DEPARTMENT OF HEALTH AND HUMAN SERVICES
CENTERS FOR DISEASE CONTROL AND PREVENTION

Advisory Committee on Immunization Practices (ACIP)

Summary Report
April 23, 2021
Atlanta, Georgia

Final - April 23, 2021

MEETING OF THE ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES (ACIP)
Centers for Disease Control and Prevention
Atlanta, Georgia 30329
April 23, 2021

AGENDA ITEM		PRESIDER/PRESENTER(s)
Friday, April 23, 2021		
11:00	**Welcome & Introductions**	Dr. José Romero (ACIP Chair) Dr. Amanda Cohn (ACIP Executive Secretary, CDC)
11:30	**Coronavirus Disease 2019 (COVID-19) Vaccines**	
	Introduction	Dr. Beth Bell (ACIP, WG Chair)
	Pathogenesis and Management of Thrombosis with Thrombocytopenia Syndrome (TTS)	Dr. Michael Streiff, MD (Johns Hopkins University School of Medicine)
	Thrombosis with thrombocytopenia syndrome (TTS) following Janssen COVID-19 vaccine	Dr. Tom Shimabukuro (CDC/NCEZID)
12:30	***Break***	
1:00	**Public Comment**	
1:30	***Break***	
1:45	Update on Janssen COVID-19 vaccine	Dr. Mathai Mammen (Global Head of Janssen Research and Development) Dr. Joanne Waldstreicher (Johnson & Johnson Chief Medical Officer)
	VaST assessement	Dr. Grace Lee (ACIP, VaST Co-chair)
	Thrombosis with thrombocytopenic syndrome (TTS) after COVID-19 vaccines: Applying the Evidence to Recommendation Framework Discussion	Dr. Sara Oliver (CDC/NCIRD)
	VOTE	
	Janssen COVID-19 Vaccine: Updated recommendations for use	Dr. Sara Oliver (CDC/NCIRD)
5:00	**Adjourn**	

Acronyms

CDC	Centers for Disease Control and Prevention
CMS	Centers for Medicare and Medicaid Services
COVID-19	Coronavirus disease 2019
EtR	Evidence to Recommendations Framework
FDA	Food and Drug Administration
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HRSA	Health Resources and Services Administration
IHS	Indian Health Service
NCHHSTP	National Center for HIV, Hepatitis, STD and TB Prevention [of CDC/OID]
NCIRD	National Center for Immunization & Respiratory Diseases [of CDC/OID]
NCEZID	National Center for Emerging and Zoonotic Diseases [of CDC/OID]
NIAID	National Institute of Allergy and Infectious Diseases
OIDP	Office of Infectious Disease and HIV/AIDS Policy
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
WG	Work Group
WHO	World Health Organization
VaST	Vaccine Safety Technical Subgroup
VE	Vaccine Effectiveness

Acronyms

AAFP	American Academy of Family Physicians
AAP	American Academy of Pediatrics
AC Forum	Anticoagulation Forum
ACHA	American College Health Association
ACIP	Advisory Committee on Immunization Practices
ACOG	American College of Obstetricians and Gynecologists
ACP	American College of Physicians
Ad.26	Adenovirus 26
AE	Adverse Event
AGS	American Geriatric Society
AHIP	America's Health Insurance Plans
AIM	Association of Immunization Managers
AMA	American Medical Association
AOA	American Osteopathic Association
APhA	American Pharmacists Association
APTR	Association for Prevention Teaching and Research
ASH	American Society of Hematology
ASTHO	Association of State and Territorial Health Officers
AZ	AstraZeneca
BIPOC	Black, Indigenous, and People of Color
BLA	Biologics License Application
CDC	Centers for Disease Control and Prevention
CICP	Countermeasures Injury Compensation Program
CISA	Clinical Immunization Safety Assessment
CMS	Center for Medicare and Medicaid Services
CNS	Central Nervous System
COCA	Clinician Outreach and Communication Activity
COD	Cause of Death
COI	Conflict of Interest
COVID-19	Coronavirus Disease 2019
CSTE	Council of State and Territorial Epidemiologists
CT	Computed Tomography
CVA	Cerebrovascular Accident
CVST	Cerebral Venous Sinus Thrombosis
DNA	Deoxyribonucleic Acid
DoD	Department of Defense
DSMB	Data Safety Monitoring Board
DVA	Department of Veterans Affairs
DVT	Deep Vein Thrombosis
ED	Emergency Department
EHR	Electronic Health Record
ELISA	Enzyme-Linked Immunosorbent Assay
EMA	European Medicines Agency
EUA	Emergency Use Authorization
FDA	Food and Drug Administration
GACVS	Global Advisory Committee on Vaccine Safety (WHO)
GBS	Guillain-Barre Syndrome

HAN	Health Alert Network
HCP	Health Care Personnel / Provider / Professional
HCW	Health Care Workers
HHS	(Department of) Health and Human Services
HIPAA	Health Insurance Portability and Accountability Act
HIT	Heparin-Induced Thrombocytopenia
HITT	Heparin-Induced Thrombocytopenia with Thrombosis
HIV	Human Immunodeficiency Virus
HRSA	Health Resources and Services Administration
ICU	Intensive Care Unit
IDSA	Infectious Disease Society of America
IHS	Indian Health Service
IM	Intramuscular
IPV	Inactivated Polio Vaccine
ISO	Immunization Safety Office
ISTM	International Society for Travel Medicine
ITP	Immune Thrombocytopenia Purpura
ITT	Immune Thrombotic Thrombocytopenia
IVIG	Intravenous Immune Globulin
JCVI	Joint Committee on Vaccination and Immunisation
J&J	Johnson & Johnson
MedDRA	Medical Dictionary for Regulatory Activities
MMR	Measles, Mumps, Rubella
MMWR	*Morbidity and Mortality Weekly Report*
mRNA	Messenger Ribonucleic Acid
MRV	Magnetic Resonance Venography
NACCHO	National Association of County and City Health Officials
NACI	National Advisory Committee on Immunization Canada
NAPNAP	National Association of Pediatric Nurse Practitioners
NCEZID	National Center for Emerging and Zoonotic Infectious Diseases
NCIRD	National Center for Immunization and Respiratory Diseases
NEJM	*New England Journal of Medicine*
NFID	National Foundation for Infectious Diseases
NIH	National Institutes of Health
NMA	National Medical Association
NYC	New York City
OCP	Oral Contraceptive Pills
OPV	Oral Polio Vaccine
PCR	Polymerase Chain Reaction
PE	Pulmonary Embolism
PF4	Platelet Factor 4
PHAC	Public Health Agency Canada
PhRMA®	Pharmaceutical Research and Manufacturers of America®
PI	Principal Investigator
PIDS	Pediatric Infectious Disease Society
PRAC	Pharmacovigilance Risk Assessment Committee
PT	Preferred Terms
PVT	Portal Vein Thrombosis
RCA	Rapid Cycle Analysis

RCT	Randomized Controlled Trial
RNA	Ribonucleic Acid
SAE	Serious Adverse Event
SAHM	Society for Adolescent Health and Medicine
SARS	Severe Acute Respiratory Syndrome
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus-2
SHEA	Society for Healthcare Epidemiology of America
SLUSOM	Saint Louis University School of Medicine
SMEs	Subject Matter Experts
SRA	Serotonin Release Assay
SVT	Splanchnic Vein Thrombosis
TTP	Thrombotic Thrombocytopenic Purpura
TTS	Thrombotic Thrombocytopenia Syndrome
UK	United Kingdom
US	United States
VA	(US Department of) Veteran's Affairs
VAERS	Vaccine Adverse Event Reporting System
VaST	ACIP COVID-19 Vaccine Safety Technical Subgroup
VSD	Vaccine Safety Datalink
WG	Work Group
VWF	Von Willebrand Factor
WHO	World Health Organization

Opening Session: April 23, 2021

José Romero, MD, FAAP
ACIP Chair

Amanda Cohn, MD
Executive Secretary, ACIP / CDC

Dr. Romero called to order the April 23, 2021 emergency meeting of the Advisory Committee on Immunization Practices (ACIP), the purpose of which was to discuss the pause of the Janssen Coronavirus Disease 2019 (COVID-19) vaccine and a potential vote. He welcomed everyone and conducted a roll call, which established quorum. ACIP member, Dr. Sharon Frey, reported that she is a Principal Investigator (PI) for Saint Louis University School of Medicine (SLUSOM) on the Moderna and Janssen COVID-19 vaccine trials. No other no conflicts of interest (COIs) were declared for this meeting. A list of Members, *Ex Officio* Members, and Liaison Representatives is included in the appendixes at the end of the full minutes for the April 23, 2021 ACIP meeting.

Dr. Cohn welcomed everyone and indicated that copies of the slides being presented during this meeting were made available on the ACIP website for members of the public and through a ShareFile link for ACIP members. She emphasized that engagement with the public and transparency in its process is vital to ACIP's work. For this meeting, one oral public comment period was planned at approximately 1:00 PM Eastern Time (ET). People interested in making an oral comment were invited to submit a request online in advance of the meeting, with priority given to those advance requests. A blind, randomized lottery was conducted to determine who the speakers would be. Speakers selected in the lottery for this meeting were notified in advance of the meeting. Members of the public may also submit written public comments through https://www.regulations.gov using Docket Number CDC-2021-0044. Further information on the written public comment process can be found on the ACIP meeting website.

As noted in the ACIP *Policies and Procedures Manual*, ACIP members agree to forgo participation in certain activities related to vaccines during their tenure on the committee. For certain other interests that potentially enhance a member's expertise, CDC has issued limited COI waivers. Members who conduct vaccine clinical trials or serve on data safety monitoring boards (DSMBs) may present to the committee on matters related to those vaccines and participate in discussion, but are prohibited from participating in committee votes on issues related to those vaccines. Regarding other vaccines of a concerned company, a member may participate in the discussion, but must abstain from all votes related to the vaccine of that company. At the beginning of each meeting and prior to each vote, ACIP members will state any COIs.

Coronavirus Disease 2019 (COVID-19) Vaccines: April 23, 2021

Introduction

Beth Bell, MD, MPH
ACIP, COVID-19 Vaccine WG Chair
Clinical Professor, Department of Global Health
School of Public Health, University of Washington

Dr. Bell introduced the session, reminding everyone that it had not been long since they met for the last emergency meeting on April 14, 2021. During the week of April 12, 2021, there was a meeting of the ACIP COVID-19 Vaccine Safety Technical Subgroup (VaST) followed on Tuesday by a joint CDC and Food and Drug Administration (FDA) statement that recommended a pause in the use of the Janssen/Johnson & Johnson (J&J) vaccine and the release of a Health Alert Network (HAN) notification. Also on Tuesday, the ACIP COVID-19 Vaccines Work Group (WG) met. On Wednesday, April 14th, an emergency ACIP meeting was convened to consider the implications of reported cases of thrombosis and thrombocytopenia after receipt of the J&J vaccine on vaccination policy. After discussions regarding United States (US) cases of cerebral venous sinus thrombosis (CVST) and thrombocytopenia, the ACIP agreed that more information was needed before policy recommendations could be made regarding the Janssen vaccine.

During the week of April 19th, the VaST met again on Monday. On Wednesday, there was an additional special meeting of the ACIP COVID-19 Vaccines WG. This led to the convening of the April 23rd meeting, the purpose of which was to review the updated cases of thrombosis and thrombocytopenia after that Janssen COVID-19 vaccine, discuss the risk-benefit analysis, and consider the policy options for updated recommendations for use of this vaccine. Dr. Bell indicated that the day's agenda would include presentations on the following topics, which would be followed by a public comment session:

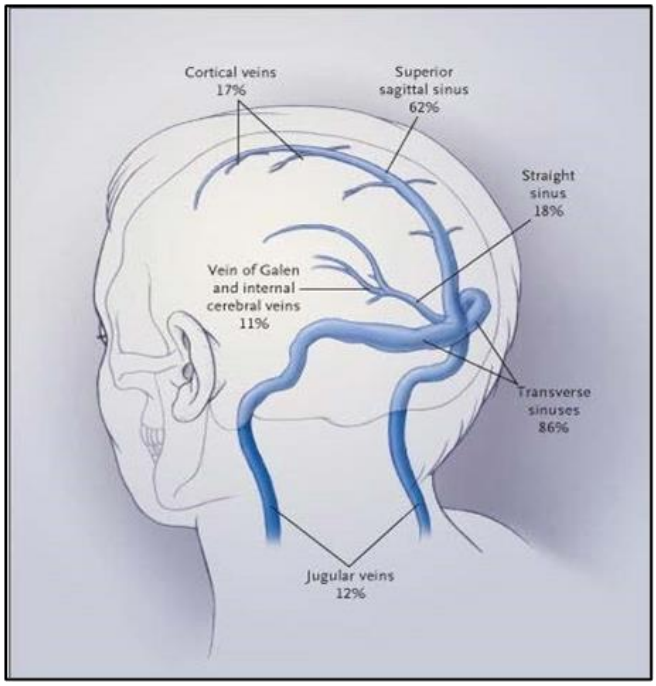
- ❑ Pathogenesis and Management of Thrombosis with Thrombocytopenia Syndrome (TTS)
- ❑ Thrombosis with thrombocytopenia syndrome (TTS) following Janssen COVID-19 Vaccine
- ❑ Public Comment
- ❑ Update on Janssen COVID-19 Vaccine
- ❑ VaST Assessment
- ❑ TTS After COVID-19 Vaccines: Applying the Evidence to Recommendation (EtR) Framework
- ❑ ACIP Discussion Period
- ❑ Potential Vote: Updated Interim Recommendations for use of Janssen/J&J COVID-19 Vaccine

Dr. Bell acknowledged and expressed gratitude to all of the WG members, *ex officios*, liaisons, consultants, CDC leads, and the large number of CDC participants who have been working diligently to assemble the information to be presented during this meeting.

Pathogenesis and Management of Thrombosis with Thrombocytopenia Syndrome (TTS)

Michael B. Streiff, MD
Medical Director
Johns Hopkins Anticoagulation Management Service and Hemostatic Disorder Stewardship Program
Johns Hopkins Special Coagulation Laboratory
Professor of Medicine & Professor of Pathology
Johns Hopkins University School of Medicine

Dr. Streiff first provided an overview of CVST, given that it is an unusual thrombotic event compared to what is typically seen in clinical practice. Much more common events would be deep vein thrombosis (DVT) and pulmonary embolism (PE). CVST is similar in the fact that it is a thrombotic event that occurs in the deep veins or superficial veins of the brain as depicted in this illustration:



In terms of the incidence[1], this is quite a rare event in that there are about 10 to 15 cases per million in the population compared to about 1 in 1000 cases of DVT and PE in the general population on an annual basis. The mean age for patients with CVST is about 35 years of age, which is a younger patient population than is typical for other venous events. It tends to occur more frequently in women than men by about a 2:1 ratio. In terms of typical clinical presentation for patients, the vast majority have a headache. More severely affected patients can have seizures related to the injury, limb weakness, a reduced level of consciousness, or even coma. Risk factors for CVST in the general population include use of estrogen-containing oral contraceptives, clotting disorders, pregnancy, cancers, infections, or surgery. Diagnosis is generally made with either a contrast computed tomography (CT) or magnetic resonance

[1] Capecchi M, Abbattista M, Martinelli I. J Thromb Haemost. 2018 Oct;16(10):1918-1931. Stam J. N Engl J Med. 2005 Apr 28;352(17):1791-8

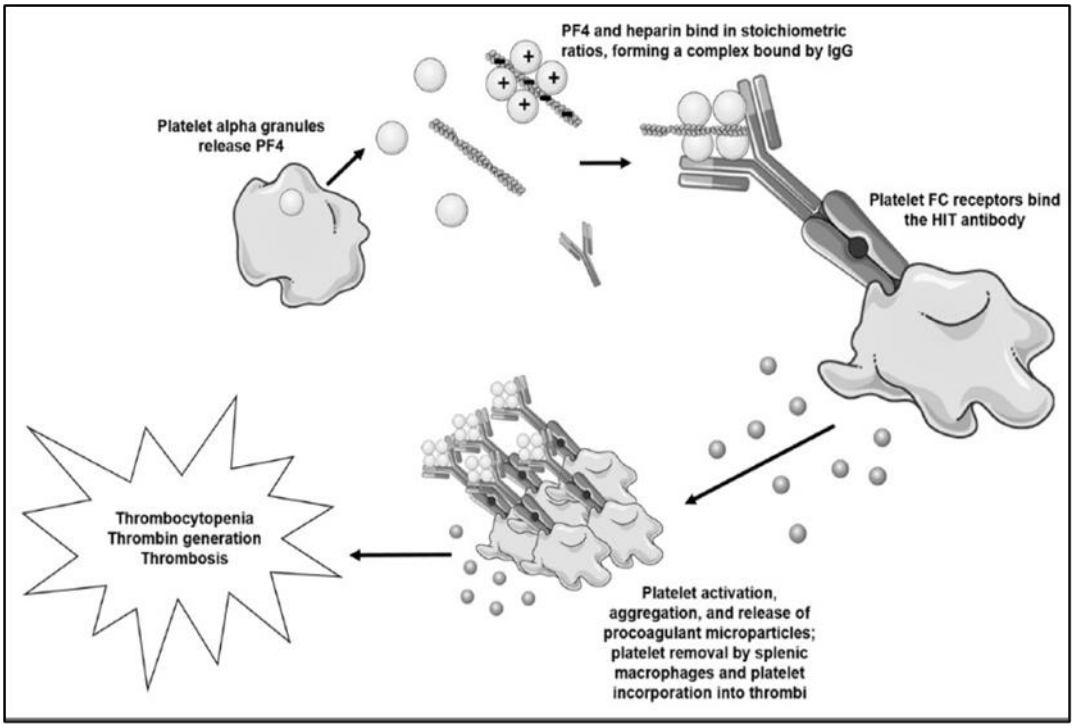
venography (MRV). Treatment is generally anticoagulation. In extreme cases, thrombolysis or clot busting medications or devices will be used.

The clinical characteristics of TTS are a moving target thus far because it is still early in the acquisition of cases. So far, TTS appears to be a thrombotic response associated with receiving an adenoviral vector vaccine against SARS-CoV-2. Based on the European and United Kingdom (UK) experience, the incidence is estimated to be between 1 case per 100,000 to 1 case per 250,000 vaccine recipients. The age range is very broad from 21-77 years of age, with 90% occurring in vaccine recipients less than 60 years of age and female to male distribution being 2.5:1. The median onset is 9 to 10 days with a range from 5 to 24 days after vaccination. The most common thrombotic events are CVST (N=27), DVT/PE (N=10), abdominal vein clots (N=7), and arterial clots (N=6). A couple of patients have presented with just DVT or PE and not CVST. Unique about this compared to other thrombotic events is that these patients tend to have positive tests for heparin-induced thrombocytopenia (HIT), which is a reasonably infrequent adverse event (AE) to receiving unfractionated heparin therapy. When this testing has been done on patients who have been reported so far, they seem to be uniformly positive for platelet factor 4 (PF4) heparin antibody immunoassay. This is in particular an enzyme-linked immunosorbent assay (ELISA). Some of the other immunoassays have been negative, although rarely. Platelet activation assays that typically are used for diagnosing this entity have been positive in some cases, although not uniformly positive in the US cases. Platelet nadir is generally about 27,000/µL, but ranges from 7000 to 113,000. Fibrinogen values tend to be low at about 125 mg/dL, with a range of 40 to 568 mg/dL. Normal ranges from 200 to 250 to 400 to 450 mg/dL. A rare patient had an elevated fibrinogen, but most patients tend to be normal or low. D dimer levels tend to be markedly elevated, reflecting a thrombotic process. When treated chronically with unfractionated heparin, these patients have had a progression of thrombotic events upon presentation. Platelet recovery tends to occur with use of a non-heparin anticoagulant as well as intravenous immune globulin (IVIG).

Comparing the characteristics of thrombotic events after Oxford-Astra Zeneca (AZ) and Janssen/J&J SARS-CoV-2 vaccines, the age ranges were similar between the two vaccines. However, there have been many more cases with the Oxford-AZ vaccine. Gender distribution is similar with more women than men. The onset is about the same at anywhere from 5 days up to 3 weeks or so. Presentations have been similar. Headache is prominent since most patients are presenting with CVST, but abdominal and back pain also are prominent. There also are similar signs of stroke, such as leg or arm weakness or disturbances in consciousness. Thrombotic events have been in similar locations, and platelet nadirs have been similar. The ELISA assay has been uniformly positive. Functional platelet activation assays have been positive in the European experience and less positive in the US experience using a different assay, the serotonin release assay (SRA). A lot of the work on HIT is based on the published work thus far, primarily from Europe from Andreas Greinacher who has spent his entire career on this work[2].

[2] Greinacher A, et al. N Engl J Med. 2021 Apr 9. PMID: 33835769. Schultz NH, et al. N Engl J Med. 2021 Apr 9. PMID: 33835768. Scully M, et al. N Engl J Med. 2021 Apr 16. PMID: 33861525.

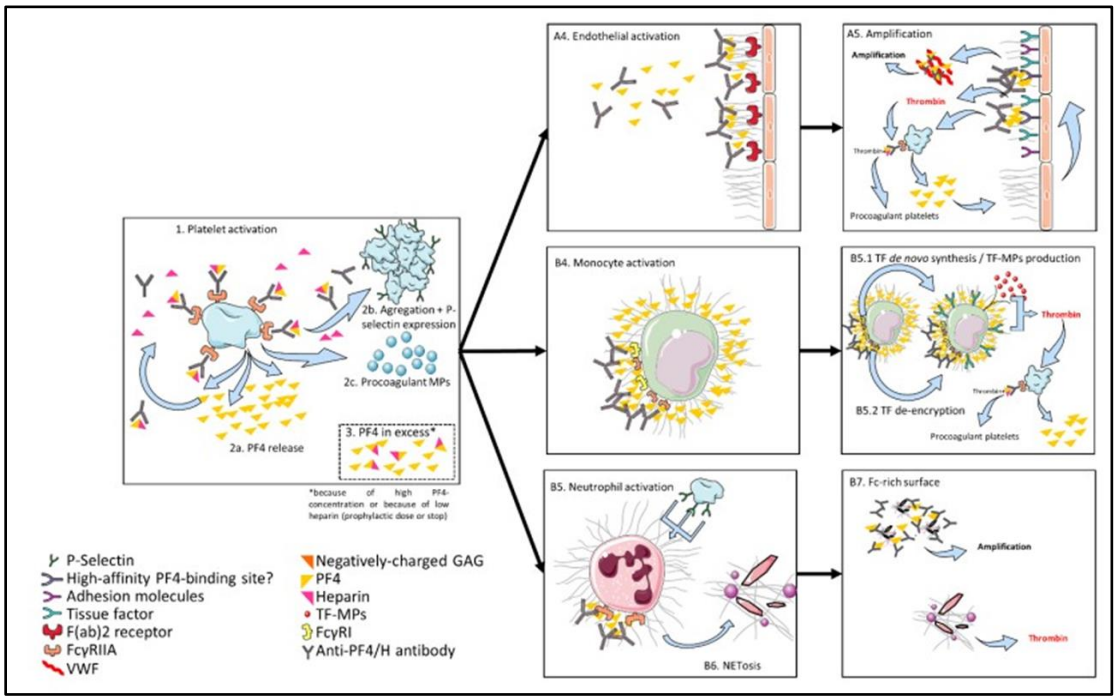
The following diagram[3] illustrates what is believed to be occurring in this syndrome in terms of how these thrombotic events are developing and why these patients have thrombocytopenia, based on the work of Greinacher and Schultz:



On the left side of the illustration is a platelet with an alpha granule. Inside alpha granules is a protein called PF4, which is a chemokine that is important for controlling and suppressing endogenous anti-coagulants like heparin sulfate. It also is involved in the wound healing process. Patients who have a lot of activation of platelets will release a lot of PF4 to help in the thrombotic and healing process. If someone is exposed to a polyanion such as unfractionated heparin, these complexes of PF4 and heparin can form as shown on the top of the diagram. This then converts a portion of PF4 into an immunogen that the immune system responds to in a small percentage of patients, who develop antibodies against this neoantigen on PF4 that is generated by the interaction between the polyanion heparin and PF4. Then these antibodies can bind to the FC receptors on platelets, which results in profound platelet activation. Thus, there is profound consumptive thrombocytopenia in a situation where platelets are being activated and form lots of platelet microparticles as depicted in the bottom righthand side of the diagram, which increase the surface area of platelets. Because they are activated, they have a lot of phosphatidylserine exposed that serves as a “playground” for the clotting factors and activates the coagulation cascade. This generates a vicious cycle of a thrombotic storm that consumes more platelets, activates more platelets, and causes clotting.

[3] Hogan M, Berger JS. Vasc Med. 2020 Apr;25(2):160-173.

This is a beautiful, though complex, diagram from the literature that outlines that it is not just platelets that are activated by the antibodies that are involved in HIT:[4]



The endothelial is activated, expresses tissue factor, and is injured, releasing von Willebrand factor (VWF) that can cause platelets to aggregate. Monocytes, one of the white cells, are activated and they express tissue factor as well. Again, that activates the coagulation cascade. Finally, neutrophils are activated and express these in their activation in neutrophil extracellular traps (NETs) and then form a place where platelets and the coagulation cascade can be activated.

Dr. Streiff pointed out that what he had discussed so far focused completely on heparin because that is the most common trigger for this syndrome. However, a small number of patients have been reported who have developed autoimmune thrombocytopenic purpura (ATP). In this case, patients develop the syndrome without receiving heparin at all. This has been seen in people who have had surgery. It is thought that endogenous polyanions such as heparan sulfate, chondroitin sulfate, or even deoxyribonucleic acid/ribonucleic acid (DNA/RNA) complexes combine with PF4 and generate these antibodies. This is what is thought to be the pathogenesis being seen with the vaccine based primarily on Andreas Greinacher's studies that are published in the *New England Journal of Medicine* (*NEJM*).

In summary, this is a compilation of the data that supports the current concept on what is causing this syndrome. Based on laboratory testing and clinical presentation, there appears to be a syndrome similar to a case of autoimmune HIT because none of these patients have been exposed to heparin, yet they develop a syndrome that looks very much like HIT. This is supported by laboratory testing that is consistent with autoimmune HIT in that patients have positive PF4 immunoassays. In Greinacher's laboratory with his platelet activation assays, they also are uniformly positive. If PF4 is added to the reaction mixture, it amplifies the reactions,

[4] Marchetti M, Zermatten MG, Bertaggia Calderara D, Aliotta A, Alberio L. J Clin Med. 2021 Feb 10;10(4):683.

which is typical of autoimmune HIT. Platelet activation also can be inhibited in vitro with either high concentrations of heparin that blocks the formation of the multimolecular complexes that activate platelets or with IVIG, which is why it is used for the treatment of this syndrome. The clinical course also mirrors HIT in that it is typical for patients to present with thrombocytopenia and a thrombotic episode that is resistant to and promoted by heparin treatments and improves when a non-heparin anticoagulant and IVIG are used. The etiology of thrombotic thrombocytopenia syndrome (TTS) is unclear. Dr. Greinacher has published a preprint article on Research Square that has not yet been peer-reviewed in which he looked at patients who had SARS-CoV-2 infection and analyzed PF4 structure and the spike protein. He could not find any patients with SARS-CoV-2 infection who had platelet activating antibodies, so he does not think that there is molecular mimicry as seen with human immunodeficiency virus (HIV) and idiopathic thrombocytopenic purpura (ITP) based on this research[5].

Management of thrombosis thrombocytopenia is based largely on the American Society of Hematology (ASH) guidelines[6], although the International Society on Thrombosis and Haemostasis (ISTH) and the Anticoagulation Forum (AC Forum) also have recommendations in this regard. Clinicians should maintain a high index of suspicion for any patient that presents with symptoms of any thrombotic event associated with thrombocytopenia within 3 weeks of administration of the J&J SARS CoV2 vaccine, this syndrome should be considered. The thrombotic event should be confirmed with imaging and simultaneously send testing for HIT with a PF4 immunoassay and platelet activation assay. Physicians should consult a hematologist to confirm the diagnosis and rule out other diagnostic possibilities that can present similar to TTS. Patients should be treated with a non-heparin anticoagulant. The thrombocytopenia should be treated with IVIG, which blocks antibody activation of platelets and speeds recovery of platelets. Platelet transfusions should be avoided because that seems to “feed the fire” of this syndrome.

Discussion Points

Dr. Lee pointed out that some reports have noted that the depth of thrombocytopenia might be associated with worse outcomes, and she wondered whether this reflected how long the process had been going on and if it is possible that if IVIG were administered early that could impact the patients’ overall outcomes.

Dr. Streiff said that the depth of thrombocytopenia could suggest that the process has been ongoing longer or perhaps reflects the titer, antibodies, and immune reaction that has been triggered. In those patients, IVIG really needs to be used. IVIG is not always used for typical HIT patient treatment, but it is used in people with severe syndromes. These patients seem to have a very severe clinical presentation, so IVIG should be used for their treatment if it is available.

Given that the role of ethylenediaminetetraacetic acid (EDTA) has been implicated in the AZ COVID-19 vaccine in terms of causing vascular permeability, Dr. Sanchez asked how that might fit into looking at other constituents of the vaccine.

Dr. Streiff said he could not see how that might trigger the antigen unless it is causing release of heparin sulfate or dermatan sulfate bound at the end of the epithelium. A vaccine triggering release of those compounds at higher proportions so that they can bind to PF4 and the vaccine is also activating platelets is possible, but this remains to be seen and tested as a hypothesis.

[5] Geinacher A et al. Research Square April 16, 2021.

[6] American Society of Hematology COVID-19 Resources at https://www.hematology.org/COVID-19/vaccine-induced-immune-thrombotic-thrombocytopenia.

Dr. Bernstein recalled that Dr. Streiff listed 6 risk factors associated with TTS and wondered if excluding people with those risk factors from getting this vaccine would therefore decrease the incidence of TTS after vaccine.

Dr. Streiff said that he did not think so based on reported comorbid conditions or treatments that some patients have had. However, there also have been patients who have not been taking oral contraceptives or hormonal therapy, were not obese, et cetera. A patient or two have had thrombophilic or clotting states, but the vast majority have not had any of the associated risk factors. The major way to focus on patients who are at risk is that it seems to affect people who are younger and women more than men.

Dr. Daley asked to what extent treatment is improving outcomes and what is on the horizon in terms of treatment.

Dr. Streiff thinks that recognition among physicians that this syndrome exists and among the public that those who have severe headache and severe abdominal pain need to see their doctor for further evaluation is helping to improve outcomes. It is clear that at least in some of the published cases, patients tried to treat their symptoms at home for a number of days before they presented and when they presented, they were severely ill. Educating the physicians and the public about early presentation will improve outcomes. As far as other medications, they are stuck with what they have. The message to physicians is to avoid heparin therapy, use non-heparin anticoagulant, and use IVIG early in these patients which will improve outcomes.

Dr. Long asked whether the population range of CVST was without thrombocytopenia and whether he knew what the number would be without vaccine or TTS.

Dr. Streiff indicated that the published studies suggested that the incidence of CVST is about 1 in 100,000 or 10 per million roughly. The number of people presenting with thrombocytopenia is extraordinarily rare in his experience. He has not seen that reported in the published literature for CVST. It generally is not a feature of CVST. The thrombocytopenia in association with these clotting events is unique. While he could not say how many people with CVST have thrombocytopenia upon presentation, he has never seen it based on his experience treating these patients. There typically is a clot and the platelets are in the normal range. The incidence with the vaccines is based on estimates he saw in an editorial of the European data that looked at the number of vaccines delivered in Europe and the UK, which estimated between 1 in 100,000 and 1 in 250,000 vaccinated patients.

Dr. Romero pointed out that Dr. Oliver would be sharing additional data later in the day that might clarify that question further.

Dr. Poehling asked whether there is a female predominance in the autoimmune form of this syndrome with heparin.

Dr. Streiff indicated that for HIT, there is not a predominance of women. There may be slightly more women than men, but there is not a dramatic difference as far as developing HIT. It is not clear what the gender breakdown is for autoimmune HIT, because it is a much less common form of HIT.

In terms clinicians thinking about using IVIG early, Ms. Stinchfield (NAPNAP) asked whether there is any information about the IVIG supply in the US. Over the years, there have been times when supplies were low.

Dr. Streiff said that he did not have this information. If clinicians do not have IVIG available in their area, they should start a non-heparin anticoagulant, which is typical of what has been done for years with HIT, and try to order IVIG as early as possible or get the patient to a medical center where they could get it.

Dr. Duchin (NACCHO) asked whether there is a difference in either severity of the syndrome or clinical outcomes between CVST with and without TTS.

Dr. Streiff said that it seems that patients who develop TTS have more severe outcomes, but that may be due to the fact that initially some of these patients have been treated with heparin, which may promote progression. That is an added wrinkle that may mean they do not get the right anticoagulant treatment and do not receive the IVIG in as timely a fashion. This is not a concern with CVST patients who are just treated with heparin. Education may help with making the outcomes more closely parallel typical CVST.

Dr. Sanchez noted that there are animal studies in mice where adenovirus-induced thrombosis has been seen with thrombocytopenia, so trying to delineate what it is with these vaccines may involve the vector.

Dr. Streiff agreed that this is a hypothesis that may explain why there are differences between typical CVST and TTS, but he does not know of any data showing that the vaccine is activating platelets and then somehow there is an endogenous polyanion that is forming. But it could be and that could be why it is different. That is probably being explored by many investigators. There has got to be something different about it compared to the typical CVST patient.

Dr. Romero said his understanding from reading the literature from the German group is that not all of the vaccine enters the cell and some of it spills over into the bloodstream and is breaking down in the bloodstream. It is the DNA contained within the adenovirus that sets up the anion and then attracts the platelets.

Dr. Long asked Dr. Streiff to give an opinion on the relative outcomes of patients who have the true heparin-induced syndrome appropriately treated compared with what is presumed to be vaccine-induced TTS.

Dr. Streiff responded that generally, he thinks that patients with the typical HIT have better outcomes than patients with TTS. The primary reason for that is the location of the clot. He could not think of a patient he has managed with HIT who developed CVST. Typically, they develop DVT, PE, or an arterial clot. Having clots in the central nervous system (CNS) and secondary intercranial hemorrhage is just a bad place to have a clot, which is why he thinks the fatality rate of this syndrome or the rate of people having permanent or at least ongoing neurological problems is much higher than seen with typical HIT patients who are not clotting in their brain.

Dr. Gluckman (AHIP) asked about the incidence of thrombotic events with complications that are secondary to COVID-19 infection and how that compares to the complications related to the vaccines.

Dr. Streiff indicated that there is a preprint article from Oxford that looked specifically at CVST in patients who had COVID-19. This is all based on observational administrative data, but CVST appeared to about 10-fold more common in COVID-19 infection patients than in patients with

vaccine-associated CVST. It is known from all of the published reports on COVID-19 disease that DVT and PE are not uncommon events in critically ill patients. About 5% to 10% of critically ill COVID-19 patients will develop a DVT or PE during their COVID-19 infection.

Dr. Shah (ASTHO, Maine CDC) noted on Dr. Streiff's Slide 5 that among the AZ recipients the median age was 40 years, which struck him as being roughly the median age of the background population. The range among J&J recipients was from teens to those in their 50s, which suggests a much lower median age. He asked whether there is a biological basis to believe that there is an age component to this and to the extent that there are differences with those 2 vaccines, whether the lower age among the J&J recipients may merely be a function of the way in which vaccines were rolled out in the US. That is, older individuals perhaps received an mRNA vaccine earlier in the vaccination effort and it is just now that younger individuals are receiving J&J vaccines.

Dr. Streiff said that because the data acquisition phase is still underway, there have not been that many cases and these numbers may change. In terms of the numbers of published cases, AZ has had a lot more time to accumulate cases and it is still very early in the process of examining J&J cases. The higher age range of some of the older patients from the UK experience seem to be a little different than the patients reported by the German/Austrian group and the Swedish group. He is wary that a couple of patients may have been accumulated who did not have the syndrome. Some people in the UK experience had PE and did not have CVST or the abdominal thrombotic events. HIT testing, particularly the functional assays, are very challenging. He thought the data were too preliminary to confirm whether there are differences in the vaccines and that is why the age range is a little older with the AZ versus the J&J vaccine. He thought that Drs. Shimabukuro and Oliver drew a closer analysis of the US cases and perhaps would be sharing additional information.

Dr. Lee asked for an explanation about why the functional assays in the US cases were different from the European cases, and if the assay is negative, it means that platelets are activated in that instance.

Dr. Streiff emphasized that functional HIT assays are very challenging tests to do which is why very few laboratories do them. Only a handful of laboratories in the US perform the serotonin release assay, which is the functional assay that predominantly was used in the US cases. The reliability of that assay varies depending on the expertise of the laboratory doing the test. In the European cases, several different assays were used. Andreas Greinacher used his homegrown platelet activation assay that he has been using since 1990, so he is literally the world's expert on doing that assay. He has more experience with that assay than anyone else, so Dr. Streiff tends to place a lot of faith in Greinacher functional HIT testing. The UK paper used a flow assay. There have not been a lot of papers comparing the different functional assays in terms of their reliability, sensitivity, and specificity. It is premature to say that based on the results from the functional assays in the US, those patients did not have platelet activation. He is wary about the reliability, given that this is such a difficult test to do. As a clinician, his emphasis on diagnosis is going to be the clinical situation, clinical presentation, thrombocytopenia, and a positive ELISA, which seems to be very sensitive for this. Since all of the ELISA's have tested positive in these patients, that is what is going to be what tells him a person has TTS and needs to be treated accordingly. If he gets a negative functional assay back, he is not going to stop treating them like they have TTS. This has only been done in 5 US patients thus far, so it is likely to change with more experience.

TTS Following Janssen's COVID-19 Vaccine

Tom Shimabukuro, MD, MPH, MBA
CDC COVID-19 Vaccine Task Force
Vaccine Safety Team
National Center for Emerging and Zoonotic Infectious Diseases
Centers for Disease Control and Prevention

Dr. Shimabukuro provided a brief background and further detailed the reports of CVST with thrombocytopenia (low platelets) following Janssen COVID-19 vaccine. He explained that thrombosis occurs when blood clots block blood vessels. Thromboses can be venous or arterial and common complications include heart attack, stroke, and infarctions. Causes and risk factors include trauma, immobility, inherited disorders, certain autoimmune disease, obesity, hormone therapy or birth control pills, pregnancy, smoking, cancer, older age, et cetera. Symptoms may include pain and swelling in an extremity, chest pain, numbness or weakness on one side of the body, and sudden change in mental status. Thromboses are diagnosed primarily through imaging (e.g., CT, MRI, ultrasound) and blood tests[7].

Platelets, which also are called thrombocytes, are colorless blood cells that help blood clot. A normal platelet count is 150,000–450,000 per microliter. In the medical world that is usually short-handed to 150-450. Platelets are important in that they stop bleeding by clumping and forming plugs in blood vessel injuries. Thrombocytopenia is a condition in which one has a low blood platelet count of <150,000 per microliter of blood. Dangerous internal bleeding can occur when someone's platelet count falls below 10,000 platelets per microliter. Though rare, severe thrombocytopenia can cause bleeding into the brain, which can be fatal[8]. To provide some context around the vaccine safety issue under discussion, this issue first came to attention because of the cases of rare blood clots with low platelets that were detected following the AZ COVID-19 vaccine[9]. Many of these events involved CVST, which Dr. Streiff described quite well in his excellent presentation.

As a reminder, the focus of the last emergency ACIP meeting on April 14th was on reports of CVST with thrombocytopenia after receipt of the Janssen COVID-19 vaccine. At that time, there had been 6 reports of CVST with thrombocytopenia to the Vaccine Adverse Event Reporting System (VAERS) following 6.86 million doses administered of the Janssen COVID-19 vaccine. That translated to a reporting rate of 0.87 cases per million doses administered. In contrast, there were 0 reports following 97.9 million Pfizer-BioNTech COVID-19 vaccine doses administered. For the Moderna COVID-19 vaccine, there were 3 reports following 84.7 million doses administered. However, all 3 of those reports had normal platelet counts. This was essentially 0 reports following just over 180 million doses of the messenger ribonucleic acid (mRNA) vaccines. This was considered to be a reporting rate imbalance.

The take-home message at that time was that CVST is rare, but clinically serious, and can result in substantial morbidity and mortality. It is not usually associated with thrombocytopenia, so this is unusual. An observed versus expected analysis was conducted, but it was somewhat of an "apples and oranges" comparison because the expected was based on CVST. There is not good information on the background incidence of CVST with thrombocytopenia. It is extremely rare. The observed cases following Janssen COVID-19 vaccines appear to exceed

[7] https://www.hopkinsmedicine.org/health/conditions-and-diseases/thrombosis
[8] https://www.mayoclinic.org/diseases-conditions/thrombocytopenia/symptoms-causes/syc-20378293
[9] https://COVID.cdc.gov/COVID-data-tracker/#vaccinations

expected cases based on background rates of CVST among women aged 20–50 years by at least 3-fold or greater. All 6 reports were in women 18–48 years of age and all had thrombocytopenia. No obvious patterns of risk factors have been detected. By contrast, CVST with thrombocytopenia had not been observed after the 2 authorized mRNA vaccines. The clinical features of the Janssen cases were similar to those observed following the AZ COVID-19 vaccine in Europe. Both the Janssen and AZ vaccines contain replication-incompetent adenoviral vectors, human (Ad26.COV2.S) for Janssen and chimpanzee (ChAdOx1) for AZ.

Based on information prior to the last ACIP meeting, CDC issued a HAN. The bottom line in that HAN was that CDC recommended a pause in the Janssen COVID-19 vaccine out of an abundance of caution while further assessment of the signal could occur. An important message to healthcare providers (HCP) was that they should be aware of these potential AEs so they could provide proper management due to the unique treatment requirement of this type of blood clot, which is not giving heparin if the HIT test is positive and treating with other non-heparin anticoagulants[10].

After this safety signal was detected in the VAERS system, a supplementary analysis was conducted in the population-based Vaccine Safety Datalink (VSD) system to ascertain what kind of data it included on the rare condition of CVST. The initial focus was on assessing the Pfizer/BioNTech and Moderna mRNA vaccines and Dr. Shimabukuro presented data on the Janssen vaccine. As of April 17, 2021, there were 2.7 million doses of Pfizer-BioNTech and 2.5 million doses of Moderna COVID-19 vaccine doses administered in VSD. There were 10 total cases of CVST identified following the mRNA vaccines, of which 5 cases were ruled out (historical n=2, history of head injury n=2, chronic cavernous sinus syndrome n=1) and 5 cases were found potentially to be CVST, but all without thrombocytopenia. After this supplemental VSD analysis for mRNA vaccines, there were no confirmed cases of incident CVST with thrombocytopenia after 5.2 million doses of mRNA COVID-19 vaccines administered in the VSD. The assessment at that time was that a safety signal was detected for CVST with thrombocytopenia following Janssen COVID-19 vaccine. There were 6 cases observed in women aged 18-48 years of age in early post-authorization monitoring. There was 1 case observed in pre-authorization clinical trials in a 25-year-old male[11]. Currently, there is a lack of evidence of an association between mRNA COVID-19 vaccines and CVST with thrombocytopenia.

The Brighton Collaboration has a draft case finding definition for a condition called “thrombosis with thrombocytopenia syndrome (TTS),” which is broader than just CVST with thrombocytopenia in that it includes other clots. A hallmark of their draft case definition is that one needs to thrombocytopenic, so a platelet count of $<150 \times 10^9$/L. In addition to rare thromboses, the definition currently includes more common thromboses, such as DVT, PE, ischemic stroke, and myocardial infarction[12].
Moving on to the data sources and the TSS cases that have been detected and assessed, the primary source is VAERS. This is the nation’s early warning system for vaccine safety. It is a spontaneous or passive surveillance reporting system that is co-administered by CDC and FDA. VAERS accepts reports from anyone (patients, parents, caregivers, HCP, vaccine manufacturers). As a national system, it has a large population under surveillance and is good at detecting rare AEs and rapidly detecting safety signals. It is subject to the limitations of

[10] https://emergency.cdc.gov/han/2021/han00442.asp

[11] https://www.nejm.org/doi/full/10.1056/NEJMc2106075; https://www.fda.gov/media/146217/download

[12] https://brightoncollaboration.us/wp-content/uploads/2021/04/TTS-CaseFinding-and-Definition-Process.v9.0-April-16-202115853.pdf

passive surveillance in general, and it is not designed to assess causality[13]. In addition to the VAERS system and VAERS team of reviewers and abstractors, the analyses relied upon CDC's Clinical Immunization Safety Assessment (CISA)[14] project team and consultants at the CISA sites to help review and evaluate these cases.

Case finding for TTS following Janssen COVID-19 vaccine occurs in a number of ways. Often, HCP directly contact CDC with potential TTS cases as they present to the hospital or as they are hospitalized. CDC initiates an investigation and facilitates submission of a VAERS report if it has not already been reported to VAERS. Also, FDA physicians review incoming VAERS reports daily to identify potential TTS cases. The VAERS database is also searched for possible TTS reports. This includes the Medical Dictionary for Regulatory Activities Preferred Terms (MedDRA PTs) for any report on large vessel thrombosis and/or embolism. For this particular analyses, the common thrombosis events were not included (e.g., acute myocardial infarction, ischemic stroke, deep vein thrombosis, pulmonary embolism). These events will be evaluated in subsequent analyses. Medical records are requested for all potential TTS cases to confirm thrombosis with laboratory evidence of thrombocytopenia. CDC and FDA medical officers reviewed TTS reports and available medical records and CISA experts, including hematologists, were consulted as needed.

In terms of the high-level reporting line for reporting rates of TTS after Janssen COVID-19 vaccine, 7.98 million vaccine doses had been administered[15] and 15 TTS cases were confirmed as of April 21, 2021. Some age- and sex-specific doses administered data were imputed because they were missing variables for age or sex, but that was a small minority of the data. There are additional potential TTS cases under review, including potential male cases. Notably, 1 case was excluded from the final analysis. This was a female <50 years of age who had a concurrent diagnosis of COVID-19 and TTS following receipt of Janssen vaccine. She had a very complicated clinical picture. While they were not comfortable including that as a case, they wanted to mention if for transparency. This table shows date for age groups, females, males:

	Females			Males		
Age Group	**TTS Cases**	**Doses Admin**	**Reporting Rate‡**	**TTS Cases**	**Doses Admin**	**Reporting Rate‡**
18-49 Years Old	**13**	1,866,294	7.0 per million	**0**	1,977,330	0 per million
50+ Years Old	**2**	2,125,239	0.9 per million	**0**	2,010,144	0 per million

‡ Reporting rate = TTS cases per 1 million Janssen COVID-19 vaccine doses administered

All 15 cases were in females, but that does not mean there is no risk to males. There could be cases that were not identified in the database. VAERS also is subject to under-reporting, so there could be cases that simply were not reported and cases that may become apparent later on that have not yet appeared. Looking at the graph of confirmed reported cases among women by age, there is an apparent clustering of individuals in the mid to late 30s. When this clustering was observed, the decision was made in consultation with CDC's VaST and COVID-19 Vaccine

[13] http://vaers.hhs.gov
[14] http://www.cdc.gov/vaccinesafety/Activities/CISA.html
[15] https://COVID.cdc.gov/COVID-data-tracker/#vaccinations

WG colleagues that it would be prudent to take a closer look by splitting the age intervals into finer age groups as shown in this table:

	Females		
Age Group	**TTS Cases**	**Doses Admin**	**Reporting Rate‡**
18-29 years old	**3**	579,709	5.2 per million
30-39 years old	**7**	594,215	11.8 per million
40-49 years old	**3**	692,370	4.3 per million
50-64 years old	**2**	1,367,529	1.5 per million
65+ years old	**0**	757,710	0 per million

‡ Reporting rate = TTS cases per 1 million Janssen COVID-19 vaccine doses administered

For this analysis, nearly 4 million doses of Janssen COVID-19 vaccine had been administered to women[16] as of April 21, 2021 and all 15 cases were confirmed to be in women. Focusing on the group 30-39 years if age, this is where the most cases were seen and this was where doses administered and highest reporting were based, which was 11.8 cases per million doses administered. In the older age groups of 50-64 years and 65+ years, the reporting rates were lower than in the younger age groups.

In terms of some of the characteristics of the 15 patients with TTS after Janssen COVID-19 vaccine, the median age was 37 years with a range of 18-59 years of age. The median time to symptom onset was 8 days with a range of 6-15 days. All cases occurred in females. Of the 15 cases, 12 cases were CVST. None of the women were pregnant or post-partum. There were 2 cases with COVID-19 disease; however, these were both by history and fairly remote with no documentation of serology testing. In terms of the identified risk factors for thrombosis[17], 2 of the case patients were using oral contraceptives, 7 were obese, 2 had hypothyroidism, 2 had hypertension, none had diabetes, and none were known to have coagulation disorders.

Regarding signs and symptoms in patients with CVST after Janssen COVID-19 vaccine in a subset of the TTS cases (N=12) at least 2 patients experienced initial symptoms starting 6 or more days after vaccination of headache, chills, fever, nausea/vomiting, malaise/lethargy, and/or abdominal pain. Some of the signs and symptoms later in the clinical course included severe headache (several with neck pain or stiffness), nausea/vomiting, abdominal pain, unilateral weakness, speech difficulty, gaze deviation, loss of consciousness, and/or seizure. The important message is that these initial symptoms are fairly vague and non-specific, mainly headache. Importantly, these headaches started 6 or more days after vaccination. The is important because headache is a commonly reported adverse reaction after vaccination, particularly for COVID-19 vaccines. The reactogenic headache typically occurs on the day after vaccination and not starting 6 or more days after vaccination, which is unusual.

[16] https://COVID.cdc.gov/COVID-data-tracker/#vaccinations
[17] https://www.hopkinsmedicine.org/health/conditions-and-diseases/thrombosis

The locations of the thromboses in the TTP patients are shown in the table below, and these are not mutually exclusive:

Cerebral Venous Sinus Locations (N=12)*	Other Locations (N=11)
Transverse sinuses	Portal vein†
Sigmoid sinuses	Hepatic vein
Confluence of sinuses	Superior mesenteric artery†
Straight sinus	Splenic artery†
Superior sagittal sinus	Pulmonary artery†
Inferior sagittal sinus	Lower extremity vein†
Cortical veins	Internal jugular vein
	Carotid artery†
	Brachial vein†
	Femoral vein and artery†
	Iliac artery†

* 7 patients with cerebral venous sinus thrombosis experienced an intracerebral hemorrhage: temporoparietal junction, temporal lobe, frontal lobe, occipital lobe, cerebellum, intraventricular, subarachnoid.
† Patients without CVST had thrombosis in these locations.

Regarding selected laboratory findings in TTS patients, all were thrombocytopenic. Among these, 10 were severely thrombocytopenic with platelet counts of less than 50,000; 3 had platelet counts between 50,000 to 100,000; and 2 had platelet counts between 100,000 to 149,000. When testing was done, 11 of the cases had a PF4 HIT-positive ELISA antibody test result and testing was either not available or was not done for 4 of the cases. The results were fairly unremarkable for the SARS-CoV-2 testing results in TTS patients, with the exception of the 1 potential case that was excluded based on the determination that it was somewhat of a complex and unique case. SARS-CoV-2 viral assays were negative in 10 patients and results were not available for 5 patients. SARS-CoV-2 serology was negative in 4 patients and not available for 10 patients. Treatment and outcomes are shown in the table below:

Treatment*	Outcomes †
– Heparin (n=6)‡	Death (n=3)§
– Non-heparin anticoagulants (n=12)	Remain hospitalized (n=7)
– Platelet transfusion (n=7)	Intensive care unit (n=4)
– Intravenous immunoglobulin (n=8)	Discharged home (n=5)

* Based on 14 patients
† As of April 21, 2021
‡ All patients who received heparin were hospitalized before HAN release
§ None of the patients who died received heparin

Initial analyses have been done in the VSD, which the population-based system that CDC uses for near real-time surveillance and research. The VSD contains data on over 12 million persons per year, primarily from electronic health records (EHR) and administrative data. In terms of VSD specific to thrombosis events after Janssen COVID-19 vaccine, over 142,000 Janssen COVID-19 vaccine doses were administered in VSD through April 17, 2021. There have been no statistical signals detected for any prespecified Rapid Cycle Analysis (RCA) outcomes. Of course, there is a relatively small number of doses administered—at least compared to the mRNA vaccines. No CVST cases have been identified following the Janssen vaccine. There were 22 VTE and/or PE cases identified in the 1 to 42 days following vaccination that were quick reviewed. These are not mutually exclusive, so this includes 2 with both VTE and PE. Of the 22 cases, 6 were ruled out as not VTE, 16 were confirmed VTE and/or PE cases; 4 (3 PE, 1 VTE) had symptom onset prior to vaccination, and that includes 1 case with thrombocytopenia documented prior to vaccination; 1 had an indeterminate symptom onset; and 11 were incident cases following vaccination. Among these 11, there were 6 females (2 PE, 4 VTE) and 5 males

(1 PE, 4 VTE), ages ranged from 50-79 years, none had a history of COVID-19 infection, and none had thrombocytopenia at the time of VTE/PE. A broader case definition was used in the VSD analysis than in the VAERS analysis. The VSD assessment included some of the more common thromboses for the Janssen assessment. The bottom line is that while there is a relatively small number of Janssen vaccine doses in the VSD, no potential cases of thrombosis with thrombocytopenia were seen based on this analysis.

In summary, TTS is a rare, but clinically serious and potentially life-threatening AE that has been observed in association with the Janssen COVID-19 vaccine. Symptom onset appears to occur at least several days after vaccination, typically around 1-2 weeks after vaccination. The clinical features of TTS following Janssen COVID-19 vaccine appear similar to what is being observed following the AZ COVID-19 vaccine in Europe. It is important to recognize TTS early and initiate appropriate treatment. TTS should not be treated with heparin unless HIT testing is negative. The US vaccine safety monitoring system is able to rapidly detect rare AEs following immunization and quickly assess safety signals. Safety surveillance and research on TTS continues, and CDC is committed to open and transparent communication of vaccine safety information.

Regarding next steps, enhanced monitoring in VAERS and surveillance in other vaccine safety systems (e.g., VSD, CMS, VA electronic health record) will continue. An expanded VAERS database search strategy is planned for TTS reports to include the following:

- ❑ MedDRA PTs for large vessel thrombosis and embolism (all reports regardless of presence of thrombocytopenia)
- ❑ MedDRA PTs for more common thrombotic events AND MedDRA PTs for thrombocytopenia OR text string for “thrombocytopenia” or “low platelets”
- ❑ Medical record review for all potential TTS cases reports to confirm thrombosis with thrombocytopenia

Dr. Shimabukuro emphasized the importance of reporting AEs to VAERS, especially the clinically serious and unexpected AEs occurring after vaccine. The information for doing so follows:

- ❑ Go to vaers.hhs.gov
- ❑ Submit a report online
- ❑ For help:
  - Call 1-800-822-7967
  - Email info@VAERS.org
  - Video instructions https://youtu.be/sbCWhcQADFE

He stressed that CDC appreciates the work and cooperation of HCP on the frontline as partners in vaccine safety to help CDC/FDA detect and rapidly assess potential safety problems and make evidence-based public health decisions. It is extremely important for HCP who report AEs if contacted and asked by VAERS or CDC to send records to VAERS as soon as possible. The Health Insurance Portability and Accountability Act (HIPAA) permits reporting of protected health information to public health authorities, including CDC and FDA when they are conducting these activities as a public health function.

Discussion Points

Dr. Poehling emphasized that these data clearly demonstrate that the safety systems that have been set up with the FDA and the CDC are working to detect events and provide much needed information as planned. She asked how many of the potential cases are under review status and if Dr. Shimabukuro could share additional information about the case that was excluded.

Dr. Shimabukuro indicated that the number of cases under review is dynamic and changes on a daily basis, but at this time of this meeting there were 10 cases under review. That is using the relatively restrictive case definition looking at large vessel thrombosis in unusual locations and the presence of thrombocytopenia. As mentioned, the case definition will be expanded to make it more consistent with the draft Brighton Collaboration case definition. That includes other thrombosis events like VTE, DVT, PE, ischemic stroke, and acute myocardial infarction. When the case definition is expanded beyond that, he anticipates that there will be a substantially larger number of cases under investigation, which is normal. In terms of additional information on the report of TTS that was excluded from the case count, it was in a female less than 50 years of age who was polymerase chain reaction (PCR)-positive for COVID-19 and had a complex clinical course. She was hospitalized twice, with admittance the first time at 22 days after vaccine with COVID-19 pneumonia. She presented with nausea, hematemesis, and shortness of breath. The date of symptom onset was not clear. During the first admission, she had a normal platelet count. She was readmitted to the hospital for a second time at 28 days after vaccination when she presented with nausea, hematemesis, abdominal pain, shortness of breath, and cough. At that time, she had a platelet count of 100,000. Imaging studies showed CVST, lower leg VTE, and a PE. She subsequently died during hospitalization. The reported cause of death (COD) was respiratory failure, shock, and COVID-19 pneumonia. This was a complex clinical course in which it was not so clear whether this should be included as a case. In consultation with colleagues at the FDA, the CDC decided not to include this as a case in the final analysis but certainly would mention that this case existed and for transparency have this information available for ACIP.

Dr. Bernstein requested a reminder of the incidence of TTS was following receipt of AZ's COVID-19 vaccine in Europe and the UK.

Dr. Oliver indicated that she would be sharing further information on this in her upcoming presentation.

Ms. McNally observed that while this is a rare outcome, it is potentially life-threatening. She is mindful that the complication is listed under the Countermeasures Injury Compensation Program (CICP). She wondered whether an Injury Table is being developed for the COVID-19 vaccine.

CAPT Mishler (HRSA) indicated that a Vaccine Injury Table will be developed but is not presently under development. There will be injuries on the table, but people also will be given consideration to non-table injuries as well.

Dr. Long commented that the Brighton Collaboration uses a very liberal definition for thrombocytopenia. It is very likely that that will become contaminated and will have to be ratcheted down a lot to get to this syndrome, which is by definition an autoimmune-type syndrome that is characterized by extremely low platelets in many patients. She asked whether there are any data about the time between onset of symptoms, especially headache, and first coming to medical attention in order to better understand if this is rapidly progressive and

potentially fatal before any medical intervention could occur or if there are 5 or 6 days in which they could educate and potentially save lives. Timewise, that could be contaminated by fever and other symptoms that still could have been reactogenic to vaccination. Perhaps hospitalization could be taken as a possible marker, although patients could have been sent home from Emergency Departments (EDs) if they had non-specific headaches.

Dr. Shimabukuro said he thought what Dr. Long was asking for was the median time in the range from symptom onset to hospitalization, which is 5 days with a range of 0 to 14 days.

Dr. Duchin (IDSA) asked what the plan is for updating available information and how that will be made available to the public. He emphasized that this level of scrutiny leaves no doubt that vaccine safety is a top priority for CDC, FDA, and the national program. The public will be interested in hearing ongoing updates of what is being found.

Dr. Shimabukuro indicated that enhanced surveillance will continue for this condition, case finding, rapid assessment of cases, requests for medical records, review, and consultation with CISA colleagues to do a deep dive into these cases. CVST has been added to the VSD RCA and CDC is looking into ways to automate and become more efficient at detecting thrombosis with thrombocytopenia in its population-based systems. They will continue to brief VaST, which meets weekly, on a routine basis. They also are happy to brief the COVID-19 WG as requested, who will certainly present safety data to the full ACIP whenever asked, and will try to publish this information as soon as possible. There are currently publications in the works.

Dr. Daley echoed the comments of Drs. Poehling and Duchin. The very fact that something this rare can be detected is an indication of the strength of vaccine safety monitoring system and that that monitoring is going to continue. By his count, the pause had been in place for 11 days. He asked whether it was Dr. Shimabukuro's sense that the pause achieved the goal of better understanding and better characterizing these cases.

Dr. Shimabukuro stressed that this work would have been done regardless of whether there was a pause. The totality of the situation caused them to focus in on rapidly assessing these cases. They changed the procedures and staffed up to do this, so one could argue that the fact of the pause focused the efforts to getting to the bottom of this quickly in order to report back to the ACIP 10 days later to provide the data hopefully needed to make an evidence-based recommendation.

Dr. Wharton (CDC) added that a very important objective was achieved by the pause in that it allowed clinicians to be informed about the condition, raised public awareness, and provided time to better assess risk in order to have the conversation they were having during this meeting.

Dr. Fink (FDA) agreed with the statements by Drs. Wharton and Shimabukuro regarding the benefit of the pause. In terms of ongoing efforts, FDA will continue to work closely with CDC to evaluate and characterize these cases and this AE. If any further information comes to light that would warrant additional safety communications or changes to the warning statement to ensure adequate risk communication, that will be done.

Dr. Romero stressed that this pause was essential to ACIP's ability to inform the public and physicians and to acquire more data for presentation and analysis.

Public Comments

José Romero, MD, FAAP
ACIP Chair

Dr. Romero opened the floor for public comment during the April 23, 2021 ACIP emergency meeting at 1:00 PM ET. He welcomed and thanked the public speakers for addressing ACIP and emphasized that ACIP takes public comments very seriously. Given the limited timeframe available, speakers were requested to limit their remarks to the 3 minutes allotted. All speakers submitted a request in advance of the meeting, with the final selection of public commenters made randomly via a lottery. The comments made during the meeting are included here. Members of the public also were invited to submit written public comments to ACIP through the Federal eRulemaking Portal under Docket No. CDC-2021-0044. Visit http://www.regulations.gov for access to the docket or to submit comments or read background documents and comments received.

Frank Han, MD
Pediatric Cardiologist, University of Illinois
Testifying as a Private Citizen

Good afternoon. My name is Dr. Frank Han. I am a Pediatric Cardiologist at the University of Illinois. I am testifying as a private citizen. My goal is simple and is to demystify the scientific method for the members of the public as it relates to vaccines. The Mayans thought it was necessary to sacrifice a human life in order for people to be protected from starvation, and many other cultures have similar belief systems. One thread rang true throughout all those centuries and that is that nobody thought to verify those beliefs. While some folks did attempt earlier versions of the scientific method, it was not really documented and widely used until the Modern Age. While you might hear many different opinions about the modern scientific method, at its core the rules of the science playbook are very simple. If the natural world could just speak English, we could talk to it. Instead, we must make educated guesses about how something works, then devise an experiment to see if our thought is correct, then collect and analyze evidence. So, that's it. There's nothing mysterious or scandalous about it and it's all about gathering observations to figure out how the natural world works. We've benefited from the scientific method when we turned on the light bulbs in our houses. We've benefited from the scientific method when we took the train to work. We've benefited from the scientific method when we've received protection against vaccine-preventable diseases. You all have benefited from the scientific method any time you try to fix something in the house. As long as a person is dedicated enough, that person can perform science. It does not have to be born into aristocracy. With the current vaccine investigation, we're witnessing what it's actually like to discover new knowledge. It's good old-fashioned hard work and interpreting the data. It's not controversial to ask the pilot if you want to learn how to fly. In the same way, it should not be controversial to ask a pediatrician or infectious disease physician about vaccine science. In the same way, it shouldn't be controversial that the best minds in the US are working on analyzing the vaccine safety profile of the Janssen Vaccine. I want the pandemic to end just as much as anyone else does. However, it is not going to end through disinformation. It's going to end through teamwork and the sharing of quality science. I would go to vaccinetalk.org to get your questions answered if you don't have easy access to a healthcare worker. There are many verified healthcare workers there who would love to share information with you. Memberships is free with a Facebook account. Everyone starts somewhere. There's no shame in having last touched a science book in high school. I would be thrilled if you want to try out the scientific method for yourself. Guess what? We all tried it as children when we jumped into puddles in the rain and

learned about splashing. Science literacy benefits everyone and it's never too late to start. Thank you for your time Mr. Chairman.

Ms. Jeanette Contreras
National Consumers League

Thank you. Good afternoon. My name is Jeanette Contreras. I am representing the National Consumers League (NCL) who for over 120 years has championed vaccine education and access for consumers to these life-saving medical interventions. We extend our gratitude to the Advisory Committee on Immunization Practices for the opportunity to serve as a voice for consumers. We commend the CDC and FDA for their concerted efforts to promptly address the recent adverse events (AEs) observed by the Johnson & Johnson COVID-19 vaccine. The decision for a momentary pause in the distribution of the vaccine enacted out of an abundance of caution illustrates just how swiftly the agencies acted on vaccine surveillance data. Consumers should be comforted to know that the vaccine safety monitoring system in place to protect them is working effectively, and further encourages transparency following the reports of severe cases of a rare form of blood clots observed in young women. The pause allowed the agencies to gather and review additional evidence to ensure the safety of the American people. Over 560,000 Americans have already died from COVID-19. The risk Americans face for dying from COVID-19 is 1 in 600 persons. While the risk of dying from COVID clearly outweighs the risk of forming blood clots from the vaccine, we commend the efforts of public health officials to evaluate the specific effects of the vaccine on women to help ensure further safety and efficacy. Due to its ease of transport and one-shot delivery, the Johnson & Johnson COVID-19 vaccine is the accessible and convenient vaccine presently available. The vaccine has been administered to over 7 million Americans with overwhelming success. Further delay of administering this vaccine only delays our ability to end the pandemic that much sooner. The reports of adverse events experienced by patients who received the Johnson & Johnson COVID-19 vaccine are concerning and we appreciate the transparency afforded to the public during this time to identify and resolve the situation. The National Consumers League has long advocated for vaccine safety and for consumers to feel confident that they are safe, especially in the midst of a mass vaccination campaign. In closing, we encourage the CDC to maintain effective public messaging to instill vaccine confidence. Consumers should rest assured that vaccines are effective measures to protect public health and vital to national efforts in ending the pandemic. Thank you for your consideration of our views on this important public health issue.

Janci Chunn Lindsay, MD, PhD
Director, Toxicology and Molecular Biology
Toxicology Support Services, LLC

Hi. My name is Dr. Janci Chunn Lindsay. I hold a Doctorate in Biochemistry and Molecular Biology from the University of Texas and have over 30 years of scientific experience, primarily in toxicology and mechanistic biology. In the mid-1990s, I aided in the development of a temporary human contraceptive vaccine which ended up causing unintended autoimmune ovarian destruction and sterility in animal test models despite efforts against this and sequence analyses that did not predict this. I strongly feel that all the gene therapy vaccines must be halted immediately due to safety concerns from several fronts. First, there is credible reason to believe that the GTs will cross-react with the syncytin and reproductive proteins in sperm, ova, and placenta leading to impaired fertility and impaired fertility and reproductive outcomes. Respected virologist, Bill Gallaher, has made excellent arguments as to why you would expect cross reaction due to beta sheet conformation similarities between spike proteins and syncytin-1 and syncytin-2. I have yet to see a single immunological study which disproves this, despite the

fact that it would literally take the manufacturers a single day to do these syncytin Enzyme-Linked Immunosorbent Assay (ELISA) studies to ascertain this. It has been over a year since the assertions were first made that this could occur. We have seen 100 pregnancy losses reported in the Vaccine Adverse Event Reporting System (VAERS) as of April 9th and there have been reports of impaired spermatogenesis and placental findings from both the natural infection, vaccinated, and syncytin knockout animal models that have similar placental pathology, implicating a syncytin-mediated role in these outcomes. Additionally, we have heard multiple reports of menses irregularities in those vaccinated. These must be investigated. We simply cannot put these GTs in our children who are at 0.002% risk for COVID mortality, if infected, or anymore of the child-bearing age population without thoroughly investigating this matter as we could potentially sterilize an entire generation. Speculation that this will not occur and a few anecdotal reports of pregnancies within the trials are not sufficient proof that this is not impacting on a population-wide scale. Secondly, all of the gene therapies are causing coagulopathy. This is not isolated to one manufacturer and this is not isolated to one age group, as we are seeing coagulopathy deaths in healthy young adults with no secondary comorbidities. There have been 795 reports related to blood clotting disorders as of April 9th in the VAERS reporting system, with 338 of these being due to thrombocytopenia. There are forward and backward mechanistic principles for why this is happening. The natural infection is known to cause coagulopathies due to the spike protein. All GTs direct the body to make the spike protein. Zhang et al in September 2020 showed that if you infuse spike protein into mice that have humanized ACE-2 receptors on blood platelets that you also get disseminated thrombosis. Spike protein incubated with human blood in vitro also caused blood clot development, which was resistant to fibrinolysis. The spike protein is causing thrombocytic events, which cannot be resolved through natural means. And all vaccines must be halted in the hope that they can be reformulated to guard against this adverse effect. Third, there is strong evidence for immune escape in that inoculation under pandemic pressure with these . . . [time expired].

Kelly L. Moore, MD, MPH
Deputy Director, Immunization Action Coalition
Adjunct Associate Professor of Health Policy at the Vanderbilt School of Medicine

Good day. My name is Dr. Kelly Moore. I'm the Deputy Director of the Immunization Action Coalition and Adjunct Associate Professor of Health Policy at the Vanderbilt School of Medicine. I'd like to take this opportunity to thank the members of the ACIP, the CDC subject matter experts (SMEs) and administrative staff, as well as all of the outside consultants for their approach to the issue of thrombosis with thrombocytopenia syndrome, which we're now calling TTS. I suspect very few of you have slept much at all in recent days. Since last summer, the ACIP has been engaged in a thorough and very public process to prepare the nation for a rational approach to the most complex mass vaccination program ever attempted in human history. As with any new vaccine, CDC and FDA were prepared for the possibility that adverse events too rare to be detected in clinical trials could emerge after vaccine administration to the public had begun. Our public investments in the multiple facets of the US vaccine safety surveillance system proved their worth by detecting these extremely rare TTS case reports within a few weeks enabling FDA and CDC to pause vaccinations, evaluate these events, and most critically to inform vaccine recipients and clinicians how to recognize, diagnose, treat, and report these cases all while 52% of recipients were still within the risk window. I cannot overstate what an extraordinary public health accomplishment this is. We are faced with a situation where a very serious rare event is possible with this vaccine, while the vaccine also is very capable of preventing a serious and very common pandemic disease and it does so with a refrigerator-stable, one-dose formulation with considerable operational advantages. It's admittedly a difficult position to be in. Nonetheless, US public health and the ACIP have been

swift, transparent, and clear in their communications and this clarity is just what is needed to support the resilience of our national COVID-19 vaccination program as we adapt to this new variable in the program and in our public education efforts. Regardless of the ACIP's ultimate recommendations today, and reasonable experts may disagree on the nuances, your commitment to maintaining ACIP's tradition of open scientific inquiry, debate, and evidence-based policymaking through this TTS situation has served the public's interest and will help individuals feel confident they have the information they need to make a well-informed personal decision about vaccination with the Jansen COVID-19 vaccine or the mRNA vaccines to protect themselves and help end the COVID-19 pandemic. Thank you for your service.

Mrs. Tia Severino
Concerned Citizen

Hello. This is Tia Severino. Thank you for allowing me to speak. As you may remember, I have spoken to you many times before about the injuries and deaths associated with CDC/ACIP-recommended vaccines and the fact that when you recommend a vaccine, that recommendation is translated into mandates. The deception, coercion, and bullying that follows is in direct violation of the Nuremberg Code. The human subject must be fully informed of risks and their involvement in any medical experiment must be voluntary. Anyone receiving any of the emergency use authorized COVID-19 vaccines is part of an experiment. Experimental drug trials are meant to be carried out on subsets of the population and the results carefully examined for any signals, especially death, before that drug can be offered to the public. And yet, here we are with the advising administration insisting that the goal is to vaccinate the entire country and characters like Bill Gates saying we can't go back to normal until the entire world is vaccinated. This is pure insanity. These experimental vaccines have no long-term data to say they are safe or effective, but the short-term data is staggering. I was just on the Vaccine Adverse Events Reporting System this morning and the most recent data for deaths associated with COVID-19 vaccines is 3186 for all manufacturers: Pfizer 1476, Moderna 1540, Jansen 155, and 23 where the vaccine manufacturer is unknown. A study done by Harvard concluded that 1% of actual events are reported, so the real number is much higher. But let's talk about the "elephant in the room." Why is ACIP focusing on a few rare events of blood clots with low platelets and ignoring thousands of reports of death. Even if your focus is on blood clots, the Moderna and Pfizer vaccines have much higher reported deaths due to blood clots. Why are you pausing Janssen over 6 deaths while completely ignoring or dismissing the thousands of deaths caused by Moderna and Pfizer? I have to be honest, it seems like a political move—a way to pretend that you care about rare events enough to stop a problematic vaccine, which really only benefits Moderna and Pfizer and forces those who want to be vaccinated to only be able to receive the risky mRNA technology. If you truly cared about the safety of vaccine recipients, you would examine all the data regarding injury and death following any COVID-19 vaccine. To finish, I'll remind you again—those you label anti-vaccine are against vaccines because we have experienced or witnessed injury. This COVID vaccine agenda is waking people up faster than I ever dreamed possible and each and every injury and death from COVID vaccines will only grow our numbers. By the way, I'm happy to be part of the control group. Thanks again.

Mr. William Zielinski
Citizen of the United States

Hey. My name is William Zielinski. I'm the father of Willow Zielinski. Willow received Prevnar 13®, DTaP, and hepatitis B at four and a half months old and her brain hemorrhaged from it because it had a thousand micrograms of aluminum injected into her and the FDA only approves 5 micrograms to be a safe amount. I am highly concerned about all the COVID-19 vaccines and their clinical studies. In 2018, ICAN (Informed Consent Action Network) and Robert F. Kennedy Jr. filed a lawsuit against HHS (Health and Human Services) for not conducting any vaccine studies in over 30 years, which I cannot believe. In 1986, Ronald Reagan took all liability away from any vaccine manufacturer and it blows my mind that vaccine manufacturers cannot be held accountable for any of the deaths caused from the vaccines that they created. My wife, Priscilla, is a first responder in Milledgeville, Georgia and the amount of calls that come through the dispatch office pertaining to shortness of breath or non-responsiveness following the COVID vaccine is unreal. I also have a childhood friend that works in the dispatch office in our area, and they aren't even allowed to talk about the vast amount of calls that come through following the COVID vaccine. I mean, it just doesn't make any sense why nobody can talk about what's going on in the real world versus these clinical studies that are so-called "being done." Since we have stopped vaccinating our children, they are healthier and happier. I love my family and my children and I'll do anything to protect my family. From what I have seen and encountered with the vaccines, they don't work from my family. My wife and I have our story on YouTube under Will and Priscilla Zielinski that pertains to all of the details following our child's, vaccines at four and a half months old. But the main focus needs to go to all of the deaths that are deriving from the COVID-19 vaccines, which I haven't seen any good clinical studies pertaining to how they are healthier and they are working. I appreciate your time and I thank you for allowing me to speak. Thank you.

Mr. Joel Thompson
Concerned Member of the American Public

Good afternoon everyone. My name is Joel Thompson and I come to you today as a concerned member of the American public. To the ACIP members present today, I first went to commend you on the tremendous thoughtfulness, thoroughness, and care you have repeatedly demonstrated in considering COVID-19 vaccines. The American public can take comfort knowing dedicated public servants such as yourselves are continually examining the COVID-19 vaccines. Unfortunately however, with regard to the Janssen COVID-19 vaccine, my compliments end here. First and foremost, I am dismayed by the paternalistic attitude displayed by members of ACIP towards the American public. Their concerns noted over the last week towards Janssen's COVID-19 vaccine would be an appropriate basis to withhold vaccination if individuals were being compelled or coerced into receiving the Janssen vaccines. That is not the case. Every person who is receiving the vaccine is doing so consensually. Your actions, or rather your lack of actions a week ago, have taken the decision away from individuals to make their own personal health decisions about what they feel is best for their own individual situations. They are now not able to choose to take the Janssen vaccine. The overwhelming recommendation of public health officials is to take the vaccine you are able to first. While the first vaccine I was able to receive was Moderna's, if the first vaccine I had been able to get was Janssen's, I would have gladly taken that even knowing what we all know today, and furthermore I would have been thoroughly dismayed if I had had to delay vaccination because I had originally been scheduled to receive Janssen's. Second, regardless of my concern about paternalism, it has been clear since before last week's ACIP meeting that the benefits of the Janssen COVID-19 vaccine vastly outweigh the risks, especially in hard-hit areas that will

benefit from the vaccine's single dose regimen, such as the frightening surge we are seeing in Michigan. Don't just take my word for it. For example, last week, Dr. Jeremy Samuel Faust of Brigham and Women's Hospital and an instructor at Harvard Medical School and Dr. Ashish K. Jha, Dean of the Brown University School of Public Health, both posted threads on Twitter explaining why they believe the decision to continue the pause is a mistake, because the benefits of the Janssen COVID-19 vaccine clearly outweigh the risks in the current environment we are in today. There's only a single responsible path for ACIP to take today. That path is to correct last week's mistake and let Americans make their own decisions about their bodies and their own health care, including a decision about whether or not to take the Janssen COVID-19 vaccine. Thank you very much for letting me speak to you today.

Mr. Brett Farruggia
Citizen of the United States

Hello. I'm Brett Farruggia. I'm representing myself as a private citizen today. Since the pause of Johnson & Johnson vaccines nearly 2 weeks ago, vaccination rates across the nation have fallen by 13%. In more hesitant states, vaccination rates have fallen further, including 33% in Texas and nearly 50% in Wyoming. This cannot fully be attributed to reduction in supplies due to the pause. Across several states, there have been mass cancellations of all 3 manufactured vaccines. In addition, including in my State of New York, homebound programs were halted for over a week due to the pause. Today, I urge the committee not only to immediately reinstate the Johnson & Johnson vaccine in order to reassure the public, but also make efforts to repair the severe damage done to vaccine confidence across the nation by this overzealous pause. I also urge the committee to re-evaluate risk assessment practices. It is a near statistical certainty that more people will die of COVID-19 due to 10 million doses of vaccine sitting idle at vaccination sites across the nation combined with renewed skepticism induced by the pause than would die from exceedingly small chances of blood clots. Further, during the pandemic the ACIP's decisions have had much more far-reaching effects than just vaccine safety. When the pace of vaccination is full of life and death for people and livelihoods, the committee should weigh the communal good against individual safety. I also urge the committee to take into account how many people will never get vaccinated due to the pause of this vaccine and weigh it against the exceedingly rare chance of death from blood clots. This pause may end up being the worst blow to vaccine confidence since the fraudulent link between vaccines and autism was made 23 years ago. If we still have this falsehood about autism and vaccines spreading 23 years later, how long will it take to quell the myth that vaccines cause blood clots in any statistically meaningful way? Again, I urge the committee to immediately reinstate the Johnson & Johnson vaccine, the necessary warnings to boost public confidence, increase vaccine supplies, and allow homebound and underserved communities access to a one-dose vaccine. Further, I urge the committee to re-evaluate risk assessment practices to better reflect the risk-benefit balance during the unique times of a pandemic. Thank you for your time.

Ms. Sarah Barry
Independent Pro-Vaccine Advocate

Hello. My name is Sarah Barry and I am an independent pro-vaccine advocate who operates online under the username 42believer. I was incredibly grateful to share my public comment with you last time and I'm equally excited to do so again. Over a month ago, I received the Johnson & Johnson vaccine and experienced no other side effects other than a sore arm and mild flu symptoms. I was and still am very grateful to have received this vaccine and I am grateful to the ACIP for continuing to monitor the situation and for having these transparent discussions. Last time I gave comment, I ended with a strong phrase that was "anti-vaxxers

abuse autistic children." I am often asked what I mean by this, so I would like to take the time to educate you all on this lesser known but crucial aspect of the anti-vaccine community. I truly believe that highlighting these transgressions is the only way to win against them. When I have discussions with people whether they think that they're super pro-vaccine or whether they're on the fence or not, most of them have heard of people like Andrew Wakefield, but they really don't know about Andrew Wakefield and the things that he's done beyond getting his license taken away and beyond having the study that he published be retracted. When I hear Andrew Wakefield, the first name that I think of is Jack Piper because he was one of the 12 children that was part of the original study, the original *Lancet* study, and Jack Piper's family was able to get hundreds of thousands of pounds in compensation from the hospital because he suffered intense cuts to his interior colon as a result of the procedures that were performed on him during the study. This is the first example of the modern anti-vaccine movement using children, autistic children in particular, as experiments to try and cure them. Another person that most people, pro-vaccine or not, most people haven't heard of people like Mark Geier. Much like Andrew Wakefield, Mark Geier lost his medical license, but instead of the experiments that Wakefield did, he gave autistic children a drug called Lupron, which ended up chemically castrating autistic children, and he charged parents $12,000 a month for the privilege of experimenting on their children without informed consent. There's a lot of anti-vaxxers who talked about we need informed consent, and we need everything to go through the proper process and be tested against placebos. I genuinely, genuinely want them to look in their own communities and see that their own communities endorse and enable people like Mark Geier to continue to hurt autistic children and flout the very standards that they are trying to hold big pharmaceutical companies to. And again, I strongly feel that this particular argument is the only way to win against people who are on the fence and I . . . [time expired]. Thank you very much.

Mr. Juan Cambeiro
Hunter College
Concerned Member of the Public

Hi. I'm Juan Cambeiro. I'm in the Biology Department at Hunter College. I do COVID forecasting work for Metaculus and most importantly, I'm a concerned member of the public who fears that this pause is having a very negative impact on getting life-saving vaccines into as many arms as possible. I would like to strongly urge the committee to recommend lifting the pause on the J&J vaccine and to recommend rollout be resumed with no age or sex restrictions. There are four key reasons that support this. First, the risk-benefit profile of the vaccine is very favorable, even for young people, as was presented by Dr. Shimabukuro earlier. Data that has come in since the pause has confirmed that TTS is an extremely rare event. Risk is somewhere in the range of less than 1 to 10 in 1 million. The positive risk-benefit profile has also recently been affirmed by the European Medicines Agency (EMA) on April 20th. This positive risk-benefit profile is clear even for young people for whom the risks of COVID are clearly far greater than the risks from this vaccine, including as Dr. Streiff mentioned, even the risk of TTS, which is somewhere around 10 times higher from COVID than from the J&J vaccine. Current polling indicates that there is a significant group of young people, including young women, who are somewhat vaccine-hesitant and who favor this vaccine as "one and done." For this group, resuming J&J vaccine rollout is crucial since these people might otherwise not get vaccinated. Second, as was pointed out by Dr. Kotton at the last meeting, the J&J vaccine lacks storage requirements and the fact that it's a single dose means it's by far the best vaccine to vaccinate disadvantaged groups like the homebound and homeless. Fully vaccinating these vulnerable populations with 2-dose mRNA vaccines that require cold-chain is, in many cases, not possible. I urge the committee to take into account these equity considerations. Third, although vaccine hesitancy in the general population doesn't seem to have increased as a result of this pause, polling by

YouGov shows that the public's perceived safety of the J&J vaccine specifically has plummeted by 15%. Moreover, in a Harris poll out this morning among the "wait and see" group of Americans, 67% say that the pause is negatively impacted their impression of the J&J vaccine's safety and 62% say that it has negatively impacted their confidence in vaccine safety overall. An extension of the pause seems likely to impact public confidence even more, especially among this crucial "wait and see" group. Finally, although ACIP is responsible for making recommendations for the US, I urge the committee to also keep the global context in mind. Many countries that take cues from what the US does have also suspended rollout of the J&J vaccine even though they don't have access to other vaccines yet. Dr. Lee made this point at the last meeting and I thought it was worth re-emphasizing since it is so important. The longer everyone else remains unvaccinated, the longer this tragedy of the pandemic will go on, people will die, and new variants will arise. A lot hinges on your vote today and I really hope you consider lifting the pause instead of continuing to restrict use of this life-saving vaccine. Thank you so much for your work and for considering my comments.

Scott Ratzan, MD, MPA
Public Health Physician
Dean/Professor, CUNY Graduate School of Public Health
Editor, *Journal of Health Communication*
National Academies Board on Global Health

Thank you for the opportunity to speak at the ACIP today. My name is Scott Ratzan. I'm a Public Health Physician, Professor, and Editor of the Journal of Health Communication. I teach at City University of New York (CUNY) Graduate School of Public Health and Health Policy New York and serve on the National Academies Board on Global Health. Previously, I was a member of the Board of Scientific Counselors (BSC) for the CDC's Office of Infectious Diseases (OID). Last year, along with Dr. Heidi Larson and others, I helped found a global initiative called CONVINCE[SM], which stands for COVID-19 New Vaccine Information Communication and Engagement. Since last March, CUNY and CONVINCE have convinced more than 20 COVID-related consumer research studies in the US and internationally. Earlier this year, I shared some of these learnings from this work with the HHS National Vaccine Advisory Subcommittee on Vaccine Confidence and made a number of recommendations to help build public confidence in vaccines. I speak today to you with hope and concern—hope that we can get this vaccine back in the pipeline and hope that we can rebuild confidence in it; concern though that a key element of our current approach may not be sufficient to attain the levels of confidence and trust we need to reach the herd immunity and end this pandemic. A study we did just last week nationally confirms it a substantial percentage, 78%, of the American public believes vaccination is the only way to end the pandemic. At the same time, our study and others suggest that at least 1 in 5 Americans did not believe that COVID-19 is that big of a risk and are not likely to receive this for any other vaccine. As we cross the threshold of a 50% vaccination rate in this country, our efforts to control COVID-19 are clearly at a tipping point. Demand for COVID-19 vaccines has fallen significantly in the past weeks and many county health departments are shuttering their mass vaccination sites. Vaccinating the next 25% of Americans will require new strategies and better systems. I believe the benefit-risk data you are considering today will support returning the single shot Janssen vaccine to the pipeline with better surveillance. However, I do not believe that the current surveillance system provides data that are strong enough, prompt enough, or convincing enough to give unvaccinated people the confidence they need to roll up their sleeves. Our current VAERS system is a passive one. It identifies vaccine injuries based on people's reporting adverse events through the local, state, or Tribal health authority. We need a more active approach. I strongly recommend that the ACIP consider supporting the development, at the federal and state levels, of a new unified system for real-time collection of

data—a registry of everyone who gets a COVID-19 vaccine, which vaccine they received, and when they got it. A proactive registry will greatly strengthen what the FDA calls "post-marketing surveillance" by generating better and prompter data on the safety and efficacy of this and other vaccines. This is data that can be reported to Congress and the public to build confidence in the safety of COVID-19 immunization and reinforce emerging statistical evidence on the positive effect of vaccination. Finally, ACIP's actions today will have national and global impact. The steps you recommend should bring this enormously useful single dose vaccine back into the global pipeline. You can all help build awareness . . . [time expired]. Thank you.

Janssen COVID-19 Vaccine Update

Mathai Mammen, MD, PhD
Global Head, Research and Development
Janssen Pharmaceuticals Companies of Johnson & Johnson

Joanne Waldstreicher, MD
Chief Medical Officer, Johnson & Johnson

Dr. Mammen emphasized that Jansen believes that the Johnson & Johnson COVID-19 vaccine, which he referred to as the J&J vaccine, has important and even unique benefits for the global effort to end COVID-19. In the weeks since Janssen's vaccine was authorized for use in the United States, 7.9 million people have received the J&J COVID-19 vaccine. During that time, it has been observed that this vaccine is not only a vital and important option across a wide range of people, but that it may be uniquely good and, in some cases, the only practical option for some people. For example, for those who face barriers to healthcare services. The vaccine has proven highly protective with single-dose efficacy also against concerning variants of SARS-CoV-2 that are emerging as viral replication and selective pressures continue at a global scale, and that the benefit thus holds. As a real credit to the US, European, and Janssen's own safety surveillance systems, they worked in close collaboration with the US, Canadian, and European health authorities to identify a very rare but very serious side effect of thrombosis with thrombocytopenia that appears at a higher rate than the background rate in the population. Janssen recognizes that this is a very rare but very important and serious risk and fully supports awareness, education, and labeling. With these efforts, Janssen's goal is earlier recognition, making this event more identifiable, diagnosable, treatable, and with improved chances of successful outcomes. Janssen's priority since the discovery of these events has been to work very closely with health authorities to increase awareness among the general public and healthcare professionals. Janssen fully supports the important information addressing this event in the vaccine fact sheet and prescribing information.

This presentation focused on a few relevant features of the current COVID-19 pandemic, a description of the benefits of the J&J vaccine, highlights regarding efficacy and other key attributes relevant to the current COVID environment, the safety of the vaccine with a focus on the characterization of the very rare but serious risk of thrombosis with thrombocytopenia, and Janssen's framework for thinking about the risks and benefits of this vaccine for the US and the globe while responsibly managing its risks.

Dr. Mammen pointed out that in the past week, there were nearly 40,000 hospitalizations and over 4700 deaths in the US and around 10 times more of that number globally. The pandemic continues to rage even in the face of the vaccine rollout. Importantly, many people face obstacles to accessing a vaccine and it is known that the J&J vaccine has been particularly important to people who live in rural or remote areas, for example, and who lack the type of

health care infrastructure required for other options. A particularly important feature of the J&J COVID-19 vaccine measured in Janssen's Phase 3 trials is that the trials demonstrated strong protection offered against severe disease after Day 28 of a single shot with 100% protection against hospitalization and 100% protection against death. Most notable is that this pattern of protection was true also in regions such as South Africa and Brazil where the 484K-containing mutations are dominant. In South Africa, for example, equal efficacy was seen to that measure globally, including 85% protection against severe COVID, 100% protection against hospitalizations, and 100% protection against deaths. These results are supported from an ongoing study in South Africa where over 280,000 health care workers (HCW) have been vaccinated. These HCW and these health care workers have significant and sometimes repeated exposure to B.1.351, the South African variant. Of note, the participants are primarily women and primarily under the age of 50. As with Janssen's Phase 3 study, there have been no hospitalizations or deaths after Day 28 and only 3 breakthroughs after Day 28 among the 280,000 vaccinated people.

The B.1.351 variant contains three mutations and 1 deletion on the tip of the spike protein, rendering the neutralizing antibodies induced by all of the vaccines about 80% to 90% less effective than they are against neutralizing the original strain of the virus. This is true for Janssen's vaccine as well. Janssen believes that the excellent efficacy that is nevertheless maintained against the variance is in part due to the T-cell immunity that recognizes so many epitopes of the spike protein, that it is very challenging for the virus to circumvent the vaccine. Janssen's vaccine in particular has excellent T-cell immunity and has this by design. It is quite important to monitor these variants as a particularly infectious and resistant one can take over very quickly, especially now that selective pressure is being effectively applied through natural infection and vaccination. B.1.351 went from non-existent to becoming the dominant variant in South Africa in a matter of 8 weeks. Now it is generally the only circulating variant in that country. Disturbingly, B.1.351 has been found circulating in 36 of 50 US states and territories and across Europe. As with B.1.351, other variants containing the key mutation of position E484K have been reported in the US, starting in New York City (NYC).

Beyond this important high-level protection of the vaccine against variants, the J&J vaccine has other features that allow it to play an essential role in the effort to contain COVID-19 both in the US and globally. Janssen's vaccine is the only authorized vaccine that uses a single-dose regimen. The benefits of this dosing cannot be overstated considering the urgent mass vaccination campaign that is underway. Whether it is in rural communities that lack access to health care or transient populations like farming communities that may not be able to be in the same location for a second dose, the one-shot benefit is critical. The vaccine also has a relatively quick onset, with vaccine efficacy against severe disease seen as of Day 7 in the pivotal trial. Available immunogenicity data from the Phase 1 study up to Day 115 are in line with the historical platform data. That is very promising with regard to durability of protection also in the elderly. In addition, the vaccine is compatible with existing vaccine distribution channels and can be stored for 3 months at normal refrigerator temperatures. What this means for achieving vaccine goals should not be underestimated. The J&J vaccine has the ability to reach locations in the US that other vaccines may not. These features of the vaccine allow vaccination of people who might otherwise not be able to or choose not to get a shot. That is, there may remain part of an unvaccinated segment of the population.

All in all, the J&J vaccine plays a critical and complementary role to other vaccines. To be explicit, one concern is that absence of, or a restriction to, the J&J vaccine does not just the delay the full vaccination of the US population, but potentially leaves unvaccinated a proportion of the US population. If the unvaccinated population is large enough, this puts at risk reaching

herd immunity in the US. The global context is also critical. As global mobility resumes, there is no question that US residents remain vulnerable so long as large swaths of the globe remain undocumented and variants, therefore, continue to emerge. For many parts of the globe, the single dose and easy transport and storage features of the vaccine are absolutely critical. A restriction in use in the US could have a negative impact on the success of achieving global herd immunity. The pandemic in the US will not truly end until the world has indeed achieved herd immunity. Janssen believes this perspective is critical for the day's discussion.

Dr. Waldstreicher emphasized that safety is Janssen's highest priority and that they have been laser focused on identifying and understanding the very rare occurrence of CVST and other thromboses together with thrombocytopenia, as well as working with the FDA and other regulators on appropriate labeling to ensure awareness and guidance on diagnosis and treatment. There has been extensive outreach and communication of this event over the past week, which stimulated a number of additional reports on this important and serious event. As seen in Dr. Shimabukuro's presentation, there are 15 post-authorization cases of thrombosis with thrombocytopenia all in women most of whom are under 50 years old. Most of these cases were CVST and some also had thromboses at other sites. Dr. Waldstreicher stressed that while she used the word "cases," these cases are not just numbers to Janssen and they take them very seriously. These are people and it is necessary to understand and characterize their risk. In exploring the context, Janssen will show the rates in relation to other background rates. This is meant to be a general comparison of orders of magnitude of risk—not a direct comparison.

To place this into context, 15 cases have been reported post-authorization among nearly 8 million people vaccinated[18]. That gives a reporting proportion of 1.9 cases per million people. To compare this to the background rate, an initial focus was used of CVST with thrombocytopenia. Janssen's analysis of 5 large observational US healthcare databases that included over 60 million people estimated the background rate of thrombosis CVST with thrombocytopenia to be approximately 0.1 cases per million[19]. The evaluation of other thromboses with thrombocytopenia is ongoing, but many of those cases are confounded by other diagnosis such as cancer and other illnesses. In reviewing the interim Brighton criteria and speaking with experts, as well as evaluating the data thus far in healthy people, Janssen recognizes that this is likely extremely rare. In terms of the observed cases of thrombosis with thrombocytopenia per million people in comparison to other vaccine-related AEs, by no means do these need to be equated with the seriousness of thrombosis with thrombocytopenia. However, Janssen felt that it was important to note the frequency of events such as intussusception with rotavirus vaccine; immune thrombocytopenia associated with measles, mumps, rubella (MMR) vaccine[20,21]; Guillain-Barre Syndrome (GBS) in H1N1[22]; and anaphylaxis in the pre-COVID era from vaccines[23]. All of these range from approximately 1 to 70 cases per million people.

The fact sheet agreed upon with FDA describes that the clinical course of thrombosis with thrombocytopenia after Janssen's vaccine shares features with autoimmune HIT. This is estimated to occur between 1,000 and 50,000 cases per million heparin users, which is a different patient population than the vaccinated population[24]. HIT can be associated with a life-threatening thromboses, requires proper diagnosis, and importantly, consideration of alternatives to heparin as with thrombosis with thrombocytopenia.

[18] Cases, # people vaccinated: CDC (April 22)
[19] Incidence based on CVST + Thrombocytopenia in 2018 from 5 observational sources (n=63 million persons)
[20] Rha, B. et al. 2014. DOI: 10.1586/14760584.2014.942223
[21] Jiang, J. et al. 2013. https://doi.org/10.1371/journal.pone.0068482
[22] Salmon. et al. Lancet. 2013 (IR = IRR*baseline risk = 2.5*1.2/100,000py)
[23] McNeil, M. et al. JACI. 2016. http://dx.doi.org/ 137.3.2015.10.1016/j.jaci.2015.07.048
[24] Hogan, M. et al. Vasc Med. 2020. DOI: 10.1177/1358863X19898253. Epub. PMID: 32195628

Turning to the focus to women under age 50, amongst the 1.9 million women in this group, there were 13 cases. This is a reporting proportion of 7 cases per million women. To contextualize the risk for women under age 50 further, Janssen looked to consideration of the labeling and known and labeled association of oral contraceptives and thromboembolic events, including stroke, myocardial infarction, and CVST. Again, Dr. Waldstreicher emphasized that by no means were they equating these types of events with one another. However, she was using this as an example of where there are options for healthy younger women. Each product has its own benefit-risk and product profile among a variety of other options and each with unique characteristics such as long-acting injections, transdermals, different hormonal generations, and even non-hormonal methods. Each has risks that are addressed with warnings in product labeling and clear information in the patient information leaflet[25,26,27,28].

Ultimately, the risk of thrombosis with thrombocytopenia should be put into context with the benefits of vaccination. In a benefit-risk assessment in adults 18 years of age and older based on the efficacy data from the randomized pivotal trial and the reporting rate from spontaneous reporting, it could be expected that if 1 million people in the US were vaccinated with the J&J single shot vaccine, there would be over 2000 fewer deaths[29] and 6000 fewer COVID-related hospitalizations[30] on the benefit side and at the same time, approximately 2 additional cases of thrombosis with thrombocytopenia[31]. Looking at the benefit-risk assessment in women under 50 years of age, if 1 million women in the US were vaccinated, there would be 2,600 fewer COVID-related hospitalizations[30] and 116 fewer deaths[29] on the benefit side and approximately 7 more thrombosis with thrombocytopenia[31].

Janssen fully supports the public health recommendations from regulatory agencies and medical societies to create general public awareness, as well as to provide specific guidance for medical professionals regarding this very rare but serious event following vaccination. Janssen is committed to active follow-up to identify and investigate all cases and have an ongoing effort to fully understand the pathophysiology. Janssen's observational study protocols are designed and they are examining the feasibility of multiple databases not only from the US, but also from the rest of the world. Janssen fully supports the guidance from the CDC and professional societies that outline awareness, education, diagnosis, and treatment. In addition, Janssen is implementing several initiatives, including HCP and consumer support, professional education, posting fact sheets on its websites, and a 24-hour global hotline. Janssen absolutely agrees with the FDA on the implementation of a warning within the label and patient and physician fact sheets describing this very rare event, including how it can be identified early and diagnosed and treated. To that end, following is the language from the Janssen label that has been agreed upon with the FDA regarding thrombosis with thrombocytopenia. In addition to the description of the events, HCPs are alerted in the fact sheet to the signs and symptoms of thrombosis with thrombocytopenia in individuals who receive the COVID vaccine from Janssen. It also states that symptoms began approximately 1 to 2 weeks following vaccination, that most people have been females 18 through 49 years of age, and that some cases have been fatal. HCP are also directed to the published American Society of Hematology (ASH) considerations relevant to the

[25] Lidegaard, O. et al. NEJM. 2012
[26] Weill, A. et al. BMJ. 2016
[27] Azoomegar. et al. Frontiers in Neurology. 2015 (IR=background rate * OR = 0.4/100,000 * 7.59)
[28] Yasmin package insert: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=d7ea6a60-5a56-4f81-b206-9b27b7e58875
[29] CDC COVID-19 mortality rate as of Apr 14, 2021, 2018 US census population, COV3001 interim analysis assuming 100% efficacy on death for 1-year post-vaccination
[30] CDC COVID-19 hospitalization rate from Mar 7, 2020 – Mar 6, 2021, COV3001 interim analysis assuming 100% efficacy on hospitalization for 1-year post-vaccination
[31] Observed: Reporting proportion; Background: Assumed 0 cases/million

diagnosis and treatment. In addition, the patient fact sheet contains a clear warning and instructions. J&J strongly supports this enhanced labeling:

FDA-Agreed Warning and Precaution Regarding Thrombosis with Thrombocytopenia
5.2 Thrombosis with Thrombocytopenia Reports of adverse events following use of the Janssen COVID-19 Vaccine under emergency use authorization suggest an increased risk of thrombosis involving the cerebral venous sinuses and other sites (including but not limited to the large blood vessels of the abdomen and the veins of the lower extremities) combined with thrombocytopenia and with onset of symptoms approximately one to two weeks after vaccination [see Overall Safety Summary (6.2)]. 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. Based on currently available evidence, a causal relationship between thrombosis with thrombocytopenia and the Janssen COVID-19 Vaccine is plausible. Healthcare professionals should be alert to the signs and symptoms of thrombosis with thrombocytopenia in individuals who receive the Janssen COVID-19 Vaccine. The clinical course shares features with autoimmune heparin-induced thrombocytopenia. In individuals with suspected thrombosis with thrombocytopenia following the Janssen COVID-19 Vaccine, the use of heparin may be harmful and alternative treatments may be needed. Consultation with hematology specialists is strongly recommended. The American Society of Hematology has published considerations relevant to the diagnosis and treatment of thrombosis with thrombocytopenia following the Janssen COVID-19 Vaccine (https://www.hematology.org/COVID-19/vaccine-induced-immune-thrombotic-thrombocytopenia). Recipients of Janssen COVID-19 Vaccine should be instructed to seek immediate medical attention if they develop shortness of breath, chest pain, leg swelling, persistent abdominal pain, neurological symptoms (including severe or persistent headaches or blurred vision), or petechiae beyond the site of vaccination.

In conclusion, the benefits of Janssen's effective single dose and easy-to-use COVID vaccine continue to outweigh its risks. We continue to face a deadly pandemic and existing and emerging variants are making containment even more challenging globally. Every day matters in the campaign to control the virus and all options available are needed as the effects of COVID infection can be both serious and long-term. The Janssen vaccine offers many benefits in this context, including early efficacy; demonstrated efficacy in South Africa with the B.1.351 variant predominating; and simplicity in terms of its single-dose administration, shipping, storage, and handling. As such, the vaccine provides access to people who are underserved as well as certain populations that typically face barriers to healthcare services. As Dr. Mammen mentioned, Janssen's concern is that with a restriction it is not just about delaying vaccination, but potentially leaving a portion of the US unvaccinated. If the unvaccinated population is large enough, this puts at risk reaching herd immunity. It also is important to recognize that decisions in the US have an impact globally. With delayed vaccination and potential increased vaccine hesitancy, variants that emerge globally will ultimately impact the US, especially as global mobility resumes. A restriction in use in the US could have a negative impact on the success of achieving global herd immunity both in the US and globally. The pandemic will not be over until a large segment of the global population is vaccinated. Janssen recognizes that there is a very rare but important and serious risk and danger and fully supports increased awareness, education, and enhanced labeling. With these efforts, Janssen aims for earlier recognition and making this event more identifiable, diagnosable, treatable, and with improved chances for successful outcomes. In summary, Janssen believes the J&J COVID vaccine is central to the effort to end the pandemic.

Discussion Points

Dr. Shah (ASTHO) asked whether in their experience with other adenovirus vaccine vectors, Janssen has seen cases of similar thrombosis with thrombocytopenia.

Dr. Johan Van Hoof, Janssen R&D, there are similarities between the AZ vaccine and the Janssen vaccine, it is important to note that there are also differences between these vaccines. That relates to the vector that is used, which is human (Ad26.COV2.S) for Janssen and chimpanzee (ChAdOx1) for AZ. There also are differences in host cell receptors and other interactions to host factors, which potentially could lead to differences in immune responses. There also are differences in the transgene that has been used. Janssen has a transgene that is stabilized with a deletion so that it can enter cells but cannot replicate inside them or cause illness and that is stabilized against mutations, which is not the case with the other transgenes. Janssen thinks it is somewhat premature at this stage to compare the findings from the J&J vaccine to the AZ vaccine, but does realize that the clinical picture is very similar.

Dr. Shah (ASTHO) further specified that he was thinking of other COVID-19 vaccines that utilize an adenovirus vector such as the Sputnik vaccine and other non-COVID vaccines that also may utilize an adenovirus vector.

Dr. Johan Van Hoof said that he could not comment on the Sputnik vaccine as they do not know exactly what has been used for that one. Not many other adenovirus vector-based vaccines are currently licensed, but Janssen has an Ebola vaccine that uses the same adenovirus vector and they have looked in detail in the database for that vaccine. More than 200,000 people have been vaccinated with the Ebola vaccine and none of these phenomena have been observed in that vaccine setting. Janssen has other vaccines in clinical development using the same vector, specifically an HIV vaccine with which several thousand women have been vaccinated. Because the data and numbers are limited, but no signs of a similar phenomenon have been seen in those trials.

VaST Assessment

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Dr. Lee took a moment to place the events of the last week in context, particularly given the multiple WGs involved. The ACIP VaST Subgroup reviews vaccine safety data on a weekly basis. Risk assessment is a dynamic process and VaST is constantly reviewing new data from all available vaccine safety surveillance systems in the US and have been since the first vaccine was administered. The ACIP COVID-19 Vaccines WG focuses on benefit-risk assessment, placing the information about benefits and risks in the context of the ongoing pandemic in the US. Benefit-risk assessment also is a dynamic process that is continually updated as new information emerges. Finally, the ACIP committee deliberates on all available information in order to make recommendations for use. As during this meeting, recommendations will be revisited as new information emerges.

As a reminder, the objectives of the COVID-19 VaST WG are to: 1) review, evaluate, and interpret post-authorization/approval of COVID-19 vaccine safety data; 2) serve as the central hub for technical subject matter expertise from federal agencies conducting post-authorization/approval safety monitoring; 3) advise on analyses, interpretation, and data presentation; and 4) provide updates to the ACIP COVID-19 Vaccines WG and the ACIP on COVID-19 vaccine safety. More importantly, the reason there is such a focus on vaccine safety is to ensure that the public has confidence in vaccines and in the US vaccination program.

To date, VaST has had 17 independent meetings to review and discuss post-authorization vaccine safety data across multiple surveillance systems. VaST members have joined additional meetings of the COVID-19 Vaccines WG for specific review and updates of safety data presented on those calls. Focusing in on VaST's role on risk assessment and the thought process of the VaST WG, 6 cases of CVST with thrombocytopenia were identified on April 12th as a rare, but serious potential AE following Janssen vaccine. VaST members noted that risk factors for CVST with thrombocytopenia are not well understood. The WG felt strongly that timely and transparent communication with HCP and the public would be crucial to maintain confidence in the vaccination program.

Within 24 hours, CDC and FDA colleagues released a communication along with a safety pause to ensure that there was immediate awareness by clinicians, public health colleagues, and the public of this potential AE[32]. On April 14th, ACIP convened an open meeting to discuss CVST with thrombocytopenia to ensure transparency and public awareness. At that time, ACIP reviewed reported cases of CVST with thrombocytopenia after COVID-19 vaccines and discussed the need for additional information to support evidence-based decision-making, including age- and gender-specific risk estimates and an evaluation of the benefit-risk balance of using the Janssen vaccine in specific subgroups.

During an April 19th meeting, VaST reviewed the new Brighton Collaboration definition of TTS, which was discussed earlier in the day by Dr. Shimabukuro. That broader definition is in use now, but having a standardized definition is critical to facilitate investigations across surveillance systems in the US and globally. Dr. Lee took a moment to recognize and thank the Brighton Collaboration team for their quick work on this definition. VaST noted that the HAN was extremely useful for supporting enhanced case finding in the US. During that meeting, VaST requested additional information on the age- and gender-specific rates of TTS following the Janssen vaccine for further risk assessment. Data from the VSD and the VA RCA were reviewed, and no safety signals were identified for CVST, other thromboembolic disease, or thrombocytopenia following the Janssen vaccine with over 200,000 doses administered at that time across the two systems. VaST also received an update from the World Health Organization (WHO) Global Advisory Committee on Vaccine Safety (GACVS) on TTS cases following the AZ vaccine. This included a better contextual understanding of the country-specific approaches to use of the AZ vaccine that are driven by country-specific benefit-risk assessments.

During a joint VaST and COVID-19 Vaccines WG meeting on April 22nd, additional safety data were presented. The groups discussed that the risk for TTS following the Janssen vaccine was 7 per million doses in females less than 50 years of age, with the highest rate noted in women 30-39 years of age. In contrast, the risk for TTS was less than 1 per million in females 50 years of age and older and males of any age. Other potential risk factors include obesity, oral contraceptive use, hypothyroidism, and hypertension. However, there is not enough information to make a determination about whether these are true risk factors or associations. There were 3

[32] https://emergency.cdc.gov/han/2021/han00442.asp

deaths, 7 remain hospitalized, and 5 have been discharged home. The groups also discussed benefit-risk assessment and the Evidence to Recommendations (EtR) Framework during that meeting.

In summary, VaST recognizes that TTS is a rare potential complication that is potentially associated with the Janssen vaccine and that the risks should be balanced against the benefits of preventing deaths, hospitalization, and thromboembolic disease associated with COVID-19 infection. VaST notes that the risk of TTS appears highest in females less than 50 years of age and other risk factors for TTS are not yet well-established. Risk mitigation strategies may include the following: 1) minimizing exposure in high-risk populations; 2) increasing awareness and ensuring timely diagnosis and management of TTS; and 3) educating patients and the public about the benefits and risks of available vaccines. VaST will continue to monitor TTS, thromboembolic disease, and thrombocytopenia in all available vaccine safety surveillance systems and will continue to update the ACIP COVID-19 Vaccines WG, the ACIP Secretariat, and the full ACIP committee on a regular basis.

Risk/Benefit Assessment of Thrombotic Thrombocytopenic Events after Janssen COVID-19 Vaccines: Applying Evidence to Recommendation Framework

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Dr. Oliver reminded everyone that for the previous votes for the use of COVID-19, ACIP has used the EtR Framework that is a structure used to describe information considered in moving from the evidence to the ACIP vaccine recommendations. It provides transparency around the impact of additional factors on deliberations when considering a recommendation. The policy question that was originally voted on for the Janssen vaccine was, “Should vaccination with the Janssen COVID-19 vaccine (1 dose) be recommended for persons 18 years of age and older under and Emergency Use Authorization?” This is the traditional EtR Framework used for previous recommendations:

EtR Domain	Question
Public Health Problem	• Is the problem of public health importance?
Benefits and Harms	• How substantial are the desirable anticipated effects? • How substantial are the undesirable anticipated effects? • Do the desirable effects outweigh the undesirable effects?
Values	• Does the target population feel the desirable effects are large relative to the undesirable effects? • Is there important variability in how patients value the outcomes?
Acceptability	• Is the intervention acceptable to key stakeholders?
Feasibility	• Is the intervention feasible to implement?
Resource Use	• Is the intervention a reasonable and efficient allocation of resources?
Equity	• What would be the impact of the intervention on health equity?

While helpful, this does not necessarily fit the type of questions facing ACIP currently. Therefore, the EtR framework was adapted to a risk-benefit assessment for the Janssen vaccine recommendation, though many of the same domains were used to lay out the information available:

EtR Domain	Question
Public Health Problem	• Recent COVID-19 Epidemiology in terms of COVID-19 cases, hospitalization, and deaths stratified by age, sex, race, and ethnicity • Thrombosis after COVID-19 Disease • Cerebral Venous Sinus Thrombosis (CVST) • Heparin Induced Thrombocytopenia (HIT) • AstraZeneca COVID-19 vaccines: Review of available global data
Benefits and Harms	• Benefits of Janssen COVID-19 vaccine • Harms of Janssen COVID-19 vaccine: Estimated cases of TTS after Janssen COVID-19 vaccine • Benefit/Risk Assessment of COVID-19 vaccines?
Values and Acceptability	• Intent to receive 1-dose COVID-19 vaccine and how that has evolved over time
Feasibility	• Jurisdictional use of Janssen COVID-19 vaccine and the possible impact of Janssen COVID-19 vaccine policy options based on recent rapid surveys of jurisdictions on vaccine policy options
Equity	• Possible impact of Janssen COVID-19 vaccine policy options in disproportionately affected populations
Resource Use	• No data available to inform these discussions

In terms of describing the public health problem and the trend in the number of COVID-19 cases in the US, through April 17th there have been around 31 million cases. There has been a rapid decline in cases since the winter, with a stable to slight increase in recent weeks. In addition, there have been over 560,000 deaths throughout this pandemic[33]. To illustrate the variability in the most recent 7-day case rates per 100,000, Dr. Oliver shared examples of the epidemiologic curves from Michigan where the incidence is currently high and rising and California where there is a lower stable incidence. This highlights that in a country as large as the US, the epidemiology of COVID is not the same everywhere. Given that the pandemic is dynamic, states can experience highs and lows at different times[34]. In terms of SARS-CoV-2 variants circulating in the US, the proportion of cases from variants of concern or variants of interest has increased. In recent weeks, nearly half of the cases (45%) are the B.1.1.7 variant[35]. It is important to acknowledge that what is happening with COVID in the US is only a portion of the picture as well. Recent global incidence rates are also important[36].

[33] https://covid.cdc.gov/covid-data-tracker/#trends_dailytrendscases

[34] https://covid.cdc.gov/covid-data-tracker/#cases_casesper100klast7days

[35] https://covid.cdc.gov/covid-data-tracker/#variant-proportions

[36] https://covid.cdc.gov/covid-data-tracker/#global-counts-rates

The recent COVID-19 epidemiology will be the most informative for policy decisions made now and moving forward. Focusing on the epidemiology since March 1st, the incidence by age and by sex, the highest incidence for new cases recently is among female 18 to 29 years of age. Among adults less than 50 years of age, females have a slightly higher incidence compared to males. This is reversed in older populations. Older adults have much higher rates of hospitalizations, with older males at the highest rates. Older males have the highest mortality rates, and all younger adults have a lower mortality rate. Disparities in incidence and mortality are noted by race and ethnicity[37].

To summarize the COVID epidemiology data since March 1st, the cumulative rate for incidence is just over 700 per 100,000 population, where younger females have the highest incidence of new infections. For hospitalization, the cumulative rate since March 1st is 20 per 100,000. Most hospitalization still occur in persons 65 years of age and older, but it is worth noting that the proportion of hospitalizations occurring in this population is declining. For mortality, the cumulative rate since March 1st is 3 per 100,000. Most COVID deaths are occurring in older populations, but the proportion occurring in this population is declining as well.

To briefly cover the epidemiology of several other relevant conditions, the overall incidence of CVST is around 14 to 28 per million. There is a wide range and many of the differences in incidence they heard from last week and across presentations this week is accounted for by the fact that the incidence has been steadily increasing in recent years. It is thought that this could be related to better detection by wider use of more advanced neuroimaging. CVST case rates are higher in young women. In traditional CVSTs, risk factors are identified in most cases. The mortality rate is 5% to 10%. Splanchnic vein thrombosis (SVT) incidence is higher with around 80 to 180 per million, with a higher incidence among men. It is worth noting that the incidence with thrombocytopenia of either of these conditions is much lower than the incidence without thrombocytopenia. Recent estimates for CVST with thrombocytopenia are around 0.7 to 1.6 per million. But again, estimates for this condition are impacted by time and overall increases in CVST[38].

HIT occurs in 0.5% to 1% of patients exposed to heparin. This translates to somewhere around 20 to 45 per million in the US population. Of patients with HIT, thrombosis occurs in 20% to 64%. As described earlier in the day, it is an immune-mediated event with antibodies directed against PF4. There are risk factors for transitioning from HIT to hit with thrombosis (HITT), which includes genetic factors, a lower platelet count, higher titers of PF4 antibodies, and prior surgery[39].

[37] https://covid.cdc.gov/covid-data-tracker/#demographics

[38] Data source: Health Care Utilization Project (HCUP) National Inpatient Sample (NIS) for 2018 and Marketscan Treatment Pathways (Continuously-enrolled Commercial Insurance and Medicaid) for 2019; Otite et al. Neurology 2020; 95: e2200-e2213. 2020; Silvis et al. Nat Rev Neurol 13, 555–565 (2017). Silvis et al. Semin Thromb Hemost 2016;42:622–631.

[39] Source: HCUP NIS 2018 and Marketscan (Continuously-enrolled Commercial Insurance and Medicaid) for 2019, unable to distinguish autoimmune HIT vs heparin-induced HIT Arepally et al. 2021; https://www.ahajournals.org/doi/epub/10.1161/ATVBAHA.120.315445; Nand et al. 1998 https://doi.org/10.1002/(SICI)1096-8652(199709)56:1<12::AIDAJH3>3.0.CO;2-5; Fabris et al 2002. https://onlinelibrary.wiley.com/doi/epdf/10.1046/j.1365-2796.2002.01021.x ; Greinacher et al. 2005. https://www.thiemeconnect.com/products/ejournals/abstract/10.1160/TH04-12-0825

CVST can occur after COVID-19, although it is very rare and in less than 0.1% of hospitalized COVID patients. Translating this to overall numbers, it could be estimated to be around 5 to 6 cases of CVST per million SARS-CoV-2 infections[40]. CVST plus thrombocytopenia in COVID patients appears to be extremely rare. Clots with COVID appear to be pathologically different than TTS after COVID vaccines. There was a preprint study that looked at PF4 antibodies in a history of patients with confirmed COVID. Overall, 90% of those were negative for PF4 antibodies and all were negative on functional assays. This included patients who had thromboembolic events with their COVID infection[41].

There was one study mentioned earlier in the day that looked at EHRs to look at CVST and portal vein thrombosis (PVT) in COVID patients[42]. They showed a low incidence of CVST in any 2-week period, but 2 weeks after COVID estimated an incidence of 39 per million hospitalized COVID patients. Cases of CVST were rarely seen after receipt of mRNA vaccines in this administrative data. However, there are limitations to interpretations of this administrative data. They were unable to assess the incidence of CVST after either the Janssen or AZ adenovirus vector vaccine and did not provide rates of CVST + thrombocytopenia. This limits the direct ability to compare rates of CVST + thrombocytopenia seen after COVID vaccines in the US or Europe.

Briefly walking through what is known about thrombosis with thrombocytopenia after the AZ vaccine in Europe, around 160 cases of CVST and 53 cases SVT were reported through early April 2021 in Europe. The EU estimates this to be around 10 cases per million but acknowledges a higher incidence in younger adults. Their cases were mostly in women less than 60 years of age and occurred within 2 weeks of receiving the first AZ vaccine dose. The EMA concluded that the benefit-risk was still favorable to use the vaccine and that a causal association was likely. No specific risk factors have been identified to date, but they acknowledge that the epidemiology may be related to vaccine delivery across Europe. They also added a warning for unusual blood clots and low platelets to the label as a side effect[43].

The UK recently provided updated numbers through mid-April with 168 reports of blood clots with low platelets and 72 cases of CVST. The male-female split (93 women, 75 men, aged 18–93 years) is slightly more even with a broader age range as was discussed in the first presentation of the day. They note a rate of 7.9 per million doses. The UK has also decided that the benefits continue to outweigh the risks. The Joint Committee on Vaccination and Immunisation (JCVI), the UK's version of ACIP, recommended that persons between 18-29 years of age at low risk of infection be offered other vaccines[44].

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[40] Data source: Premier Healthcare Database, January 2020-January 2021

[41] Katsanos et al. (2020) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7753413/ ; Baldini et al. (2021) https://doi.org/10.1111/ene.14727; Mowla et al. (2020) https://doi.org/10.1016/j.jns.2020.117183; Greinacher et al. Research Square preprint (Apr 9, 2021): https://www.researchsquare.com/article/rs-404769/v1

[42] Taquet et al. Open Science preprint (April 15 2021): https://osf.io/a9jdq/

[43] https://www.who.int/news/item/16-04-2021-global-advisory-committee-on-vaccine-safety-(gacvs)-review-of-latest-evidence-of-rare-adverse-blood-coagulation-events-withastrazeneca-covid-19-vaccine-(vaxzevria-and-covishield); https://www.ema.europa.eu/en/news/astrazenecas-covid-19-vaccine-ema-finds-possible-link-very-rare-cases-unusual-blood-clots-low-blood; https://www.ema.europa.eu/en/documents/prac-recommendation/signal-assessment-report-embolic-thrombotic-events-smq-covid-19-vaccine-chadox1-s-recombinant_en.pdf

[44] https://www.gov.uk/government/publications/coronavirus-covid-19-vaccine-adverse-reactions/coronavirus-vaccine-summary-of yellow-card-reporting
https://www.gov.uk/government/news/mhra-issues-new-advice-concluding-a-possible-link-between-covid-19-vaccine-astrazeneca-and-extremely-rare-unlikely-to-occur-blood-clots
https://www.gov.uk/government/publications/use-of-the-astrazeneca-covid-19-vaccine-jcvi-statement/jcvi-statement-on-use-of-the-astrazeneca-covid-19-vaccine-7-april-2021

The Pharmacovigilance Risk Assessment Committee (PRAC), EMA's safety committee, also met to review 8 of the cases of TTS after the Janssen vaccine incidents were reported in the US. They felt that the cases were very similar to cases occurring after the AZ vaccine. Similar to AZ, they concluded that a warning should be added to the product label. However, they also emphasized that it is a rare event, the benefits outweigh the risks, and emphasized the importance of HCP awareness[45].

Moving to benefits and harms, the Phase 3 trial of the Janssen vaccine demonstrated efficacy against symptomatic laboratory-confirmed cases of COVID, with an overall estimate of 66.3%. Efficacy against hospitalization was 93% and higher efficacy against severe outcomes was noted. Efficacy against severe disease remains high in various world regions, suggesting protection against severe disease with variant strains. Similar efficacy is shown across age, sex, race, and ethnicity categories and those with underlying medical conditions at ≥14 days post-vaccination. There also are benefits beyond efficacy. This vaccine is able to be shipped and stored at refrigerator temperatures and is a single-dose series, which may make it easier to reach some disproportionately affected groups. Dr. Shimabukuro described possible harms of the Janssen vaccine in detail, so Dr. Oliver did not go through it all again but instead highlighted the findings. Nearly 8 million vaccines doses have been administered[46], with 15 confirmed cases of TTS, a rate of 7 per million in women 18-49 years of age, almost 1 per million in women 50 years of age and older, and none in men noted in post-authorization surveillance. However, 1 case occurred in a man in the clinical trial.

Dr. Oliver reviewed the formal risk-benefit analysis, which she showed from two different perspectives. As ACIP thinks through these policy decisions, they will need to think through the population level risk-benefit and an individual level risk-benefit. Therefore, she presented results from two different analyses that looked at each of these perspectives. First for the population level, the WG quantified COVID infections, hospitalizations, and deaths averted under different assumptions about resuming the Janssen COVID-19 vaccine over a 6-month period, then used those data to quantify population level age-specific benefits and harms of resuming vaccination with Janssen COVID vaccine. The individual level risk-benefit analysis was a more direct patient level evaluation looking at a 1-month period to quantify the direct age- and sex-specific benefits and harms per million Janssen vaccine doses.

First for the population level, the objective of the modeling was to quantify COVID-19 infections, hospitalizations, and deaths under different assumptions about resumption of Janssen vaccination. In all scenarios, continued use of mRNA vaccines was assumed. The following scenarios were evaluated:

- ❑ Jansen vaccination was not resumed
- ❑ Janssen vaccination was resumed starting April 24, 2021 for all adults 18 years of age and older, which was modeled at 50% and then 100% of the pre-pause J&J administration rate in the 18+ age group
- ❑ Janssen vaccine resumed starting April 24, 2021 in adults 50+ years of age only, and modeled at a 50% pre-pause administration rate and then a 100% percent pre-pause administration rates

[45] https://www.ema.europa.eu/en/news/covid-19-vaccine-janssen-ema-finds-possible-link-very-rare-cases-unusual-blood-clots-low-blood

[46] https://covid.cdc.gov/covid-data-tracker/#vaccinations

CDC's modeling team developed a compartmental model used to simulate incident infections, hospitalizations, and deaths over the course of the epidemic in the US. This is an updated version of the model that was previously shared with ACIP and is stratified by age, essential worker status, and underlying conditions. The model was recalibrated with incidence data through Spring of 2021 to be consistent with the Ensemble from Round 4 of the Multiple Model Scenario Hub. Age group-specific vaccination coverage was modeled through April 2021, accounting for age group-specific vaccine hesitancy when calibrating anticipated coverage. Two types of vaccines were modeled, mRNA and the Janssen vaccine, with VE estimates informed by the clinical trials and assumed to develop 14 days after administration. The model assumed no loss to follow-up or delays in administration with the mRNA second doses and no waning immunity over the future 6-month time horizon.

Looking at time to complete vaccination for all intending adults, during and after the vaccine pause, administration of mRNA vaccines continues at the same rate as the week before the pause began until demand is fully met. If use of the Jansen vaccine is not resumed for any ages, then it takes approximately 14 days longer to meet all vaccine demand. However, in practice, the pace of administration may slow as those experiencing barriers to access and/or greater hesitancy may comprise a greater share of those unvaccinated. This model was calibrated to be consistent with the Ensemble from Round 4 of the Multiple Model Scenario Hub.

Both a low transmission scenario with a higher and longer sustained compliance with non-pharmaceutical interventions and a moderate transmission scenario with non-pharmaceutical interventions easing more quickly over time were modeled. The results of varying the resumption strategy may be influenced by the population vaccinated and administration rates under the moderate transmission scenario. There is a lower percent reduction in infections, hospitalizations, and deaths when limiting Janssen vaccines to persons 50 years of age and older. Additionally, there is a difference in model results depending on the administration rate, with the 100% administration rate resulting in greater reductions than in the 50% administration rate. Under a low transmission scenario, there is a slightly lower percent reduction. There is a benefit of resuming Janssen vaccination in terms of infections, hospitalizations, and deaths prevented under different epidemiologic assumptions compared to a scenario in which administration of the J&J vaccine does not resume.

The outputs from this model were used in the population risk benefit calculations to quantify the age-specific risks and benefits of resuming vaccinations with Janssen COVID-19 vaccines, including the risks of TTS, and the benefits including prevention of COVID-19 related hospitalizations, deaths, and ICU admissions. Estimates used from the compartmental model included numbers of hospitalizations and deaths due to COVID-19, number of persons estimated to receive the Janssen vaccine after the pause, and a variety of conditions (e.g., low and moderate transmission, 50% and 100% of prior vaccination rate, resuming in ages 18+ and 50+, versus no resumption). The estimates were modeled for a 6-month time horizon. Additionally, data were used from the CDC Pandemic Planning Scenarios on age-specific proportions of hospitalized cases admitted to the ICU, CDC counts of the observed TTS by age, and CDC data on the numbers already vaccinated with the Janssen COVID-19 vaccine before the pause.

In the scenario where vaccination is resumed in persons 18 years of age and older using the conditions of moderate transmission and vaccination with the Janssen vaccine at 50% administration right before the pause, 2 TTS cases would be expected among 50–64-year-olds and 24 cases would be expected among 18-49 years. Overall, if vaccination with Janssen COVID-19 vaccine were resumed in all adults, this model predicts that 26 cases of TTS would

occur among the 9.8 million persons vaccinated, about 1400 deaths would be prevented, and about 2200 ICU admissions would be prevented. In the scenario of resuming vaccination only for persons 50 years of age and over there, 2 cases of TTS are predicted only among 50–64-year-olds. The number of deaths and ICU admissions prevented are predicted to be much smaller than the scenario of resuming vaccinations for all adults, but the benefits still outweigh the smaller risks. The model predicts 2 TTS cases in 3.6 million vaccinations, which would prevent around 250 deaths and 800 ICU admissions.

Summarizing the risks and benefits for all of the scenarios included in the model, the model considered suggesting upper and lower bounds of populations effects for resuming Jansen COVID-19 vaccine. When resuming vaccination among all persons at least 18 years of age, 26 to 45 TTS cases would be expected depending upon vaccine uptake and between 800-2500 fewer admissions and between 600-1400 fewer deaths would be expected compared to not resuming vaccination with the Janssen vaccine. When resuming vaccination among only persons 50 years of age and older, 2 to 3 TTS cases, between 300-1000 fewer ICU admissions, and between 40-250 fewer deaths would be expected. With this approach to assessing the risks and the benefits, the benefits of vaccination apply to the whole population over a 6-month period and result from both direct and indirect effects, while the risks pertain only to the vaccinated persons.

Moving to the individual level benefits and risks, the population model did not inform the direct individual benefits and harm for vaccination of that individual and was not able to look at sex-specific effects. Therefore, a simpler direct estimation approach was used to explore risks and benefits for females and males in different age groups per million Janssen vaccine doses. The calculations were based on recent age-specific incidence of hospitalization for COVID, VE against hospitalization observed in the trials, total Janssen vaccines to date, and the number of persons already vaccinated. Estimations are calculated assuming a 30-day period of not being vaccinated.

For females 18-49 years of age, the model estimates that for every million doses of Janssen COVID-19 vaccine administered, 13 cases of TTS would be expected and 12 deaths, 127 ICU admissions, and 657 hospitalizations due to COVID would be expected to be prevented in one month. The estimations for females 50 years of age and older are that there would be only two cases expected of TTS per million vaccinations doses and prevention of nearly 600 deaths, over 1000 ICU admissions, and nearly 5000 hospitalizations due to COVID-19 would be expected.

In males aged 18-49 years, the 1 TTS case that was observed in the Phase 3 trial was incorporated into this estimate. Per 1 million vaccinations, a small member of TTS cases would be expected and prevention of 11 deaths, over 100 ICU admissions, and about 600 hospitalizations due to COVID would be expected. In males 50 years of age and older, 0 cases of TTS would be expected and around 700 deaths, 1500 ICU admissions, and 5000 hospitalizations due to COVID would be expected to be prevented.

These approaches to the risk-benefit analysis offer complementary information on the risks and benefits of resuming vaccinations and in which age groups. The population approach takes into account both direct and indirect (herd) effects of vaccination; incorporates the availability of different vaccines; simulates incidence, hospitalizations, and deaths over the course of the pandemic; and makes estimates on all outcomes over a 6-month time horizon. This approach shows a large population benefit of vaccination relative to a rare occurrence of TTS. The direct individual level approach estimates the benefits and risks to vaccinated individuals, and only considers getting a Janssen vaccine versus not getting any vaccine over a short 1-month time

horizon. This analysis shows a positive balance of benefits and risk for all ages and sex groups. However, the stratified results suggest that the relative balance and risks for individuals varies by age and sex.

The assessment of values and acceptability focused on intent to receive a 1-dose COVID vaccine, intent to receive a Janssen vaccine over time, and the effect on overall vaccine confidence. Prior to authorization of a Janssen, CDC conducted a survey[47] that asked, "If there was a 2-dose or a 1-dose COVID vaccine available, which one would you choose?" This survey was conducted in February 2021 prior to the pause. Overall results were presented on March 1, 2021 when ACIP voted on the use of the Jansen vaccines. However, these data are now examined by age, sex, race and ethnicity, and income. Overall, most responders said that they would be willing to take either vaccine offered to them. However, 6% of individuals said that they exclusively preferred a 1-dose vaccine. There were no differences in the proportion that preferred a 1-dose vaccine by age, sex, or income. However, significantly more Hispanic than White respondents exclusively preferred a 1-dose vaccine.

Several other surveys have been conducted over the past 1 to 2 weeks. At the time of the last survey, only 37% of respondents called the Janssen COVID vaccine safe after the pause was announced[48]. This represents of a drop of about 15% over 2 to 3 days. Another survey found that Americans are less likely to prefer Janssen vaccine[49], with a 13% decline in preference for the vaccine that ranged from 9% to 25% across age and race categories. In recent weeks, the willingness to receive a Janssen vaccine has declined substantially. In an effort to look at overall vaccine confidence, one survey found that the drop in vaccine confidence did not appear to extend to the Pfizer or Moderna vaccines[50] and most (59%) felt that they were safe. A recent poll did not suggest reduction in the intent to be vaccinated[51] and instead found that people were 40% more likely to receive a vaccine compared to one month ago. One survey did find a proportion of those who remain unvaccinated may be less inclined to receive a COVID-19 vaccine after the pause, regardless of the band brand[52].

Moving to feasibility, CDC was able to conduct a rapid survey of each US jurisdiction for the use of the Janssen vaccine and the impact of the Janssen vaccine pause and potential recommendation. Many jurisdictions were using this vaccine in specific populations, including persons experiencing homelessness, homebound populations, and incarcerated individuals. The settings in which jurisdictions were using the Janssen vaccine included mobile vaccination clinics, EDs, and student health centers. Jurisdictions were asked about the potential impact if the Janssen vaccine were only recommended for specific populations. Jurisdictions felt that they may need to reconfigure some of their vaccination sites, update scheduling tools, and may have difficulties serving disproportionately affected populations. Many stated that providers may need to carry multiple vaccines. Health departments also expressed concerns about communicating changes to the public and highlighted the difficulty serving disproportionately affected populations for populations at risk for not returning for a second dose, race and ethnic minorities through mobile vaccination, and in rural or hard-to-reach areas.

[47] Source: Combined Data from IPSOS and NORC, February 2021 (3 waves)
[48] https://today.yougov.com/topics/politics/articles-reports/2021/04/15/johnson-johnson-vaccine-confidence
[49] CVS Health Survey- COVID-19 Vaccine Brand Preferences and Hesitancy Post J&J Pause
[50] https://today.yougov.com/topics/politics/articles-reports/2021/04/15/johnson-johnson-vaccine-confidence
[51] deBeaumont Foundation Poll, April 15-16, 2021. Vaccine Confidence Grows Despite J&J Pause
[52] CVS Health Survey- COVID-19 Vaccine Brand Preferences and Hesitancy Post J&J Pause

In terms of jurisdictional thoughts on impact if the Janssen vaccine was no longer recommended, jurisdictions were primarily concerned around second dose management if only 2-dose vaccines were available and equity concerns. Janssen vaccines provided flexibility for jurisdictions to avoid second dose management, run mobile clinics, and fully vaccinate people who may need to complete a series quickly. Jurisdictions noted that some individuals expressed a preference for a Janssen vaccine and increasing challenges to reach homebound, transient, or rural populations.

Equity was assessed in this same jurisdictional survey. Jurisdictions raised concerns that the revised recommendations would disproportionately affect several populations. Jurisdictions continue to mention 4 populations at risk of disproportionate impact, including persons experiencing homelessness, homebound populations, incarcerated individuals, and migrant or season seasonal populations. It was felt that if the Janssen vaccine were no longer available, these populations may be disproportionately impacted. Dr. Oliver shared quotes from 2 jurisdictions to illustrate the concerns and disparities:

> **Region 2 Jurisdiction: "**The hardest to reach transient populations such as the homeless and those moving through substance use treatment programs, mental health treatment programs, etc. would be most impacted, given that they are among the most difficult individuals with whom to connect to provide second dose vaccination."
>
> **Region 10 Jurisdiction:** "…not having this vaccine would have an impact on trying to reduce the gap in vaccine disparities. We have community partners lined up to host events using the Janssen vaccine that are working with vulnerable populations in the state."

As noted during the ACIP meeting the previous week, there is a spectrum of policy options for the Janssen COVID-19 vaccine. ACIP could decide that the risks outweigh the benefits and vote to not recommend use of the Janssen vaccine due to these safety concerns. ACIP could decide that the benefits outweigh the risks overall and recommend use of the vaccine in all adults 18 years of age and older. There also is an option in the middle of the spectrum to recommend use of the Janssen vaccine in some populations. The 4 policy options discussed by the WG included the following:

- ❑ Recommend against use for all per person
- ❑ Reaffirm recommendations for all ages and sexes in the context of the FDA warning statement within the EUA
- ❑ Recommend vaccination for only adults 50 years of age and older
- ❑ Reaffirm the recommendation for use, but women less than 50 years of age should be aware of the increased risk of TTS, and may choose another COVID-19 vaccine, such as the mRNA vaccines

The following table highlights some of the pros and cons for each of these 4 options that were discussed by the WG:

Policy Option	Pros	Cons
Recommend **against use** in all persons	• No further cases of CVST/TTS after Janssen vaccine	• Would remove choice from individuals • Could lead to excess COVID-19 cases & deaths • Could disproportionately impact at-risk populations with barriers to access or difficulty returning for 2nd dose
Reaffirm recommendation for **all** ages/sex: *Setting of FDA warning	• Allows for flexibility/choice • Allows for use of the vaccine in harder to reach populations	• Burden on individual to understand risk; health department/providers to convey risk • May lead to more cases of TTS • At-risk populations for COVID-19 likely at risk for barriers to TTS identification and treatment
Recommend vaccination only for **adults ≥50 years** of age	• Would remove vaccine from most at-risk population (reduce TTS cases) • Clear to communicate	• Difficult to implement (vaccination sites could need stock two vaccines) • Would remove an option in a population with lower risk (young men) • Could disproportionately impact at-risk populations
Reaffirm recommendations for use; women <50 should **be aware of** increased risk, and **may choose** another COVID-19 vaccine	• Allow for flexibility/choice • Allow for use of the vaccine in harder-to-reach populations, while still acknowledging risk in young women	• Could be difficult to implement (vaccination sites could need stock two vaccines) • Could be difficult to communicate

To quickly summarize the WG's discussions the previous day, there was concern by many that a detailed personal level discussion of the risk-benefit balance is difficult in many current vaccination settings, such as mass vaccination clinics. Recommendations that may require vaccination sites to require two types of vaccines is difficult to implement. Access to vaccines for hard-to-reach populations remains important. The risk-benefit balance may change as the pandemic evolves and the risk of COVID-19 changes. The WG discussed the benefits and concerns with all policy options for the Janssen COVID-19 vaccine. There was no single policy option as a clear choice by the WG. However, many on the WG appreciated the flexibility of a broader recommendations for use, with the acknowledgement of the elevated risk in women less than 50 years of age. The question posed for the full ACIP to discuss was, "Given the review of the benefits and risks, what recommendation does ACIP feel is appropriate for use of the Janssen COVID-19 vaccine?"

Discussion Points

Dr. Bernstein requested further information with regard to the 4th option how women less than 50 years of age would become aware of the increased risk of TTS. He reminded everyone about the concern he expressed the previous week about adding a warning to the EUA Fact Sheet that is already 6 to 8 pages long in that such a warning might be overlooked or missed. He wondered what was being proposed to convey that important information.

Dr. Cohn indicated that CDC is awaiting ACIP's recommendation but will prepare tools to inform providers and women about the risks, signs, symptoms if this is the direction ACIP goes. This will be done through high-level infographics and other means by which to convey this information in a much simpler way than will be communicated in the very comprehensive and complete Patient FAQ form in the EUA.

Dr. Sanchez said he understand the complexity and that having a permissive acceptance of the vaccine would be shared decision-making as they have been doing for other vaccines. He was very interested in whether Janssen has information about the acceptance of the vaccine after all of these cases have been reported in media and the literature, which he saw from the presentation was down to 19%. His concern is that currently, few places have options for different vaccines. If a location has only the Janssen vaccine available and that 19% is true, many people may choose not to be vaccinated. While he understood the rationale for comparing this vaccine to an unvaccinated population and the risk-benefit for that, the US has other vaccines that to date do not appear to have cases of TTS. He remains concerned. He understands the shared decision-making and having that option for individuals, but he is concerned that the 19% might go down even further when people are informed of the risk. If any of the 4 options is recommended, it will be important to have vaccine choices available in different jurisdictions.

Dr. Long found the modeling at the population level to be quite compelling and wondered whether it was all based on the assumption that it would take 14 days longer to immunize the population than if this vaccine was available for all. Similarly, as Dr. Sanchez asked, she asked whether the decision to compare individual direct benefits of the vaccine versus none was to understand what would happen if an individual refused other vaccines. She also asked why consideration was not given to administering the Janssen vaccine only to males.

Dr. Oliver clarified that the population model included the current and projected supply of mRNA vaccines over the next 6 months. The population level was the situation as it is in the US. The individual patient level model tried to take into account the thought that there might be a time period weighing the risks and benefits if an individual is unable to get access to another vaccine in a short period of time. The reason the time horizon was short was because it was assumed that the delay would be low. The 2- to 4-week time period was an output from the first model, assuming the current situation in the US. The time delay was an output not an input of the model. In terms of the potential for recommending the Janssen vaccine only to males, the scenarios selected for the modelers was based on the initial discussions from the WG the previous week. Jurisdictions felt that age-based recommendations potentially could be communicated and discussed but having a sex-based recommendation would be incredibly difficult to communicate and implement.

Dr. Cohn added that it was not so much about someone declaring their gender as much as it was about where different groups of people access vaccines and the places that would have to carry multiple types of vaccines. The WG recognized that same challenges with the age restrictions as with the gender restriction. Over the course of the week, there have been reports of male cases. Some of those may have been ruled out, but the risk among males is still not completely clear. The risk among males appears to be low, but there is still likely some risk.

Ms. Bahta reported that one of the things she has been hearing since the pause started from several Black, indigenous, and people of color (BIPOC) communities is that they perceive the Janssen vaccine to be targeted to them. They already were concerned about the efficacy and are now also concerned that that this could be subpar vaccine in terms of safety. That needs to be thoughtfully considered. She recalled that there was information about race the previous week and wondered if there was any addition information on the impact of the pause on race and ethnicity. In addition, she wondered what the feasibility would be of vaccinators being able to carry two vaccine products and whether the flexibility to choose could be accommodated based on supply. In the context of a very rare risk, a high benefit, and the need to make all

vaccine available to everyone—flexibility is key and she would look for that decision with the 4th consideration.

Dr. Oliver responded that she was not aware of specific model outputs from risks and benefits that they were able to obtain from the population level at a race and ethnicity level. Many of those concerns came out in the jurisdictional surveys and communicate many of the concerns raised by Ms. Bahta.

Dr. Slayton added that the models looked at persons within an age group and do not distinguish between different races and ethnicities, what their contact patterns look like, or their risks for severe outcomes.

In terms of the flexibility to stock two vaccine products, Dr. Cohn indicated that vaccine distribution numbers at the national level would continue to be the same. Decisions would be local about which vaccines go to different sites.

Dr. Romero added that this would be an implementation issue that would be dealt with at a statewide level in his state, and states would have to adjust to that. He believes that Arkansas could accommodate a recommendation of that nature. He called upon ASTHO for additional thoughts.

Dr. Shah (ASTHO) said that it is feasible to accommodate multiple vaccines and prescribe different recommendations for individuals. However, it does introduce logistics challenges as Dr. Oliver point out in her presentation. One issue is that it requires adjudication and decision. At a time when trying to vaccinate as many people as possible in any given period of hours, it might slow things down. Even a couple of percentage points could have an impact. Second, he has heard from pharmacists across states that carrying multiple vaccines introduces the possibility of errors occurring, small though it may be.

Dr. Poehling emphasized that in the midst of an ongoing pandemic, the benefits are far greater at the population level than potential cases of TTS. She appreciated the many hard-to-reach populations and the very important point that Ms. Bahta made about ensuring that communication about the vaccine does not make it appear to be targeted to any one group. She found the individual assessment to provides a very important component. The benefits clearly outweigh the risk though there are differences in age groups, particularly for women less than 50 years of age. For all of those reasons, she was leaning toward the 4th policy option.

Dr. Frey stressed that a lot of time has been spent on the question regarding what to do about these very rare events with CVST and thrombocytopenia. She asked what would trigger ACIP revisiting this question.

Dr. Oliver responded that the plan is to revisit all of the recommendations. Everything was voted on under the EUA. With the transition to Biologics License Application (BLA), it will be possible to reassess larger amounts of data in the pandemic setting. Regarding a specific safety signal or issue, she would say that they would do the exact same thing as this time—very closely monitor. VaST and the ACIP COVID-19 Vaccine WG both meet weekly, so concerns would go through those channels and to ACIP as soon as possible. Hopefully, they will not have to do this again.

Dr. Romero pointed out that it is not uncommon for the ACIP to modify its recommendations. That has been done before as with the inactivated polio vaccine (IPV) and oral polio vaccine (OPV) use recommendations that were undertaken for pediatric that were completely modified over time as the benefit ratio for IPV became higher and higher.

Dr. Kotton emphasized that consideration also should be given to the impact on immunocompromised patients. It is estimated that approximately 2% to 4% of the US population is immunocompromised. Numerous trials have shown a markedly decreased level of protection from COVID-19 vaccines. Clinically, many patients are being seen infected well after 2 doses of the mRNA vaccine, many of whom have severe disease. With ongoing viral replication, there is great concern that the risk of producing novel variants is significant. Variants may be more pathogenic, more transmissible, and/or may be resistant to vaccine-produced immunity. This could impact the entire community and the ability to defeat this pandemic. In her field, there is a lot of interest in providing either booster doses or alternative vaccine administration. She has heard that this is being done, or at least is being considered, in other countries such as France and Israel. Until everyone in the US who wants a vaccine has gotten their vaccine, a pause has been placed on the ability to give additional doses of vaccine for this vulnerable population. In order to best protect this population and the general population, consideration should be given to the impact of moving forward on vaccination as rapidly as possible in order to reach the point of providing additional vaccines for this vulnerable immunocompromised population.

Dr. Talbot said her major concern in talking about risk is that people are confusing the risk of this AE to the risks of oral contraceptive pills (OCP). The risk is not the same because it is not necessarily the same type of clots or treatment. When women present to the ED with a clot, all of the protocols in all hospitals nationwide are to start heparin. That will put these patients at increased risk, even though they are not at the same risk and should not be compared to OCP. There are not individual risk factors. There are age and sex. When they talk about this, gender and age need to be discussed. She did not think they could ignore the fact that the majority of cases have occurred in women. Women often present to EDs with vague symptoms like headache or nausea/vomiting, are not taken seriously, and are sent home. This must be considered in terms of risk. In terms of those who are homebound, a recent nursing home outbreak illustrates how incredibly important it is to vaccinate those *around* the immunocompromised and those who are homebound. Everyone is worried that if there is not a one-dose vaccine to take into the home, those patients may be left at risk. However, they must educate that the public that if they are in contact with someone who is homebound or immunocompromised, they need to be vaccinated themselves to prevent the risk of transmission. The Indian Health Service (IHS) has managed to keep all 3 vaccines at the same clinics and have done just fine. We are Americans, we have a lot of ingenuity, and we can operationalize having multiple vaccines at one place. She would hate to think this would become an insurmountable obstacle. She has less confidence in the ability to educate the entire medical force and every American about the risk of this with enough detail and understanding such that a person could determine the risk-benefit for themselves.

Dr. Daley suggested that it was possible that they were underestimating the benefits of vaccination. The spread of variants that are more easily transmissible and possibly more severe would increase the likelihood of spread of disease among the unvaccinated. The models that Dr. Oliver presented do not account for longer-term morbidity and mortality from COVID disease. A report earlier in the day from the VA showed that those who had COVID who were not hospitalized had increased risk of mortality in the 6 months following their COVID infection, which he thinks should be factored in. If vaccine sites are able to publicize which vaccines they have available, then the public may be able to choose where to get vaccinated. That is an

alternative to having to have two vaccines on-site. With all of those considerations in mind, he favored the 4th recommendation.

Ms. McNally indicated that she favored Option 4 at this point. She agreed that there are important benefits to the Janssen vaccine and also thinks it is very important that people have the right to choose. She is concerned that there is very rare risk and they would be warning for those people who may have this outcome. Looking at the *Emergency Use Authorization of Medical Products and Related Authorities: Guidance for Industry and Other Stakeholders* document dated 2017[53], she noted that there is a section that talks about information for recipients and the importance for people to receive a fact sheet. She was trying to balance that against ACIP's Charter and Description of Duties[54] wherein it indicates that, "For each vaccine, the committee advises on population groups and/or circumstances in which a vaccine or related agent is recommended. The committee also provides recommendations on contraindications and precautions for use of the vaccine and related agents and provides information on recognized adverse events." She thought Option 4 accomplished that need for ACIP and balances the role of FDA and the role of CDC.

Dr. Cohn acknowledged that individuals who sign up online for vaccination in many places, including vaccinefinder.org, can put in the vaccine they want. They can ensure that at least on government websites, the information about this risk is clearly delineated. That does not account for individuals who do not have that technology, but there is an ability to identify which vaccine a person would like to choose.

Dr. Romero emphasized that this is a very rare event. Taken in the context of all other issues that have been discussed, other factors that were weighing in his decision were the issues of other risk factors that are yet to be well-understood such as neuropsychiatric problems associated with infection, long-hauler syndrome, et cetera. Limiting the vaccine to a greater population certainly would have impact on that. The issue of individuals returning for a second dose is also important to him. A recent *Morbidity and Mortality Weekly Report* (*MMWR*) look at doses given between the start of the immunization drive into the middle of January 2021 showed that 3.4% of the population surveyed did not return during the window. Data from his state as of April 22nd showed that 11.1% had not returned during the window for their second dose. Clearly, removing a vaccine that can be given as a single dose and that is a preference among Latino communities would be a detriment. These elements weigh heavily on his decision in leaning toward Option 4.

Dr. Duchin (NACCHO) thought that based on the model, it was clear at the population and individual health levels that the benefits of this vaccine justify the risks. This is an incredibly important vaccine that is needed in the armamentarium as Dr. Romero just described. He noted that the risk-benefit calculation is based on the current US exposure risk. Over time with these effective vaccines, he believes the risk will recede. He wondered what type of additional information they could get that would help better understand at what level of disease and at what incidence level this risk-benefit equation will change significantly to help guide future use of the product.

[53] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/emergency-use-authorization-medical-products-and-related-authorities

[54] https://www.cdc.gov/vaccines/acip/committee/charter.html

Dr. Slayton indicated that these models have been used in previous CDC decision-making and have been updated as additional data become available. This is also why 2 scenarios were included, low and moderate, in the population level model. That is a process that they are happy to continue to provide to ACIP as more is learned about the future incidence.

Dr. Gluckman (AHIP) called attention to Slide 51 in Dr. Oliver's presentation as he thought it put an excellent perspective on the risk of TTS versus the potential benefits. While it is important to make people aware of the risk of TTS, it is essential that people are also provided with the overwhelming benefit. For every case of TTS that occurs, there are still 12 deaths prevented, 127 ICU admissions prevented, 657 hospitalizations prevented, and potential risk for long-term sequelae of COVID. He is concerned that without a stronger statement from ACIP, a decision could contribute to vaccine hesitancy and that any contribution to vaccine hesitancy is far more likely to cause real harm to people. While information is important, ACIP should make a very strong and unequivocal statement about the overwhelming benefits and recognize that there are some issues regarding feasibility in certain populations. Of course, people should have a choice when that opportunity is available. The overwhelming risk-benefit analysis is "get the vaccine you can get."

Dr. Shah (ASTHO) pointed out that Dr. Oliver gave a clinic on the optimum way to analyze and communicate about a difficult public health policy question and he commended her for her outstanding clarity of thought and communication. He noted that there were some strands between the differences between Options 2 and 4. Both options provide flexibility of choice and allow receipt of this vaccine among hard-to-reach populations. It is important to note that both options would entail an official recommendation being appended to the EUA as their colleagues from Janssen noted. He posited that there is not much difference between Options 2 and 4 and that it may come down to their understanding collectively of the language of "may choose," so long as they understand that "may choose" is at the population level and might entail someone choosing which vaccine when making an appointment. At the practical level, most sites will not be able to offer more than one vaccine. He was not aware of a single vaccination site in Maine that simultaneously is running 2 vaccines at once. When they adjust for that understanding, he did not think there was much of a difference between Options 2 and 4. The choice, which he believed in retaining, would come at the time someone decides to seek a vaccine rather than at the point-of-care (POC). The option of choice already exists and is baked into Option 2 as well.

Dr. Oliver reiterated that absolutely all of the recommendations are in the context of FDA's warning statement. She agreed that in many instances, it will be up to the jurisdictions exactly how "may choose" another vaccine gets implemented. Very likely in many instances, it will be an individual person signing up for which vaccine appointment they are going to take. This reinforces the importance of clear public communication. Her interpretation from the WG's discussion was that Option 4 is ACIP reinforcing the risk in this specific population, but that in many situations the benefit may outweigh that risk.

Dr. Bell added that the issue is that the WG thinks it is important to reflect both truths—both the fact that benefit-risk is in favor of a large benefit, but also that there is a very small risk of a serious adverse event (SAE), which people should be aware of. That is a little bit different from Option 2, which would not reflect in the same way the ACIP's recognition of both and the opportunity for people to make an informed choice. In terms of her own perspective on where she comes down in terms of how to approach this situation, she thinks it is very important to recognize that this is a recommendation and policy for now and for the current situation in which COVID-19 is not at bay. This is a time when options and flexibility are needed and that is very much part of her thinking. The second point that the benefits do clearly outweigh the risks from

the population and individual perspectives. It is reassuring to her that while they do not have all of the information, they do have enough information to move forward. At the same time, there is a real risk. However, it is admittedly an extremely small risk that is less than many other risks people choose to take every day. Nonetheless, there are alternatives in the US. For that reason, she personally prefers wording that explicitly reflects the ACIP's recognition of both the risks and benefits. It is somewhat of a paradox that there has been a lot of discussion about vaccine hesitance and what to do about that, but her own feeling is that that is just an unknown. It is a paradox that by recognizing, detecting, and acting on a very rare risk that should inspire vaccine confidence, perhaps it has the opposite effect. In any case, going forward she thinks that the success of this policy recommendation and public confidence rest on education and communication. It is critical that CDC and state and local health department partners step up to take this task at hand and work to help people understand what the choices are.

Dr. Goldman (ACP) said he firmly believes that the "perfect should never be the enemy of the good." The risks and benefits of this vaccine clearly show tremendous disease is being prevented and they need to be cognizant of that fact. To not continue the use of the Janssen vaccine would be detrimental for the overall vaccine program in preventing tremendous amounts of deaths, hospitalizations, and ICU admissions. He pointed out a few concerns from the private practice and primary care perspective. Certainly, it would be presumed that private practitioners could stock 1 vaccine let alone 2. However, what is happening on the ground is that many of them cannot get any vaccines to administer to any of their patients. If they do not even have the option of a single dose vaccine, it will dramatically affect the ability of vaccine distribution to many in private practice and primary care. Many of his patients are expressing a preference for a single dose because they cannot take off from work for 2 visits or they do not have access to care. There is certainly the health equity component that they must be extremely aware of. He also firmly believes in patient choice and thought that Option 2 keeps it as simple as possible to make sure people have that choice and will know what the FDA recommendations are. He stressed that they need to be very careful in the wording used because what this pandemic has shown him is that many jurisdictions will misinterpret guidelines out of convenience. He pointed to the example of when they said that the second dose can be given up to 6 weeks. Many jurisdictions split the difference and just did 4 weeks across the board for both vaccines even though that is not what the recommendation said.

Dr. Fryhofer (AMA) reiterated that speaking as a practicing physician, it has been very difficult for private practices to carry more than one vaccine at one time. She is very concerned about vaccinating homeless, homebound, and incarcerated vulnerable populations. This depends on this one-dose and done vaccine with the easy storage to reach those populations. She is very concerned about the variants and was impressed with the presentation by Janssen about coverage of the B.1.351 variant. She also is concerned that a lot of vulnerable patients and populations would not be able to get a second dose of vaccine and might not return for that. She feels very strongly that the Janssen vaccine needs to be available, and that patients should have a choice. She was encouraged by Dr. Cohn's statement that there is a way to determine locations of particular vaccines, because people really care about which vaccine they are getting. She liked what Dr. Bell said about the 2 truths and the reasoning behind her choice of Option 4. She also shared Dr. Shah's and Dr. Goldman's concern that it is just a little complicated, the wording makes it sound somewhat shady and might be discouraging, and that this might increase vaccine hesitancy. If the reaffirmation for all ages and sexes and the FDA warning is in the EUA, she wondered how that would change CDC's outreach to ensure that practitioners and the public understand the risks and side effects. She stressed how proud she was of all of the hard work, detail, and research that had gone into making sure that the vaccine safety surveillance system is looking after the American public.

Dr. Cohn indicated that for either Option 2 or 4, CDC would develop the same tools, education, and communication products to help women and providers understand the benefits and risks.

Dr. Zahn (NACCHO) pointed out that everyone in public health is anticipating that over time, the mass vaccination events and points of dispensing (PODs) that have been set up will be eliminated. At that point, public health and a lot of community provider assistants anticipate reaching out to communities to reach people where they are. The homeless population is an obvious group that will need outreach. When they are reaching out, Option 2 versus Option 4 would be quite different. Trying to transport 2 vaccines in that scenario would be logistically difficult. More than that, a lot of outreach partners upon which public health is relying have done such great work vaccinating (first responders, volunteer nurses, et cetera) but may not be comfortable talking through the risks and benefits about the issue. This is not simple, but if they add the wrinkle of women under 50 needing to be aware and able to choose, the logistics of outreach can be done but will be complicated.

Dr. Lee observed that clearly at a population level, the benefit-risk balance favors vaccine use. Even in the last 11-day pause, what is striking to her is that there have been deaths and ICU admissions that potentially would have been preventable had they not done the pause. At the same time, the last 11 days have been reassuring to her in that they have not identified hundreds more cases despite enhanced awareness and case finding across the US, which was her worry last week. They now have a lot better information about the risk estimates by age and sex, which could inform their decision-making at hand. In sum, last week she would have made a different decision than what she would advocate for this week. From an access and acceptability standpoint, she thinks that ACIP's role in this instance should be to ensure access to vaccine. Individuals absolutely should be well-informed as they always should be and they should have the ability to make an informed choice and encouraged to talk to their HCP if they wish. Acceptability is not just a Janssen issue. It is a much broader issue so she thinks they cannot do enough to support and ensure that they are always educating patients and the public on all fronts. In terms of implementation, these issues are going to occur throughout. Right now, there is only one vaccine available for those 16-17 year of age. In order to ensure access, they are functionally carrying multiple products. Maybe not on the same day, but many sites are doing this in order to ensure access to 16–17-year-olds because only one product is available in the US that goes down to that age group and there are vulnerable children in that age group. From a communications standpoint, she emphasized a point that was made earlier that this is not just risk communication. It is benefit-risk communication. Similar to what has been done for anaphylaxis and making sure that people have the tools, communication, and screening available at vaccination sites should be done for this as well. Everything they do should incorporate health literacy principles and multiple languages to ensure that they are truly informing everyone who may wish to have the vaccine. From a process perspective, they need to think carefully about the implications of what the recommendations will be. Options 1 and 3 are off of her list. She has been thinking carefully and listening to the arguments for Options 2 and 4 and having spent a lot of time with the EtR Framework, she did not think that Option 4 fell within what they would normally consider as a recommendation per ACIP's usual framework. It really should fall under Option 2 to reaffirm recommendations for all age and sex with the same comment about the FDA warning and all of the information that is in Option 4. At the beginning of the day, she was feeling that she needed all of the additional information in Option 4 to feel comfortable with any recommendation as a way to state the concern about the benefit-risk balance. However, she thinks it is going to be extremely confusing because every recommendation ACIP makes is a benefit-risk balance and they cannot parse out every single benefit and risk in every single recommendation for every single vaccine, COVID or non-COVID. From a procedural standpoint, she thought they needed to incorporate all of the discussion

points that were brought up for Option 4 in the way that they implement, but that the recommendation should be consistent with the EtR Framework.

Dr. Grogg (AOA) noted that he has an immune deficiency and did not respond to the vaccine. He thinks the pause of the Janssen vaccine has caused a lot of vaccine hesitancy and there have been deaths, hospitalizations, admissions to the UCU, long-term sequelae, et cetera over the last week. While he was confused about whether it should be Option 2 or 4, he would like to see everybody vote forward on the Janssen vaccine and heavily inform HCP about insulin and other things and get this done.

Dr. Hayes (ACNM) reported that she has been working in a mass vaccination clinic and reassured everyone that they have carried all 3 vaccines. They have tents set up, the cubicles are numbered, someone in the back room draws up all of the vaccines, and she jabs the arms. It is possible to stock and organize 3 vaccines and allow people to choose which one they want when they walk in the door. She supported Option 2.

Dr. Oliver reminded everyone that the language that was voted on previously states, “The Janssen COVID-19 vaccine is recommended for persons 18 years of age and older in the U.S. population under the FDA’s Emergency Use Authorization.” This is basically Option 2. Option 4 would state, “The Janssen COVID-19 vaccine is recommended for persons 18 years of age and older in the US population under the FDA’s Emergency Use Authorization. Women aged <50 years should be aware of the increased risk of thrombosis with thrombocytopenia syndrome (TTS) and may choose another COVID-19 vaccine authorized for use in the United States.”

Dr. Cohn pointed out that with that language in the recommendation, they would then describe the risks and benefits in the Clinical Considerations sections but have the overall recommendation points to the EUA only. It is essentially Option 2 with the additional language pointing to the FDA EUA. Since they had not heard support for Options 1 or 3, they were projected for further discussion as well.

Dr. Ault did not see a huge difference between Options 2 and 4 depending on the way the warning statement is worded in the EUA.

Dr. Oliver posted the language agreed upon by FDA and Janssen for everyone’s review.

Dr. Eckert (ACOG) said that speaking not as the ACOG representative but about her individual thoughts, her concern was that Option 4 potentially may enhance obstacles to vaccination. Individuals who are pregnant have met frequently with obstacles. Since CDC will and has been doing a great job with information and information sharing, she questioned whether Options 2 and 4 were really all that different. She personally advocated for having the fewest obstacles possible and supported Option 2.

Dr. Weiser (IHS) commented that Indian Health Services arguably serves some of the most remote and hard-to-reach populations in the country. In their jurisdiction, they have been receiving and providing all 3 vaccines. Some of their sites are handling all 3 vaccines: Pfizer just for 16–17-year-olds, Moderna for the majority of the adult population, and Janssen that some people were waiting to receive and chose not to get the others. As part of a health system, they have proven that they can handle all 3 vaccines. Typically when they have a large vaccination campaign or site, they will give mainly 1 vaccine on that day if they are doing a drive-up or large-scale vaccination event. They do have the ability to keep the vaccines straight and make sure that people receive the vaccine they have asked for.

Ms. McNally requested confirmation that the FDA warning and precaution that the "FDA-Agreed Warning and Precaution Regarding Thrombosis with Thrombocytopenia" is what would appear in the EUA Fact Sheet for recipients.

Dr. Waldstreicher responded that this is the Fact Sheet for HCP. The one for recipients is different, but it is very clear and provides information for recipients about the signs and symptoms and to present if they have any of those signs and symptoms. It describes the overall event as well.

Ms. McNally found this to be very relevant to the conversation and wondered if it would be possible to see some of this proposed language. Informed consent is not required for a product authorized under EUA.

Dr. Bell called upon FDA to comment on what will be included in the patient Fact Sheet.
Dr. Fink responded that it would be best if Janssen had the ability to share the language for the Recipient Fact Sheet. Dr. Waldstreicher shared and reviewed the following excerpt:

Excerpt: Fact Sheet for Recipients and Caregivers
Blood clots involving blood vessels in the brain, abdomen, and legs along with low levels of platelets (blood cells that help your body stop bleeding), have occurred in some people who have received the Janssen COVID-19 Vaccine. In people who developed these blood clots and low levels of platelets, symptoms began approximately one to two-weeks following vaccination. Most people who developed these blood clots and low levels of platelets were females ages 18 through 49 years. The chance of having this occur is remote. You should seek medical attention right away if you have any of the following symptoms after receiving Janssen COVID-19 Vaccine: • Shortness of breath, • Chest pain, • Leg swelling, • Persistent abdominal pain, • Severe or persistent headaches or blurred vision, • Easy bruising or tiny blood spots under the skin beyond the site of the injection.

Dr. Long thought they should not talk about this as "very rare" as "rare" is difficult to quantify. In the age group of women of interest, it is 1 in 140,000. Some people would say that is rare, but she would never say that it is "very rare." People perceive and want to take risks at different levels, so they need to be sure that they allow choice. Because it is difficult to do does not mean that they can abrogate their responsibility to protect the public and individuals. She thinks if they had 3 vaccines that were all single dose, all had the same efficacy, and all were available, they would be preferring 2 other vaccines in this age group. She certainly would be preferring that. While she was not suggesting that they say that specifically, they should reaffirm that the vaccine's benefits outweigh the risk. Yes, people should receive any vaccine they can get as soon as they can get it. They have to have a different way to say Option 4. To her, it comes out as a petulant young woman rather than they are experts who recognize this risk, which may be more important to some people or maybe a single injection is more important to that young lady who is choosing between vaccines. But to say "may choose" does not seem to be saying what they recommend. She also was not for just leaving the FDA warning, because the FDA does the licensure and legality part of it and ACIP is supposed to nuance that by all of their deliberations to protect the population and individuals. In terms of the benefits outweighing the risks in that younger age population of women, she did not buy that they would not otherwise be vaccinated. Therefore, she thought they had to do justice to both truths and that they need to have something better than "may choose."

Dr. Sanchez agreed with Dr. Long. One of the women was 59 years of age. He asked whether any consideration had been given to age 60.

Dr. Oliver indicated that the WG tried to look at what is known about the current age distribution. They had to make some assumptions when they started doing this work a couple of days ago, so the work was done with the 50-year-old cutoff. The WG saw more slides and more information than what was presented during this meeting. Some information was presented for 65 and older. Ultimately, the issue is that the population 65 years of age and older that is remaining to be vaccinated is much smaller than the 50–64-year-old population. That definitely impacts the modeling results, but they did not specifically look at a risk-benefit analysis with a line drawn at 60 years of age.

Dr. Sanchez stressed that the range was 18-59 on April 14th. He said he fully understands the benefits of immunization and could not argue with that, but he also understands the risk and it is not insignificant and makes him nervous. There was 1 male during trial, so the risk does not seem to be zero in men. They way that Option 4 is worded makes it sound almost like the choice should only be given to women and to everyone, so he is hesitant about that as well.

Dr. Poehling affirmed that she was thinking along the same lines as Ms. McNally and appreciated her adding clarity to this thought process. She agreed that the exact wording for the public was a very important part of the consideration for her as well.

Molly Howell (AIM) reported that the previous day, AIM surveyed its members who are the 64 awardees implementing the COVID vaccination programs in the US and 81% were supportive of either Option 2 or 4. Aim will work with either.

Dr. Stinchfield (NAPNAP) shared her personal thoughts from the State of Minnesota that is seeing all of the variants in increasing numbers and is currently accepting young adults into its children hospital due to very high census across the state with the disease. What makes her nervous is the climbing incidence of COVID and she has an urgency to move on this with former Option 2, because it is most reflective of the data they saw during the day and the discussions. It is likely to have the least unintended consequences for those who are reading it. In a hospital that has given 20,000 doses so far of 2 products, it is very doable to have 2 different products. For example, they have been very happy to give their J&J vaccines to individuals 18 years of age and older who are young autistic males who are combative and are under an already planned sedative procedure. This has worked out very well. These vaccines can be administered on different days and different sites, so she has no concern about implementation. In terms of vaccine hesitancy, this pause has made people nervous. But because of the excellent work, including Dr. Oliver's Master Class, will help to increase the confidence in the US and across the world. She has a considerable concern about global problems right now with India and Brazil and the urgency in the US and across the world to use all of the tools possible to get the pandemic behind us. Therefore, she feels very comfortable with the original language/Option 2 with the details in the EUA.

Dr. Whitley-Williams (NMA) indicated that NMA's preliminary considerations would be supportive of reaffirming the recommendation for use of this vaccine. It is well-recognized that persons in the Black and Brown community have been disproportionately affected by this pandemic. The benefit of a vaccine that is effective far outweighs the risks, especially in hard-to-reach vulnerable populations. She also concurred with Ms. Stinchfield in terms of the global

impact. She also encouraged continued work to try to get to the bottom of the underlying cause of the TTS, particularly as it relates to age, gender, race, and ethnicity.

Dr. Arthur (BIO) suggested that whatever the decision is, this is an excellent opportunity to recommit to getting all vaccinees to use V-Safe[SM]. This is an extremely important tool for helping people pay attention to their side effects, report them, and gather the really important data on vaccine safety. There have been many reports about people not being told about V-Safe[SM] when they get vaccinated, although some places are doing a great job. This is an opportunity to change the daily information people receive in the text to encourage more citizens to enroll and fill it out.

Dr. Chen said he thought he agreed with what Dr. Shah initially articulated, which is in essence that Options 2 and 4 are not significantly different from each other. As long as they understand that in the implementation, they would not have the formal complicated consent process or the "be aware" statement and that for the ability to choose, they would not make it a requirement for the local point of immunization clinic to be required to store 2 or more vaccines. Option 4 has the potential for misinterpretation by local smaller implementation teams and programs. They heard from some large programs that they have no problem juggling 2 or 3 vaccines simultaneously on any single day. Individual medical practitioners, pharmacists, dentists, and veterinarians are starting to be trained in his State of Maryland to be able to implement these vaccines and he could not imagine that they would be able to juggle multiple products simultaneously. As long as there is an aggressive campaign for educating the public and medical community, he favors Option 2.

Dr. Lett (CSTE) asked for more information about what implementation process is anticipated if the pause is lifted in terms of whether it will be necessary for certain language to be available, materials to be available, screening forms and standing orders to be available, et cetera.

Dr. Cohn replied that if there was a decision in the next half hour, CDC is awaiting and anticipate that the FDA would publish the newly approved EUA language that was shown from the Patient Fact Sheet. At that time, if the CDC Director approves the decision made by ACIP, that would be published on the ACIP website and through other information sharing and people would be allowed to resume use of doses that they have available already. That being said, over the next 72 to 96 hours, there will be a Clinician Outreach and Communication Activity (COCA) call that describes all of this information, and *MMWR* will be published that shares all of this information, and CDC will take the input from the day and the language that FDA will publish and FDA and CDC will complete communication and education materials, including infographics, and patient fact sheets that are smaller and focused just on this issue that will be available early next week.

Ms. McNally asked whether the Janssen patient fact sheet indicates that there is an alternative of mRNA vaccines.

Dr. Waldstreicher indicated that later in the fact sheet there is a statement that reads, "Currently, there is no FDA approved alternative vaccine available for prevention of COVID-19. Other vaccines to prevent COVID-19 may be available under Emergency Use Authorization."

Dr. Cohn added that the CDC education materials will describe all options available as they are able to speak about all of the products as opposed to the EUA, which has to focus on the individual product that it is authorized for.

Dr. Bell requested clarity about how these EUA fact sheets are used.

Dr. Waldstreicher indicated that the EUA fact sheet is given to individuals prior to receiving the vaccine and it also is posted on the Janssen website.

Dr. Cohn added that sometimes this information is received in PDF format with the email confirming an appointment as well, but it should be given at some point between making an appointment and being vaccinated.

Dr. Bernstein said it was incredibly impressive to him how well our nation's vaccine safety surveillance systems work. The Vaccine Adverse Events Reporting System, VAERS, which is not designed to assess causality, identified a safety signal of real concern prompting further investigation. As Drs. Oliver, Bell, and the COVID-19 WG presented, the ACIP closely examines disease epidemiology, vaccine supply, implementation concerns, public values and acceptance, and equity. Its 3 overarching pillars of science, implementation, and equity are important. After the emergency ACIP meeting the previous week, he felt implementation and equity favored reinstituting the J&J vaccine. However, the science was much less clear to him. The brief pause measured in days appropriately continued to allow additional data to be collected and analyzed. The ACIP process works in a timely and transparent way, which should improve the public's understanding of this safety signal. The day's presentations and discussions convinced him that lifting the pause on J&J's vaccine is in the best public health interest of the US population. Any vaccine may have side effects. In this case, the risk of blood clots and low platelets, even resulting in fatality in some, has now been extensively studied and will continue to be monitored. Plus, patient education and provider recognition are expected to help improve outcomes. Important information also will now be conveyed in the FDA's EUA Fact Sheet, the CDC's materials, and through local public health officials. The 3 COVID-19 vaccines currently authorized in the US are amazingly safe and effective. In his mind, their benefits far outweigh identified or perceived risks. As many people as possible need to be vaccinated in order to reach community immunity and put the pandemic behind us. The J&J vaccine will help to do just that, so he preferred Option 2 and he thought that nuanced language could be included in the Clinical Considerations that often accompany these recommendations.

Dr. Poehling expressed concern that headache, which is one of the most common symptoms of thrombosis and thrombocytopenia, seemed buried in one of the bullets. She expressed her hope that on the CDC website, that symptom could be elevated.

Dr. Cohn indicated that CDC would take this into account when developing the materials. Regarding a comment that Dr. Talbot made earlier regarding the ED and understanding the risk of blood clots, especially in this age group of women, one of the key things that CDC has been and will continue to communicate in its provider education is that one of the first things providers should do is check the platelet count and that should inform treatment and management. CDC is grateful to its colleagues at ASH and other colleagues who have supported information regarding clinical management to ensure that this is recognized and treated early and appropriately.

Dr. Romero said that while he supported Option 2, they could see from the discussion that there was some selective interpretation of that recommendation. Women are not going to be offered an option to a second vaccine at sites across the country. That will place certain women at a disadvantage who may decide that the vaccine being offered at a particular site is not the one for them and they will have to shop for a vaccine. While that is an issue, he thought he could live

with Option 2 (now 1) because it does reinstate the Janssen vaccine, which he thinks is essential to the vaccine efforts. At this point, he ended discussion and called for a motion.

Motion/Vote: Janssen COVID-19 Vaccine

Dr. Lee motioned to approve the language stating, "The Janssen COVID-19 vaccine is recommended for persons 18 years of age and older in the US population under the FDA's Emergency Use Authorization." Dr. Ault seconded the motion. Dr. Frey abstained from voting due to her declared conflicts of interest with COVID-19 vaccine clinical trials. The motion carried with 10 affirmative votes, 4 opposed, and 1 abstention. The disposition of the vote was as follows:

10 Favored: Ault, Bahta, Bell, Bernstein, Chen, Daley, Kotton, Lee, Poehling, Romero
4 Opposed: Long, McNally, Sanchez, Talbot
1 Abstained: Frey

Subsequent to the vote, ACIP members were invited to share any additional comments they wished to further explain their votes or in general.

Dr. Bell reiterated a theme, which is the importance of CDC, state and local health departments, and partner organizations providing clear communication and education on this topic. She voted "Yes" and can live with this recommendation, but she thinks that under an EUA where there is no signed informed consent, it could be that ACIP recommendations might need to reflect some more nuanced concerns than under the usual procedure. She is concerned that consumers, particularly women in this age group, will not be adequately informed just by the FDA EUA Fact Sheets. ACIP is depending on the public health agencies and partner organizations to make sure that people actually are informed, are empowered, and that they actually get a balanced perspective.

Dr. Sanchez agreed with Dr. Bell and said that is precisely the reason that he voted "No." He has no problem with the continued availability of this vaccine. He thinks if someone makes an informed consent after having and knowing the risks involved, he is fine for them to get the vaccine. However, he thought that just making a blanket recommendation knowing the risk that seems to have biologic plausibility and severity was not adequate and that there needed to be stronger language to make sure that people are informed appropriately.

Dr. Poehling emphasized that the detection of thrombosis and thrombocytopenia after 6 cases in over 7 million doses administered clearly demonstrates that the safety systems are both sensitive and effective. The COVID-19 pandemic continues to cause significant morbidity and mortality. Not only does COVID-19 disease cause many complications including, but not limited to, increased risk of serious clots, multi-inflammatory syndrome, post-infection neuropsychological syndromes, and long-hauler syndromes, but also this pause has been effective in increasing awareness of the rare and serious events of thrombosis and thrombocytopenia; highlighting the importance of timely diagnosis, evaluation, and treatment; and gathering data needed for a risk-benefit analysis at the population at the population and individual levels. The benefit of reaffirming the Janssen vaccine is high and outweighs the risk. For all these reasons, she believes it is in the best interest of the public to reaffirm the recommendation for this vaccine with the warning added to the FDA EUA.

Dr. Long clarified that she did not object to the recommendation itself but voted "No" because she objected to the absence of any kind of guidance from the ACIP. This is an age group that is most at risk that is getting this vaccine predominantly to save other people's lives and morbidity, not their own. She thinks ACIP has a responsibility to be certain that they know this. If they choose to be vaccinated with vaccine anyway, ACIP wants to respect that choice. However, she was very sorry that they did not choose to put up front the knowledge that they have that this is unique, it is clustered, it is almost certainly related to the vaccine, and there are options.

Dr. Bernstein pointed out that some of the concerns he was hearing likely would be written into the updated Clinical Considerations in the same way they were when there was a concern about anaphylaxis with the Pfizer vaccine. Clinical Considerations are typically published on the CDC website and in the *MMWR* and are readily available to the public.

Dr. Cohn indicated that all of the language pertaining to the risks and benefits and the decision to get vaccinated that were presented in the course of the day's discussion will be included in the *MMWR* and the Clinical Considerations will be updated. If the CDC Director agrees to reaffirm this recommendation, all of this will be published during the day on Tuesday.

Dr. Lee emphasized that she agreed with all of her colleagues that she absolutely thinks this is a serious adverse event and that they need to continue to ensure that awareness is raised. Procedurally, she thought the only choice that they had was to recommend, to not recommend, or to recommend shared clinical decision-making. The emphasis and the vote itself reflect the challenge that was before them today that they need to be able to reflect the importance of this particular adverse event and elevate it. But she also thought they had to come out with a clear recommendation. She thought Option 4 would have been confusing and was actually inconsistent with all of the other priority ACIP recommendations.

Dr. Romero said that he was able to vote for Option 2 (that became 1) because he thought it stated clearly that the Janssen vaccine could and should be reinstituted. He acknowledged, as did everyone else, that these events are rare, but they are serious. At the same time, it places upon those who will make this vaccine available and will be distributing it to inform the public about the risks of the vaccine. This is not something for which they will simply be able to say that they are following the ACIP recommendation. It is the responsibility of clinicians to make sure that women understand this risk and, when possible, that they have an alternative at the same site that is administering the Janssen vaccine.

Dr. Wharton expressed CDC's gratitude to everyone for the time they put into this, their thoughtful discussions, the deliberative process in which they engaged, and for coming to a conclusion on this important matter for CDC. The agency appreciates ACIP's support and help and everything they have done to support the COVID-19 Vaccine Program.

Dr. Cohn emphasized that there have been hundreds of people working within CDC's Immunization Safety Office (ISO) and at the FDA collaboratively on all of this work over the past 2 weeks. She reminded everyone that there is an ACIP meeting scheduled for May 5, 2021 to discuss dengue and rabies vaccines. They also anticipate that if there is a future authorization by the FDA for additional age groups for COVID-19 vaccines that there will be an additional ACIP emergency meeting convened.

Certification

Upon reviewing the foregoing version of the April 23, 2021 ACIP meeting minutes, Dr. Jose Romero, ACIP Chair, certified that to the best of his knowledge, they are accurate and complete. His original, signed certification is on file with the Management Analysis and Services Office (MASO) of CDC.

ACIP Membership Roster

Department of Health and Human Services
Centers for Disease Control and Prevention
Advisory Committee on Immunization Practices
December 23, 2020 – June 30, 2021

CHAIR

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Director, Arkansas Department of Health
Professor of Pediatrics, Pediatric Infectious Diseases
University of Arkansas for Medical Sciences
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Term: 10/30/2018-06/30/2021

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BERNSTEIN, Henry, DO, MHCM, FAAP
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