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VITT

Clinical Features

Dr Sue Pavord
Oxford University Hospitals
NHS Foundation Trust

27 June 2022

Oxford University Hospitals NHS
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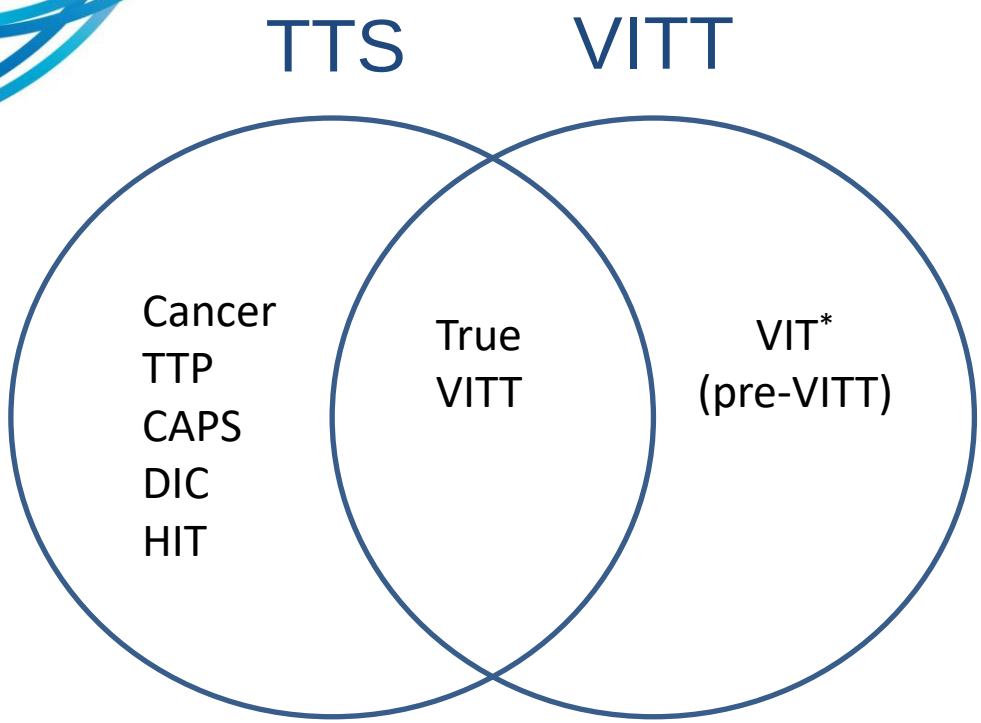
VITT

Clinical Features

Vaccine-induced **I**mmune **T**hrombocytopenia and **T**hrombosis

Vaccine-induced **I**mmune **T**hrombotic **T**hrombocytopenia

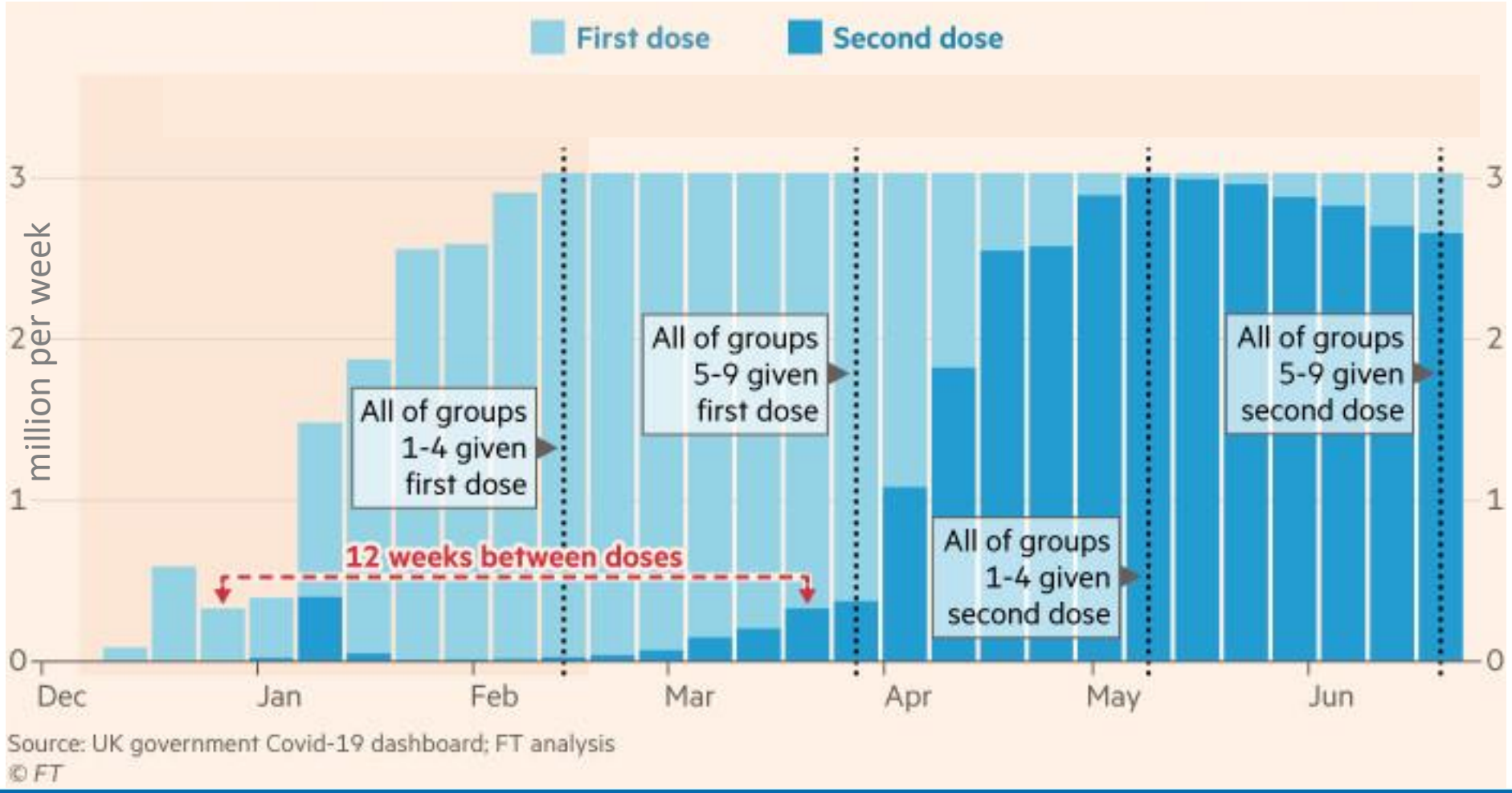
27 June 2022



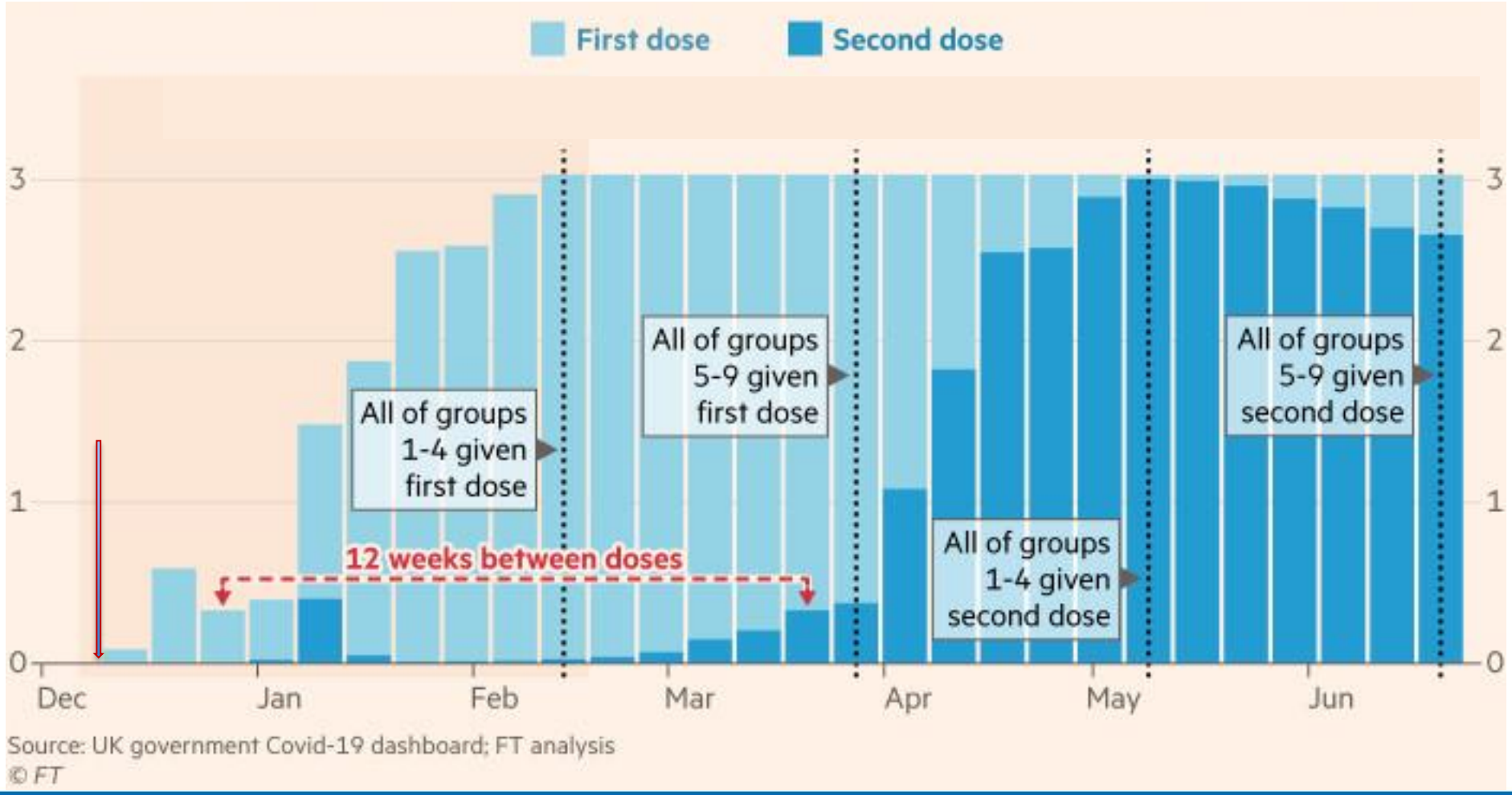
Pavord *et al,* NEJM Aug 2021
Salih *et al,* NEJM Sept 2021

TTS -Thrombotic thrombocytopenia syndrome; VITT -Vaccine-induced immune thrombocytopenia and thrombosis; TTP -thrombotic thrombocytopenia purpura; CAPS -catastrophic antiphospholipid syndrome; DIC -disseminated intravascular coagulation; HIT-heparin induced thrombocytopenia
*VIT or pre-VITT is the condition where all the VITT features other than thrombosis are present[1,2].

Covid-19 vaccine roll out in UK



Covid-19 vaccine roll out in UK



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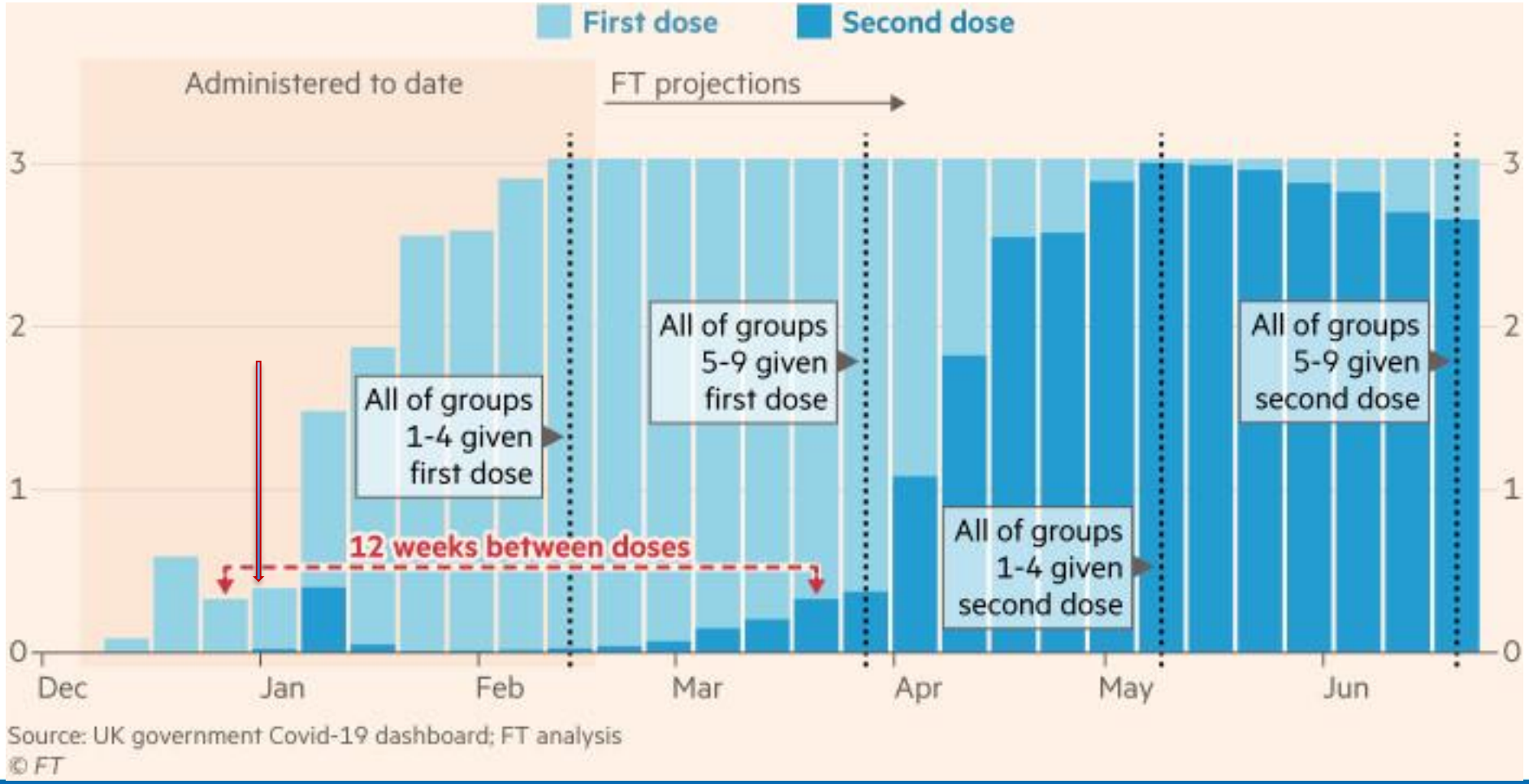

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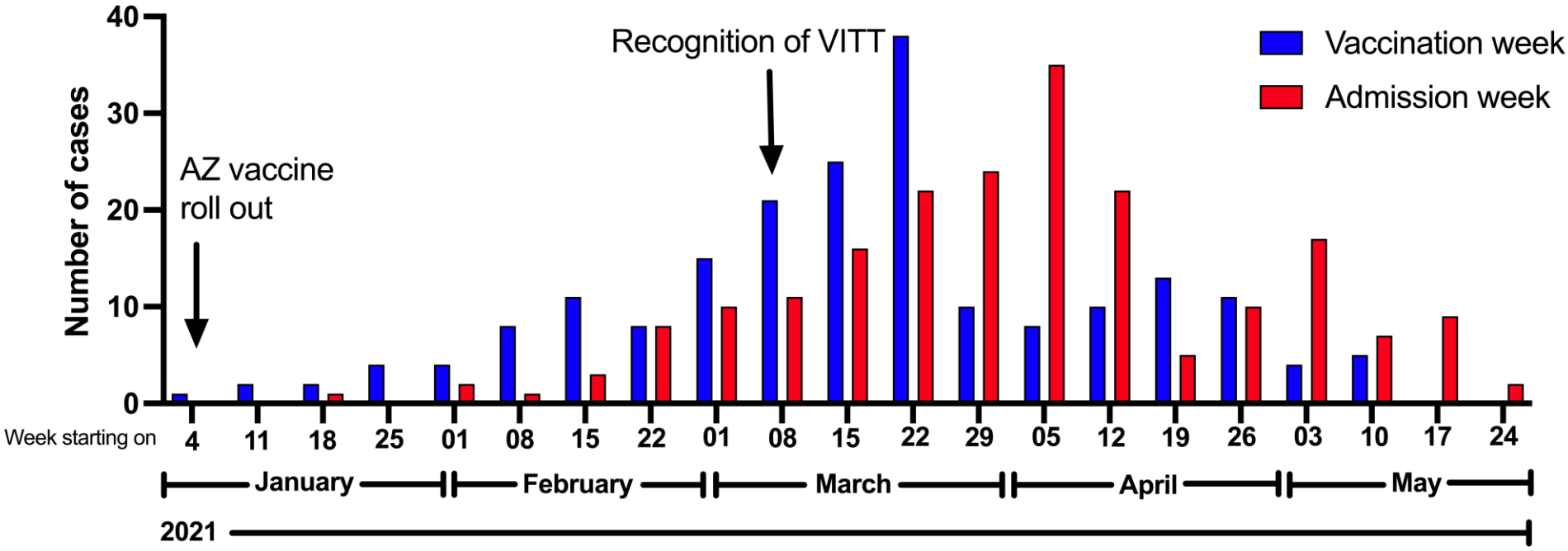
Timings of vaccines and admissions with VITT



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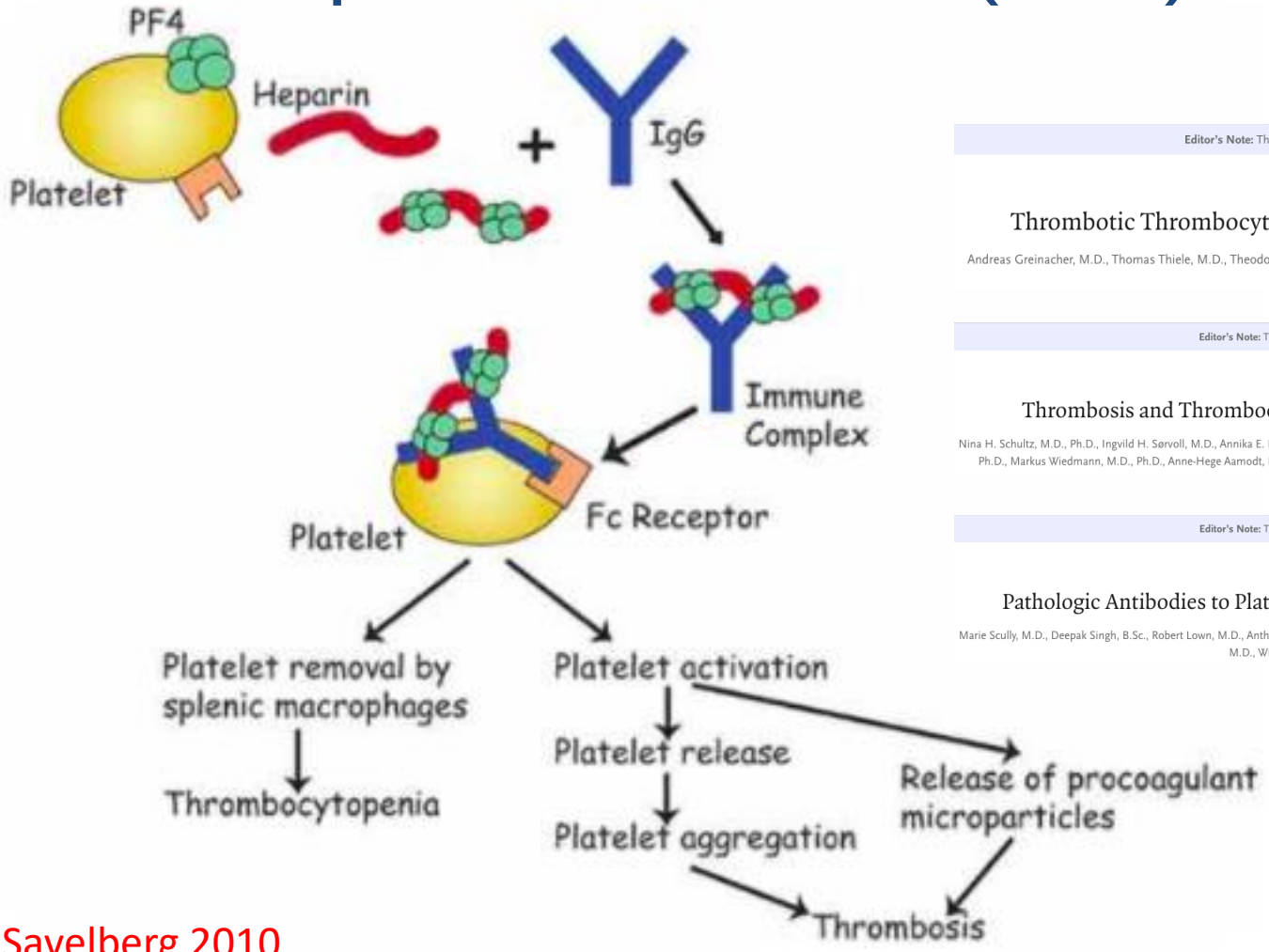
Anti-platelet factor 4 (PF4) antibodies



Editor's Note: This article was published on April 9, 2021, at NEJM.org.

ORIGINAL ARTICLE

Thrombotic Thrombocytopenia after ChAdOx1 nCov-19 Vaccination

Andreas Greinacher, M.D., Thomas Thiele, M.D., Theodore E. Warkentin, M.D., Karin Weisser, Ph.D., Paul A. Kyrle, M.D., and Sabine Eichinger, M.D.

Editor's Note: This article was published on April 9, 2021, at NEJM.org.

ORIGINAL ARTICLE BRIEF REPORT

Thrombosis and Thrombocytopenia after ChAdOx1 nCoV-19 Vaccination

Nina H. Schultz, M.D., Ph.D., Ingvild H. Sørvoll, M.D., Annika E. Michelsen, Ph.D., Ludvig A. Munthe, M.D., Ph.D., Fridtjof Lund-Johansen, M.D., Ph.D., Maria T. Ahlen, Ph.D., Markus Wiedmann, M.D., Ph.D., Anne-Hege Aamodt, M.D., Ph.D., Thor H. Skattør, M.D., Geir E. Tjønnfjord, M.D., Ph.D., and Pål A. Holme, M.D., Ph.D.

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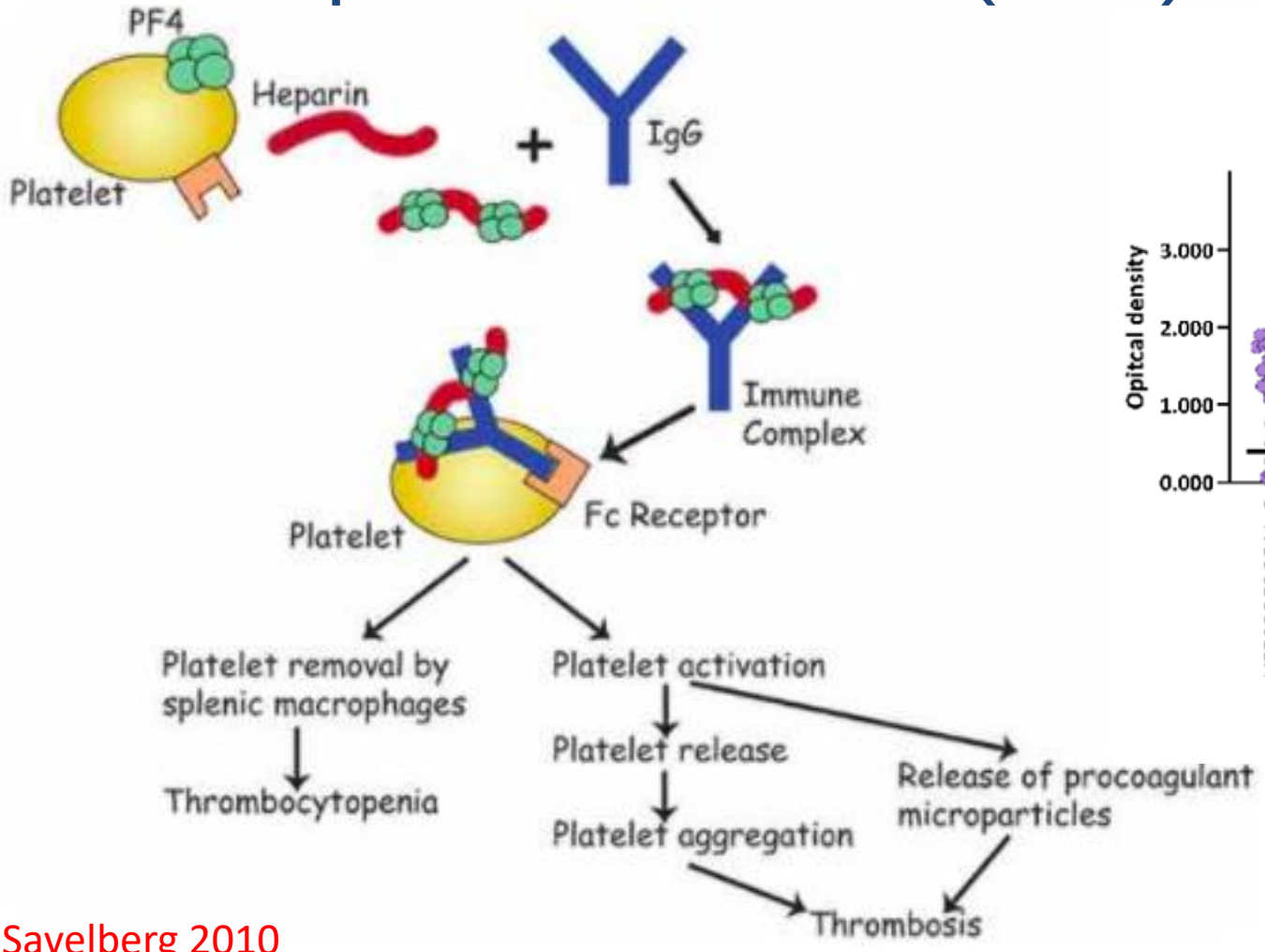
ORIGINAL ARTICLE

Pathologic Antibodies to Platelet Factor 4 after ChAdOx1 nCoV-19 Vaccination

Marie Scully, M.D., Deepak Singh, B.Sc., Robert Lown, M.D., Anthony Poles, M.D., Tom Solomon, M.D., Marcel Levi, M.D., David Goldblatt, M.D., Ph.D., Pavel Kotoucek, M.D., William Thomas, M.D., and William Lester, M.D.

Savelberg 2010

Anti-platelet factor 4 (PF4) antibodies



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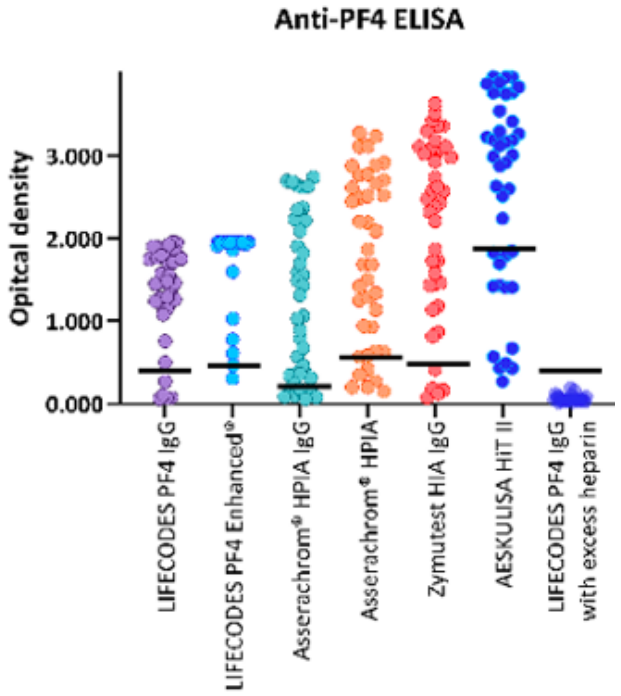

Platton 2022

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"Expert" Haematology Panel (EHP)

- Sue Pavord, Oxford
- Marie Scully, London
- Will Lester, Birmingham
- Beverley Hunt, London
- Mike Makris, Sheffield

- UK Haematologists
- Open to all disciplines

- neurologists, neurosurgeons, intensivists, ED

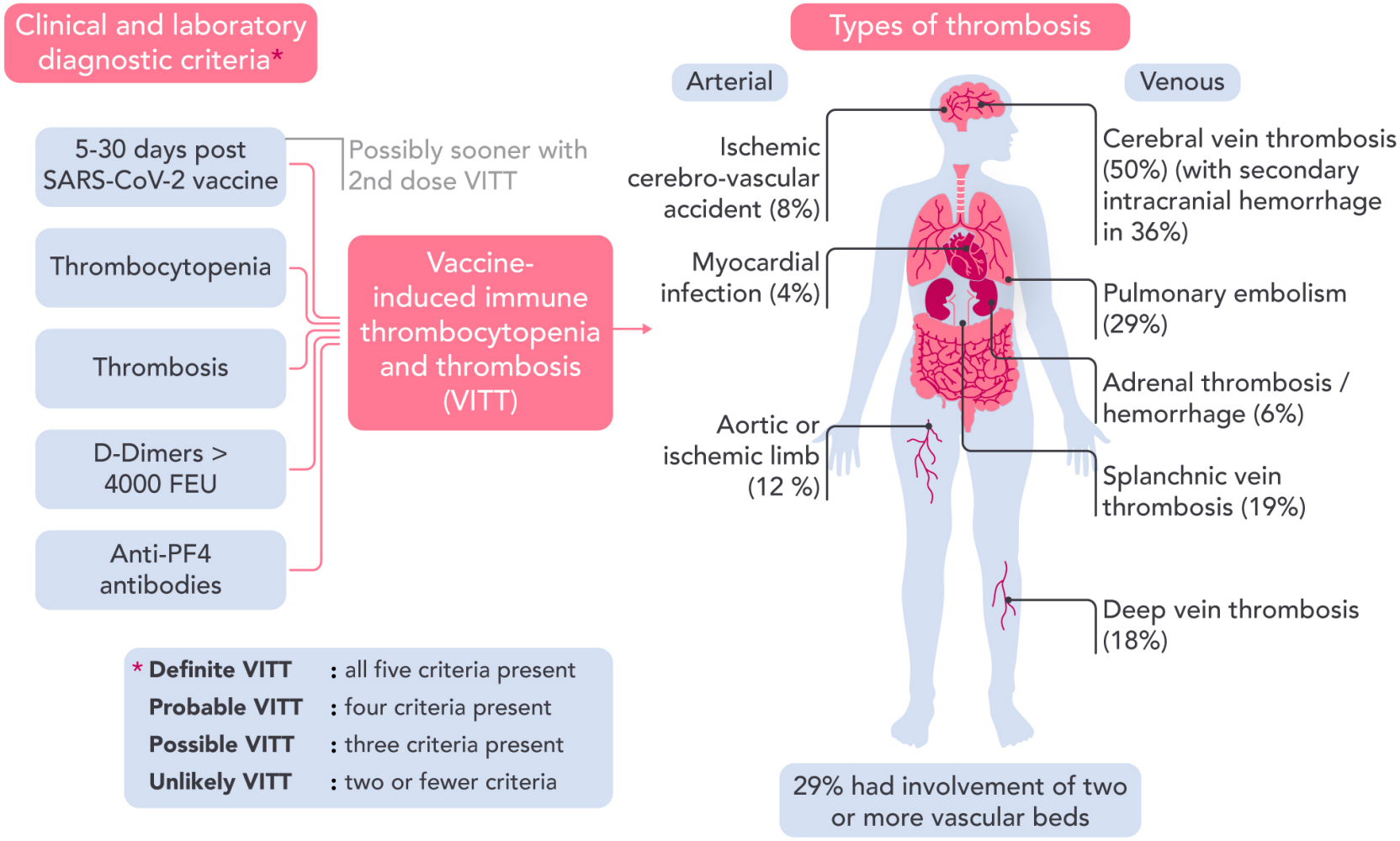
- 2pm MDT meetings 7/7
  From 22 March 2021
  To 23 June 2021

British Society for Haematology
Listening • Learning • Leading

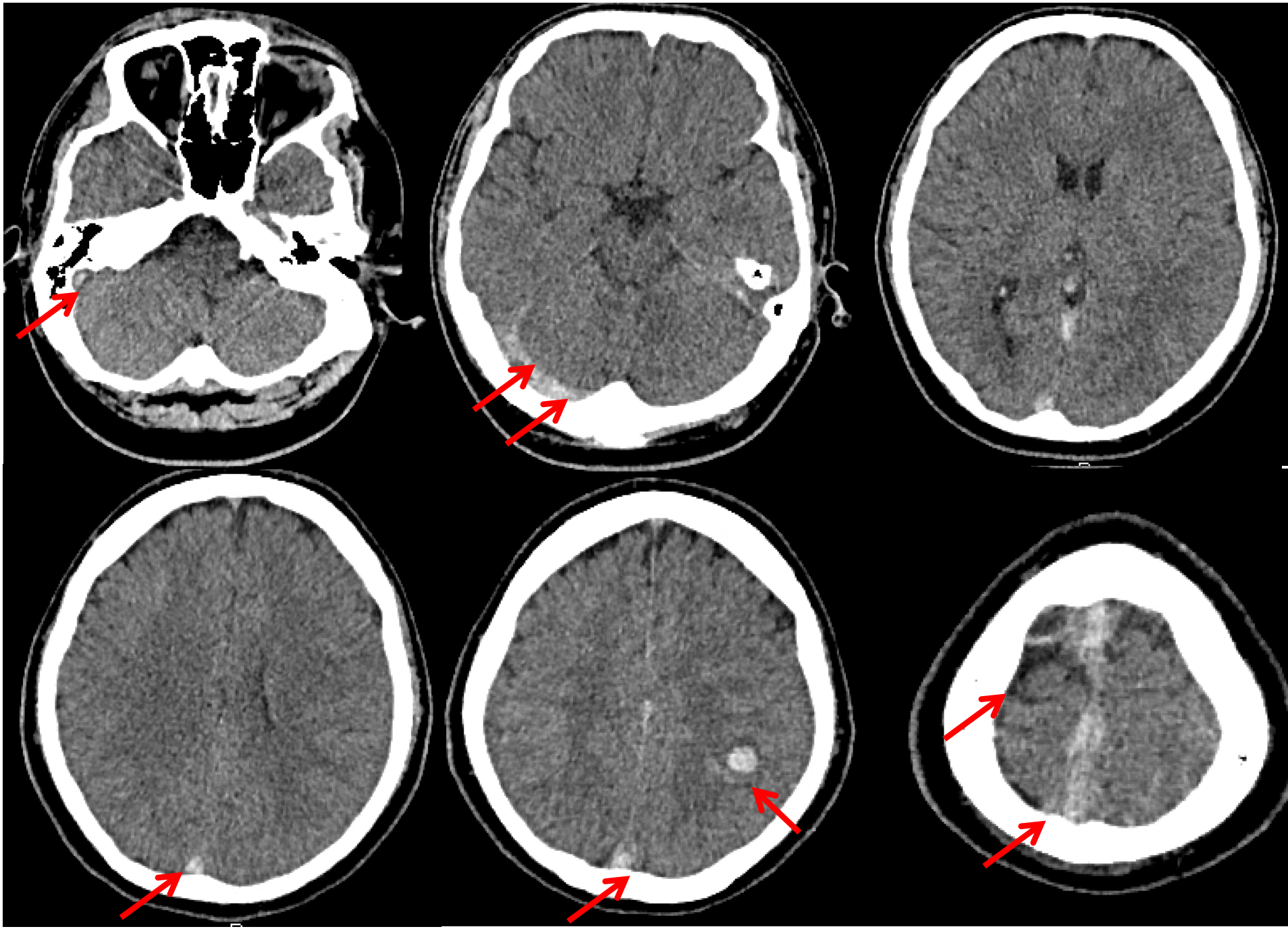
Case Example

- D14 presents with headache, extensive CVST, GCS 4
- Platelets 18, fib 1.1g/L
- D Dimer 36,000
- Major ICH - hemicraniectomy
- IvIg + plts + cryo
- anticoagulated
- prolonged hospital stay
- ?long term cognitive impairment
- awaiting cranioplasty

Clinical features of VITT



Pavord, Blood 2022



Screening for VITT

The Royal College of Emergency Medicine | sam | Royal College of Physicians

Guidance agreed with Expert Haematology Panel (EHP) April 10th 2021
Guidance agreed with British Society of Neuroradiologists (BSNR) and RCR April 11th 2021

Management of patients presenting to the Emergency Department/ Acute Medicine with symptoms

The condition of concern is **Covid-19 Vaccine induced Thrombosis and Thrombocytopenia (VITT)**

Key Decision point 0 – Does this patient's presentation raise any concern about VITT?

If no, manage as per routine practice for specific presentation

If yes , continue with this guidance

Concern- cases usually present with progressive thrombosis, with a high preponderance of cerebral venous sinus thrombosis. Splanchnic vein thrombosis is common and pulmonary embolism and arterial ischaemia are also seen. Bleeding can be significant and unexpected. Symptoms of concern are:

• Persistent or severe headaches, seizures or focal neurology, • Shortness of breath, persistent chest or abdominal pain, • Swelling, redness, pallor or cold lower limbs

Key Decision point 1 – initial assessment

Has the patient presented with symptoms >4-28 days since vaccination

Send FBC

Is the platelet count > 150 x 10^9/L

If Y -VITT is unlikely

As this is an emerging area of practice, please continue to check back for updates
https://b-s-h.org.uk/ and https://www.gov.uk/government/organisations/medicines-and-healthcare-products-regulatory-agency

The Royal College of Emergency Medicine | sam | Royal College of Physicians

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Key Decision point 2 -is patient safe to go home?

Does the patient have symptoms of another clinical condition that needs investigation

If N then home with safety net advice to return if persistent or escalating symptoms or other concern for thrombosis for repeat testing

If Y then further work up required for alternative diagnoses

Key Decision point 3- if platelets < 150 x 10^9/L

Send clotting (fibrinogen) and d-dimer test

d-dimer <2000[1], normal fibrinogen

d-dimer > 2000*, low fibrinogen

Not VITT - Ix for other diagnosis

Suspect VITT

Haematology advice

Rx as per guidance from Expert Haematology Panel

Appropriate imaging and other specialty referral [2]

[1]D Dimer as mcg/L, (includes FEU or DDU) = 2mg/L (cases -D Dimers > 4000 mcg/L but D Dimers 2000-4000 mcg/L need to be discussed as probable case)

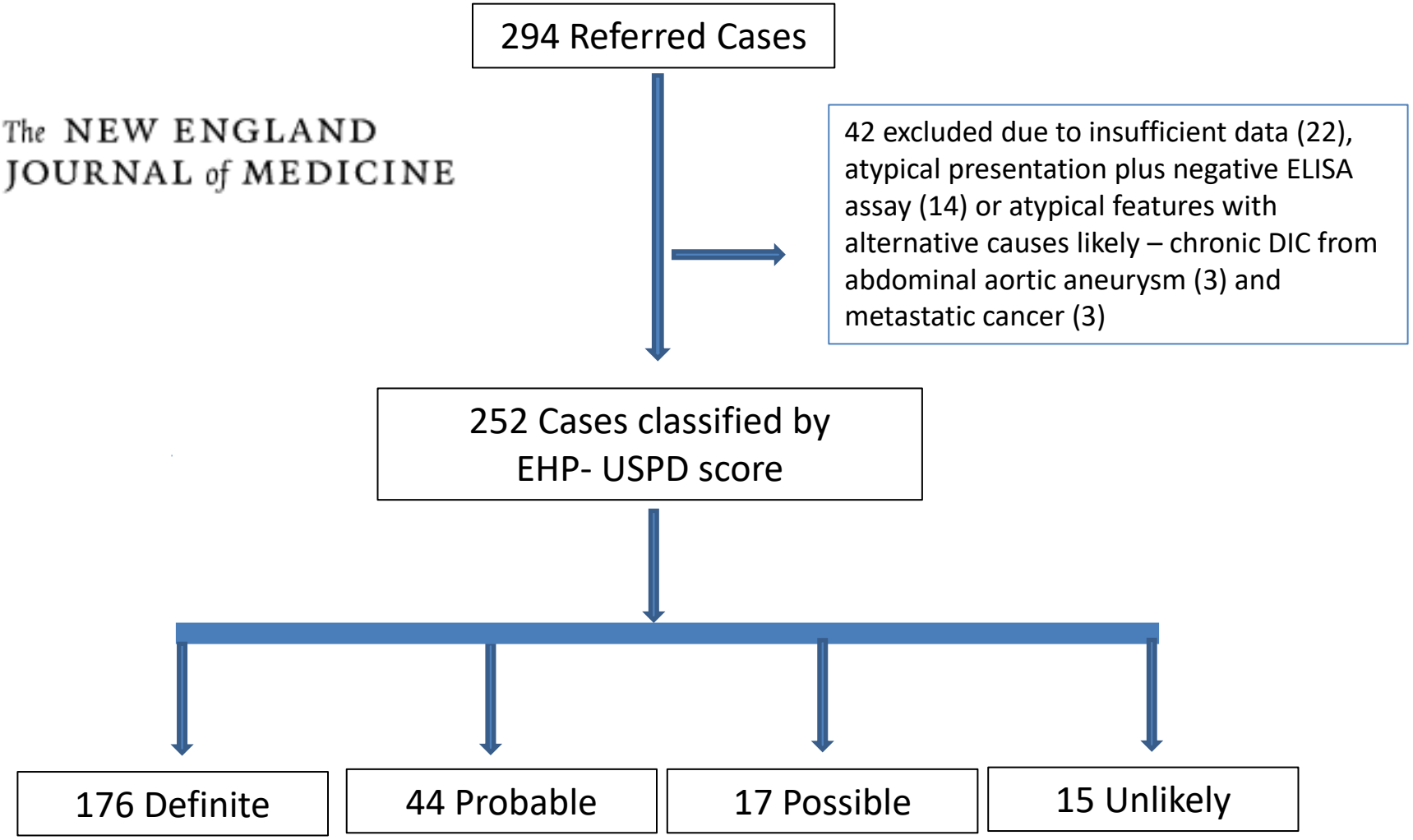
As this is an emerging area of practice, please continue to check back for updates
https://b-s-h.org.uk/ and https://www.gov.uk/government/organisations/medicines-and-healthcare-products-regulatory-agency

ORIGINAL ARTICLE

Clinical Features of Vaccine-Induced Immune Thrombocytopenia and Thrombosis

Sue Pavord, F.R.C.Path., Marie Scully, M.D., Beverley J. Hunt, M.D., William Lester, M.D., Catherine Bagot, M.D., Brian Craven, M.B., B.Ch., Alex Rampotas, M.R.C.P., Gareth Ambler, Ph.D., and Mike Makris, M.D.

The NEW ENGLAND JOURNAL of MEDICINE

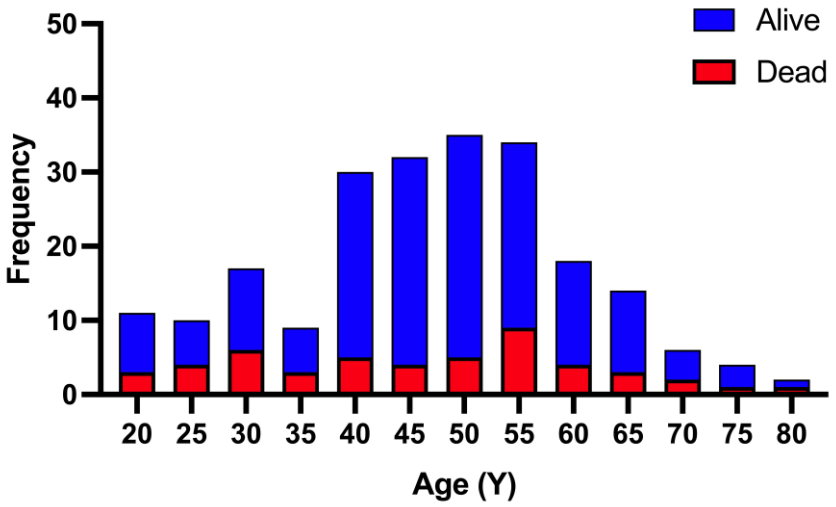


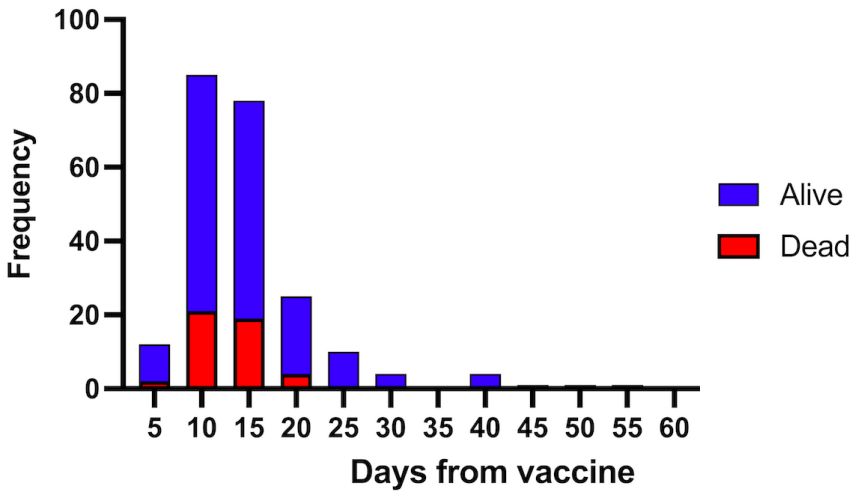
Risk factors

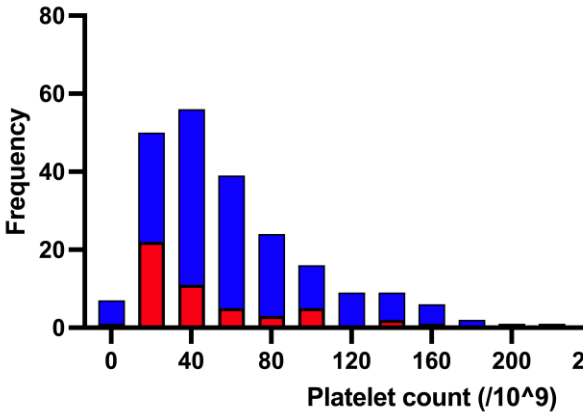
Age – average age 47yrs
Incidence 1:50,000 for individuals <50 yrs
1:100,000 for those over 50 yrs

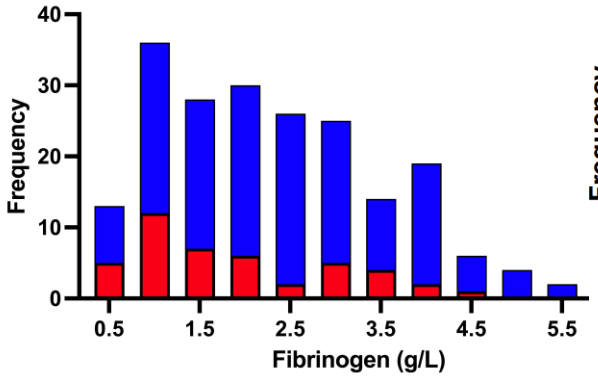
Not -
prothrombotic conditions
Cancer
Medications
gender

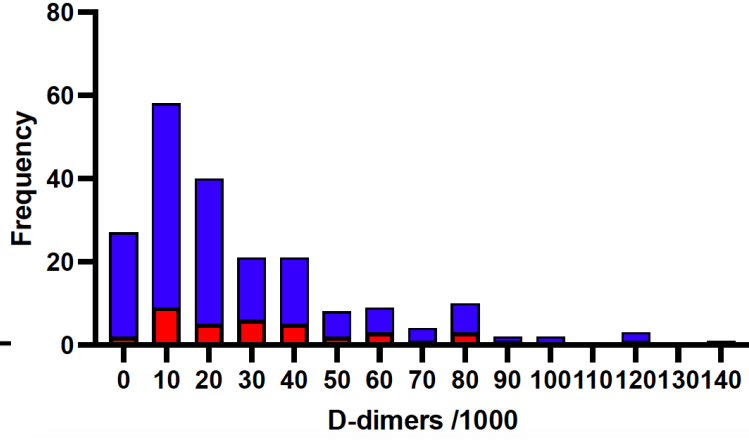
Prognostic Markers











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Clinical Features of Vaccine-Induced Immune Thrombocytopenia and Thrombosis

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Prognostic marker	Odds of death
Cerebral venous thrombosis	2.7
Low platelet count	1.7 for every 50% reduction in presenting platelet count
Raised D-Dimer	1.2 for every 10,000 FEU higher level at presentation
Low fibrinogen	1.7 for every 50% reduction in baseline fibrinogen

Prognostic markers

Presenting thrombosis	Number (%)	Age Range, (median)	Sex M:F (%fem)	Days from vaccine	Presenting platelet count	Presenting fibrinogen	D-dimer	Outcome A:D (%died)
Venous								
CVST	93 (47	18-85 (49)	40:52 (57)	5-32 (14)	7-340 (49)	0.35 – 6.5 (2.3)	1800-80,000 23,704	64:28 (30)
CVST with platelets<30	30 (15)	18-66 (48)	9:21 (70)	6-17	7-30 (20)	0.6 – 4.4 (1.6)	7000 – 116,000 (35,200)	8:22 (73)
CVST with Platelets >30	63 (32)	1-85 (50)	32:31 (49)	5-32 (12)	31-340 (64)	0.35 – 6.5 (2.3)	1800-80,000 (14,000)	28:6 (17)
ICH	35 (18)	19-67 (49)	12:24 (67)	19-67 (52)	11-182 (34)	0.66-4.7 (2.2)	760-91,000 (69,000)	19:16 (46)
DVT and/or PE	65 (33)	21-81 (54)	34:30 (47)	7-56 (15)	6-447 (50)	0.5-6.5 (1.9)	500-80,000 (20,000)	58:5 (8)
PVT and other splanchnic vein thrombosis	27 (14)	21-59 (46)	11:16 (59)	6-24 (12)	11-115 (27)	0.9-4.4 (2.0)	10,000-80,000 (27,000)	21:6 (22)
Adrenal thrombosis and haemorrhage	3 (2)	38-67 (66)	1:2 (67)	9-14 (12)	16-79 (34)	2.1-4.06 (2.1)	4160 – 30,492 (10,388)	2:1 (33)
Arterial								
Limb ischaemia or aortic thrombus	19 (9.5)	24-72 (56)	6:13 (68)	8-42 (15)	6-344 (95)	0.5-4.8 (2.5)	500-13,000 (1,300)	14:2 (12.5)
Cardiac or cerebrovascular event	19 (9.5)	21-81 (47)	10:8 (44)	7-56 (10)	6-182 (51)	0.2-4.7 (2.63)	250-53,000 (20,000)	11:6 (35)
Multiple sites								

Vaccine re-challenge

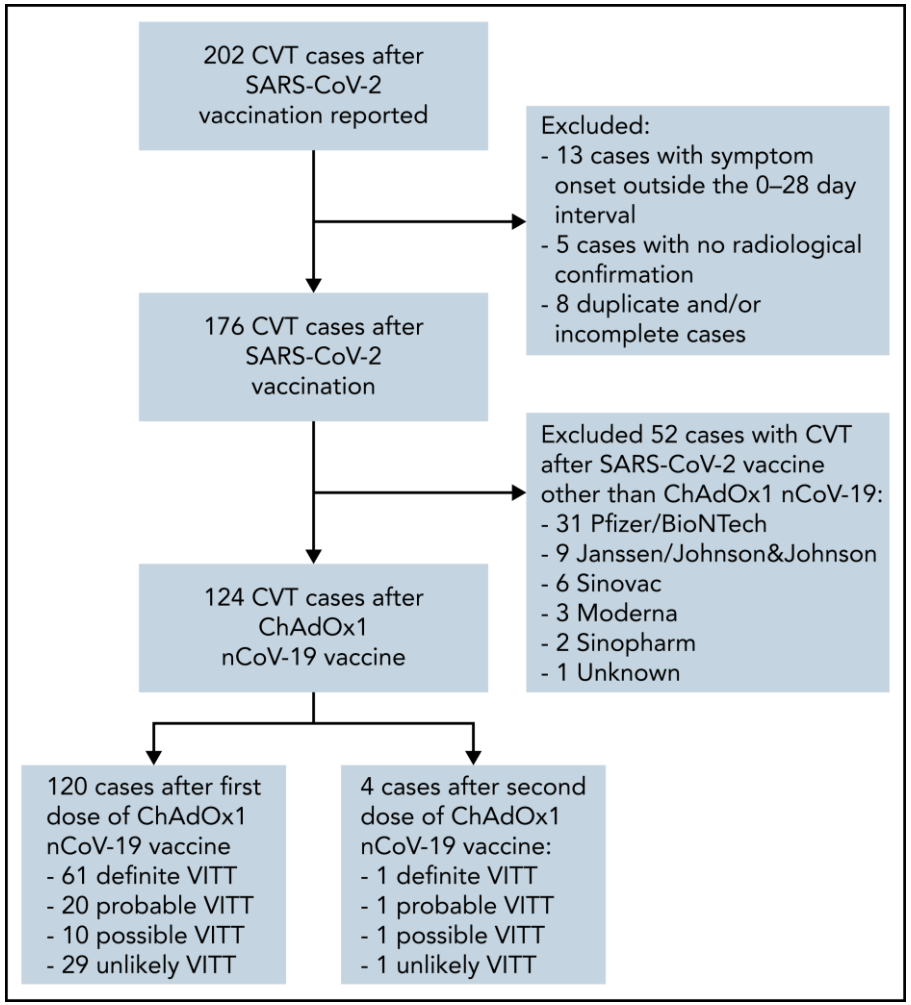
Table 1. Second Doses of Covid-19 Vaccine in Patients Who Had VITT after a First Dose of ChAdOx1 nCoV-19.*

VITT Category	ChAdOx1 nCoV-19	mRNA-1273	BNT162b2	Interval between Vaccine Doses
	no. of patients who received a second dose			*days*
Confirmed	1	2	23	53–234
Probable	0	0	2	77–122
Possible	4	0	8	63–190
Total	5	2	33	—

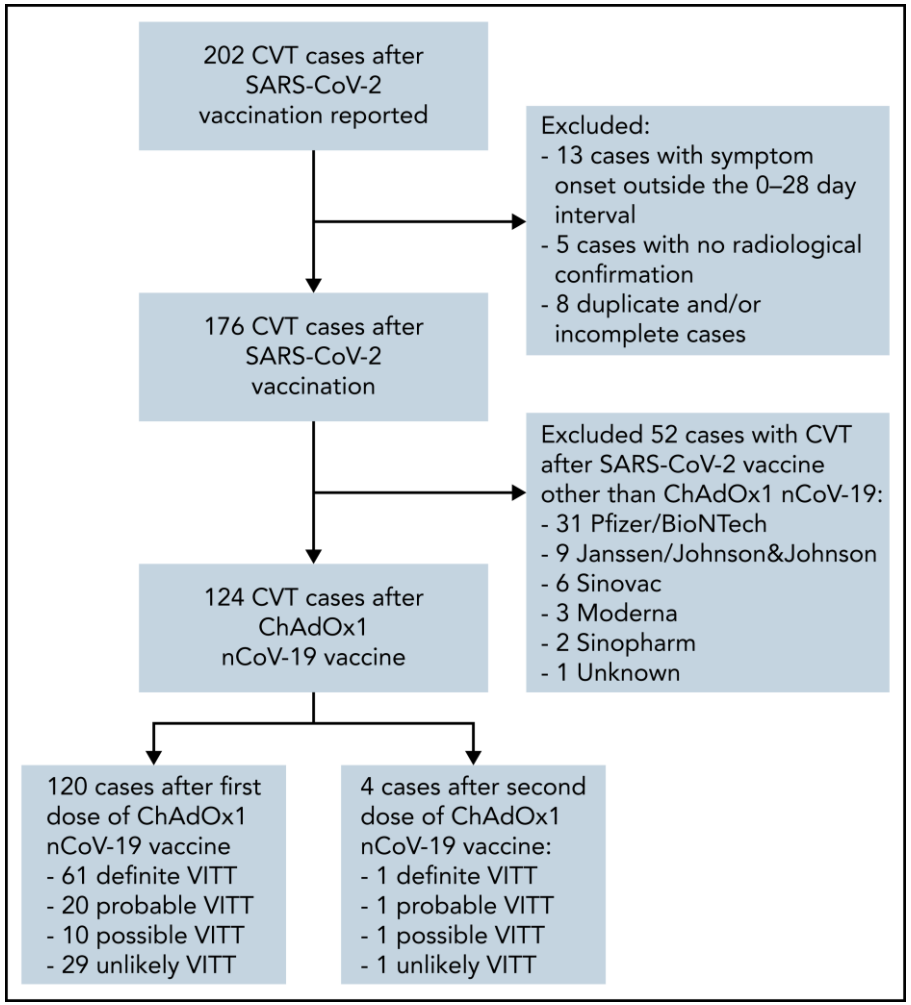
* Covid-19 denotes coronavirus disease 2019, and VITT vaccine-induced immune thrombotic thrombocytopenia.

Lacey et al, NEJM

2nd dose VITT

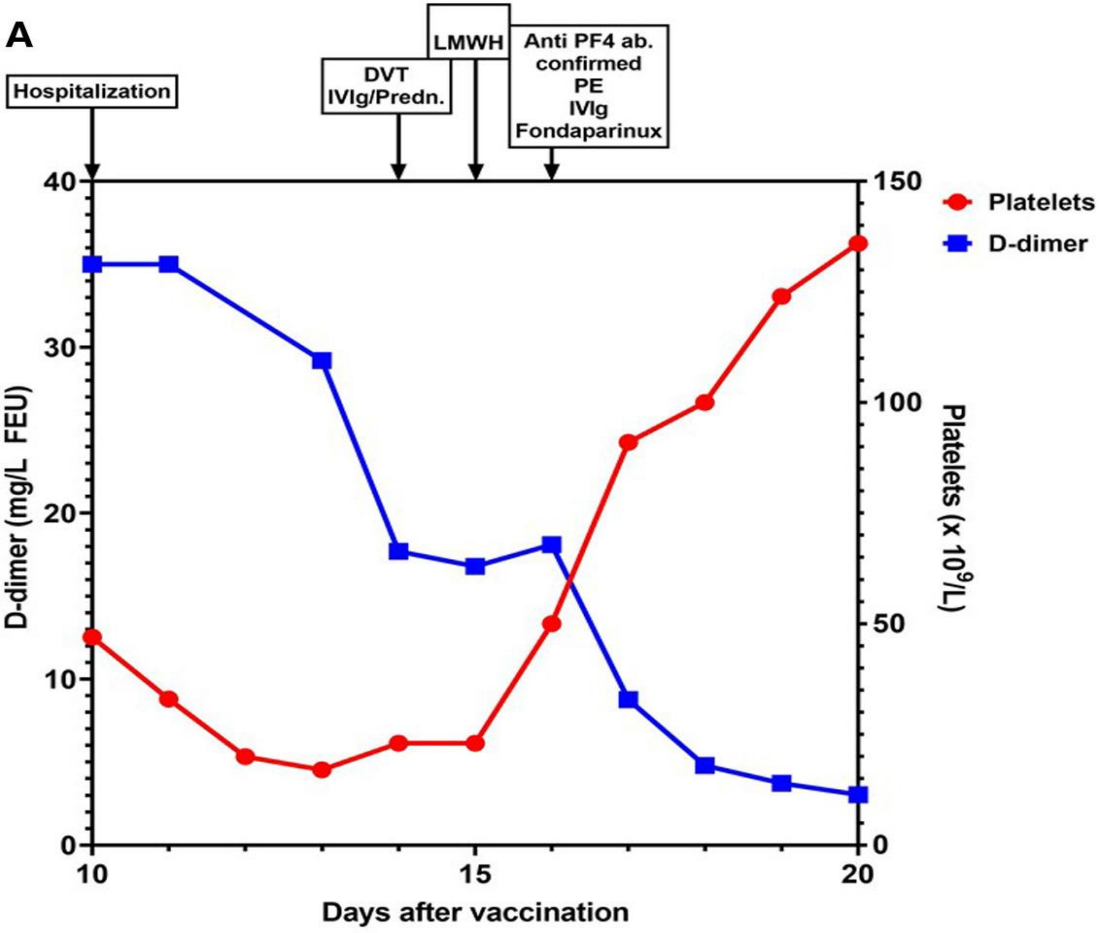


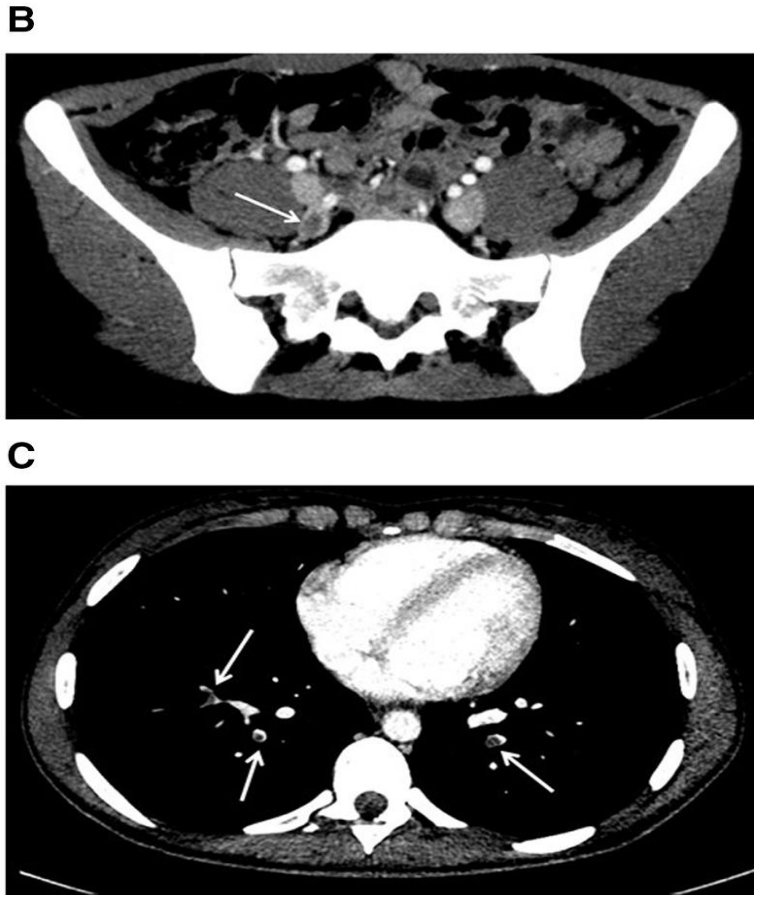
2nd dose VITT



- No confirmed cases in UK
- >11 week interval
- Pathogenicity of VITT antibodies declined by 12 weeks
- HIT antibodies transient 40-100 days
- Persistence beyond 12 weeks is <5%
- After this time it takes 5 days to mount the immune response again

VITT after HPV vaccination





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