded that a link between the use of Janssen COVID-19 Vaccine and the risk of blood clots with low platelets is possible. The risk of these events is very rare.</p> <p>The overall benefits of Janssen COVID-19 Vaccine in preventing COVID-19 outweigh the risk of very rare events of blood clots in combination with low platelets.</p> <p>Health Canada's review of available information did not identify specific risk factors, such as age or gender, for these very rare events. Therefore, Health Canada is not restricting the use of the vaccine for certain populations or age groups. The risk of severe disease associated with COVID-19 illness varies with age and continues to change as the nature of the pandemic changes.</p>
<a href="#">Health Canada</a> April 19	<p>Health Canada's review of the available information concluded that a link between the use of AstraZeneca COVID-19 Vaccine and COVISHIELD and the risk of these blood clots with low platelets is possible. The risk of these events is very rare, and the overall benefits of the vaccine in protecting Canadians from COVID-19 continue to outweigh its potential risks.</p> <p>Health Canada did not identify risk factors, such as age or gender, for these very rare events, and is not restricting the use of the vaccine at this time.</p>
<b>Australia</b>	
<a href="#">ATAGI (Australia)</a> April 23	<p>Comirnaty (Pfizer) is preferred over AstraZeneca COVID-19 vaccine in people under the age of 50 years. The AstraZeneca COVID-19 vaccine can still be given to adults under 50 years if Comirnaty is not available, if the benefit of vaccination is likely to outweigh risk, and where informed consent has been obtained.</p> <p>In people aged 50 years and over, the benefits of AstraZeneca COVID-19 vaccine outweigh the risks associated with vaccination. This is due to the ongoing potential for COVID-19 outbreaks, the widespread susceptibility of the Australian population, and the strong relationship of severe COVID-19 and mortality with increasing age.</p> <p><i>CEP NOTE: The J&amp;J/Janssen and Moderna vaccines are not approved for use in Australia.</i></p>
<b>International</b>	
<a href="#">WHO</a> April 21	<p>A very rare syndrome of blood clotting combined with low platelet counts, described as thrombosis with thrombocytopenia syndrome (TTS), has been reported around 4 to 20 days following vaccination with the ChAdOx1-S vaccine. A causal relationship between the vaccine and TTS is considered plausible although the biological mechanism for this syndrome is still being investigated. Most of these cases were reported from the United Kingdom and the European Union (EU). There is considerable geographic variation with regards to the reported incidence, with very few cases reported from non-European countries, despite extensive use of the vaccine in these countries. An estimation of the risk outside Europe needs further data collection and analysis. Data from the United Kingdom (31 March 2021) suggest the risk of TTS is approximately 4 cases per 1 million (1 case per 250 000) vaccinated adults, while the rate is estimated to be approximately 1 case per 100 000 in the EU. Current data from Europe suggest that the risk may be higher in younger adults compared with older adults; no specific risk factors have yet been identified.</p> <p>In countries with ongoing SARS-CoV-2 transmission, the benefit of vaccination in protecting against COVID-19 far outweighs the risks. However, benefit–risk assessments may differ from country to country, and countries should consider their epidemiological situation, individual and population-level risks, availability of other vaccines, and alternate options for risk mitigation. The benefit– risk ratio is greatest in older age groups as the risk of severe COVID-19 disease outcomes including COVID-19 related thromboembolic events increases with age.</p> <p>It is currently unknown whether there is a risk of TTS following the second dose. As data from additional studies become available, enabling better understanding of the pathophysiology of TTS and its relationship to the vaccine, recommendations on vaccination will be updated, if appropriate. People who have had blood clots associated with low platelet levels (TTS) after their first dose of should not be given their second dose.</p>

CEP NOTE: Guidance also includes recommendations against the use of vaccines in persons who have known allergies to specific ingredients in the vaccine, or have a history of adverse reactions to other vaccines. Details of these recommendations are not included in our tables.

## Professional society guidance on adenovirus vaccines

Source	Recommendations
<a href="#">ASH</a> (USA) April 29	<p>Following FDA/CDC review of all sources of vaccine event reporting in the United States following JJ vaccine administration, and a detailed risk/benefit analysis, the CDC Advisory Committee on Immunization Practices met on April 23, 2021, and voted to recommend that the JJ vaccine again be available for persons aged 18 years and older under the FDA's Emergency Use Authorization. The 10-day pause in administration of the JJ vaccine was believed to be sufficient to educate health care providers regarding TTS diagnosis and treatment. The overall safety, efficacy, and need for the JJ vaccine was thought to far outweigh the very low risk of TTS. The updated incidence of this constellation of findings was extremely rare at two per million for the JJ vaccine, based on a total of 15 cases reported following 7.98 million doses administered. The rate was seven per million in the highest risk group of women younger than 50 years; however, even in this group, the risk/benefit strongly favored vaccination, based on a predicted 116 deaths from COVID-19 disease per million at current infection and mortality rates. Educational materials being provided by the CDC and FDA will inform the public regarding the option of mRNA vaccines with lower risk of TSS, particularly women younger than 50 years who have developed TTS at the highest rate to date following the JJ vaccine.</p> <p>Based on current information, we strongly agree with the CDC panel that the risk of COVID-19 disease, including thrombosis, far outweighs the extremely rare risk of TTS associated with highly efficacious vaccines.<sup>5</sup> Of note, there is no information to date on any increased risk for TTS in patients with blood diseases and/or pre-existing risk factors for thrombosis or autoimmunity. The single-dose JJ vaccine may be particularly attractive for administration to patients before initiation of chemotherapy or other immunosuppressive interventions.</p>
<a href="#">Thrombosis Canada</a> April 26	<p>Thrombosis Canada acknowledges the recommendation of the National Advisory Committee on Immunization (NACI) that the AstraZeneca SARS-CoV-2 vaccine may be offered to individuals 30 years of age and older.</p> <p>Thrombosis Canada, alongside NACI and other healthcare organizations in Canada, is closely monitoring emerging evidence on the safety of the AstraZeneca vaccine and will provide timely updates to healthcare professionals and the public to enable informed decisions about the administration of this vaccine.</p> <p>In the meantime, Thrombosis Canada continues to strongly recommend that all eligible adults receive the AstraZeneca and Johnson &amp; Johnson (Janssen) vaccines, including people with a prior blood clot, those with a blood clotting tendency (e.g., factor V Leiden mutation), and people who are receiving blood thinners as the benefits of receiving the vaccine far outweigh the risks.</p>
<a href="#">ISTH</a> April 20	<p>ISTH reiterates that COVID-19 is associated with a risk of hospitalization and death. The reported combination of blood clots and low blood platelets is exceedingly rare, and the overall benefits of the AstraZeneca vaccine and the Johnson &amp; Johnson vaccine outweigh the risks of these rare thromboembolic side effects.</p>
<a href="#">BSH</a> (UK) April 8	<p>We wish to draw to the MHRA's attention that there is no evidence that individuals with a prior history of thrombosis or known risk factors for thrombosis are more at risk of developing the immune complication reported after the AstraZeneca vaccine. Furthermore, for the majority of individuals, the risk of recurrent thrombosis due to COVID19 infection is far greater than the risk of this syndrome.</p> <p>To avoid potential harm arising from unnecessary delay in vaccination for this group, we ask and strongly urge the MHRA to review their statement of 7th April 2021, and amend to be in line with the JCVI statement of the same date which weighed the relative balance of benefit and risk to advise:</p> <ul style="list-style-type: none"> <li>• Only individuals under the age of 30 years without underlying health conditions which put them at a higher risk of severe COVID-19 disease, to be offered an alternative COVID-19 vaccine, if available.</li> <li>• There are some adults &lt;30 without underlying health conditions who are in phase 1, who were prioritised due to an increased risk of exposure and/or to reduce the risk of passing the infection on to vulnerable individuals. This includes health and social care workers, unpaid carers and household contacts of immunosuppressed individuals. Acting on a precautionary basis, if these persons are still unvaccinated, it is preferable for them to be offered an alternative COVID-19 vaccine, if available.</li> </ul>
<a href="#">ETHA</a> (Europe) Not dated	<p>The benefits of the vaccine continue to outweigh the risks for people who receive it. The vaccine is effective at preventing COVID-19 and reducing hospitalization and death.</p> <p>Patients with a prior history of blood clots or with a history of thrombophilia should continue to be vaccinated.</p> <p>National authorities may provide additional guidance on the roll out of the vaccine based on the situation in your country.</p>

## Medical center guidance on use of adenovirus vaccines

Hospital	Recommendation
<a href="#">Penn Medicine</a> Not dated	We are offering the J&J vaccine to adults who face significant difficulties getting to a vaccination site. This vaccine is especially well-suited for homebound people because it is easier to transport, does not need to be stored at ultra-cold temperatures, and involves only one appointment.
<a href="#">Brigham</a> April 23	<p>There have been reports of rare venous thrombotic disease--and particularly cerebral venous sinus thrombosis--in recipients of the widely deployed Oxford/AstraZeneca and Janssen/J&amp;J adenovirus vector vaccines.</p> <p>Although the mechanism of this clotting dysfunction is not certain, it appears to be a vaccine cross-reaction that causes an auto-immune thrombocytopenia. There appears to be an increased risk in women under the age of sixty, possibly related to estrogen levels.</p> <p>For both vaccines, the frequency of these events appears to be lower than the risk of thromboembolic complications of COVID-19. As of April 15, 2021, the benefits of both Oxford/AstraZeneca and Janssen/J&amp;J vaccines in a pandemic context are still thought to outweigh potential risks.</p> <p>Given the appropriately high bar for safety of vaccines, however, deployment of both of these vaccines has been paused in many jurisdictions, as agencies try to better understand any causal link between the vaccines and these thrombotic complications.</p>
The following medical centers resumed use of the J&J vaccine after the CDC-recommended pause: Medstar (Washington DC), Columbia/New York Presbyterian, Penn Medicine, University of Washington, Yale	
The following medical centers have not stated whether they resumed use of the J&J vaccine after the CDC-recommended pause, and have not identified specific groups of patients for whom use of the J&J vaccine should be discouraged: Beth Israel Lahey Health, Cleveland Clinic, Mount Sinai, UCSF	
CEP NOTE: Some medical centers have only used mRNA vaccines (for reasons which may or may not relate to safety). These medical centers include Emory, Massachusetts General Hospital, University of Michigan	

## Guidance sources

ATAGI—Australian Technical Advisory Group on Immunisation  
 BSH—British Society for Haematology  
 EMA—European Medicines Agency  
 FDA—US Food and Drug Administration  
 IDSA—Infectious Diseases Society of America  
 JCVI—Joint Committee on Vaccination and Immunisation (UK)  
 MHRA—Medicines and Healthcare products Regulatory Agency (UK)  
 RCP—Royal College of Physicians (UK)  
 THANZ—Thrombosis and Haemostasis Society of Australia and New Zealand  
 UCSF—University of California, San Francisco  
 WHO—World Health Organization

## Sources with no relevant guidance at this time

American College of Physicians  
 Canadian Agency for Drugs and Technologies in Health  
 Cochrane COVID Review Bank  
 ECRI Guidelines Trust  
 European Hematology Association  
 Evidence Aid  
 FLARE (Massachusetts General Hospital)  
 Health Information and Quality Authority (Ireland)



National COVID-19 Clinical Evidence Taskforce (Australia)  
National Institute for Health and Care Excellence (NICE, UK)  
Oxford COVID-19 Evidence Service

### **Update history (key additions and changes only)**

May 17: Initial report.

### **About this report**

A Rapid Guidance Summary is a focused synopsis of recommendations from selected guideline issuers and health care systems, intended to provide guidance to Penn Medicine providers and administrators during times when latest guidance is urgently needed. It is not based on a complete systematic review of the evidence. Please see the CEP web site (<http://www.uphs.upenn.edu/cep>) for further details on the methods for developing these reports.

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