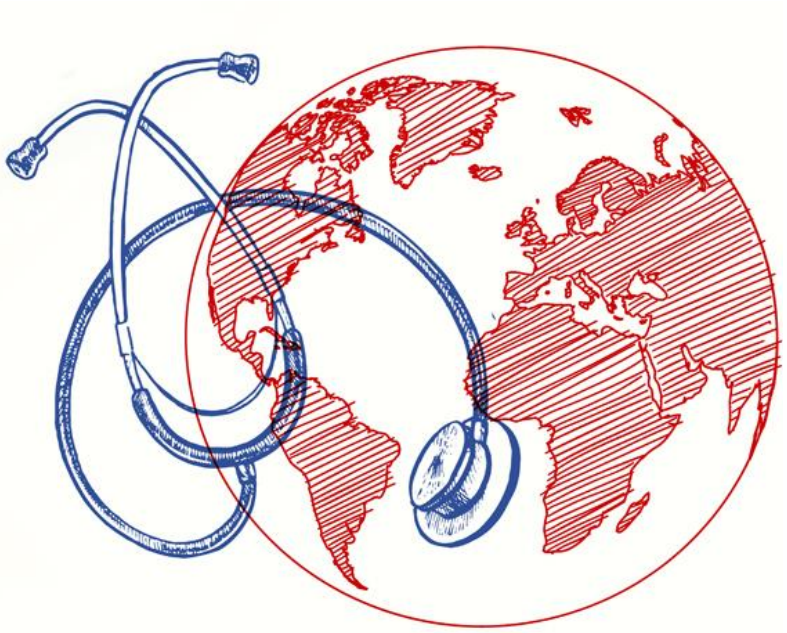
Global Health Cast 61

February 26, 2024



Dr. Melvin Sanicas
@Vaccinologist

Prof. Dr. Joe Schmitt
@Prof_Schmitt

What we talk about today

- Older adults who exercised before the pandemic were at lower risk of COVID infection and hospitalization
- Cognitive issues and depression in those with long COVID
- COVID infection linked to fatigue
- Even low intensity activities (walking/yoga) help with depression
- Vaccine induced thrombocytopenia and thrombosis (VITT)
- Measles in Europe – more to come after the COVID19-gap?
- Hepatitis E in Europe – vaccination useful?

Older adults who exercised before the pandemic were at lower risk of COVID infection and hospitalization

JAMA Network Open

Original Investigation | Public Health

Prepandemic Physical Activity and Risk of COVID-19 Diagnosis and Hospitalization in Older Adults

Dennis Muñoz-Vergara, DVM, MPH; Peter M. Wayne, PhD; Eunjung Kim, MS; I-Min Lee, MBBS, ScD; Julie E. Buring, ScD; JoAnn E. Manson, MD, DrPH; Howard D. Sesso, ScD, MPH

Abstract

IMPORTANCE Higher prepandemic physical activity (PA) levels have been associated with lower risk and severity of COVID-19.

OBJECTIVE To investigate the association between self-reported prepandemic PA levels and the risk and severity of COVID-19 in older US adults.

DESIGN, SETTING, AND PARTICIPANTS This cohort study combined cohorts from 3 ongoing prospective randomized clinical trials of US adults aged 45 years or older who provided prepandemic self-reports of baseline leisure-time PA and risk factors for COVID-19 outcomes using the most recent questionnaire completed as of December 31, 2019, as the baseline PA assessment. In multiple surveys from May 2020 through May 2022, participants indicated whether they had at least 1 positive COVID-19 test result or were diagnosed with or hospitalized for COVID-19.

EXPOSURE Prepandemic PA, categorized into 3 groups by metabolic equivalent hours per week: inactive (0-3.5), insufficiently active (>3.5 to <7.5), and sufficiently active (≥7.5).

MAIN OUTCOME AND MEASURES Primary outcomes were risk of COVID-19 and hospitalization for COVID-19. Multivariable logistic regression was used to estimate odd ratios (ORs) and 95% CIs for the association of COVID-19 diagnosis and/or hospitalization with each of the 2 upper PA categories vs the lowest PA category.

Key Points

Question Are higher prepandemic physical activity (PA) levels associated with lower risk of developing or being hospitalized for COVID-19?

Findings In this cohort study of 61 557 women and men aged 45 years or older who reported 5890 incident cases of COVID-19 and 626 hospitalizations, those who achieved at least 7.5 metabolic equivalent hours per week of PA before the pandemic had significantly reduced odds of COVID-19 diagnosis and hospitalization compared with the inactive group.

Meaning Higher prepandemic PA levels were associated with lower odds of developing and being hospitalized for COVID-19.

After controlling for demographics, BMI, lifestyle factors, underlying illnesses, and medications, compared with inactive individuals, **those who were insufficiently active had no significant reduction in infection** (odds ratio [OR], 0.96) **or hospitalization** (OR, 0.98), **while those sufficiently active had a significant reduction in infection** (OR, 0.90) **and hospitalization** (OR, 0.73).

GLOBAL HEALTH PRESS

Original Investigation | Infectious Diseases

Cognitive Symptoms of Post–COVID-19 Condition and Daily Functioning

Abhishek Jaywant, PhD; Faith M. Gunning, PhD; Lauren E. Oberlin, PhD; Mauricio Santillana, PhD; Katherine Ognyanova, PhD; James N. Druckman, PhD; Matthew A. Baum, PhD; David Lazer, PhD; Roy H. Perlis, MD, MSc

Abstract

IMPORTANCE The frequent occurrence of cognitive symptoms in post–COVID-19 condition has been described, but the nature of these symptoms and their demographic and functional factors are not well characterized in generalizable populations.

OBJECTIVE To investigate the prevalence of self-reported cognitive symptoms in post–COVID-19 condition, in comparison with individuals with prior acute SARS-CoV-2 infection who did not develop post–COVID-19 condition, and their association with other individual features, including depressive symptoms and functional status.

DESIGN, SETTING, AND PARTICIPANTS Two waves of a 50-state nonprobability population-based internet survey conducted between December 22, 2022, and May 5, 2023. Participants included survey respondents aged 18 years and older.

EXPOSURE Post–COVID-19 condition, defined as self-report of symptoms attributed to COVID-19 beyond 2 months after the initial month of illness.

MAIN OUTCOMES AND MEASURES Seven items from the Neuro-QoL cognition battery assessing the frequency of cognitive symptoms in the past week and patient Health Questionnaire-9.

RESULTS The 14 767 individuals reporting test-confirmed COVID-19 illness at least 2 months before the survey had a mean (SD) age of 44.6 (16.3) years; 568 (3.8%) were Asian, 1484 (10.0%) were Black, 1408 (9.5%) were Hispanic, and 10 811 (73.2%) were White. A total of 10 037 respondents (68.0%) were women and 4730 (32.0%) were men. Of the 1683 individuals reporting post–COVID-19 condition, 955 (56.7%) reported at least 1 cognitive symptom experienced daily, compared with 3552 of 13 084 (27.1%) of those who did not report post–COVID-19 condition. More daily cognitive symptoms were associated with a greater likelihood of reporting at least moderate interference with functioning (unadjusted odds ratio [OR], 1.31 [95% CI, 1.25-1.36]; adjusted [AOR], 1.30 [95% CI, 1.25-1.36]), lesser likelihood of full-time employment (unadjusted OR, 0.95 [95% CI, 0.91-0.99]; AOR, 0.92 [95% CI, 0.88-0.96]) and greater severity of depressive symptoms (unadjusted coefficient, 1.40 [95% CI, 1.29-1.51]; adjusted coefficient 1.27 [95% CI, 1.17-1.38]). After including depressive symptoms in regression models, associations were also found between

Key Points

Question How are post–COVID-19 condition self-reported cognitive symptoms associated with employment status, functional outcomes, and mood?

Findings In this survey study including 14 767 individuals with post–COVID-19 condition surveyed in late 2022 to early 2023, 57% reported experiencing cognitive symptoms daily, compared with 27% with prior SARS-CoV-2 infection who did not develop post–COVID-19 condition. In those with post–COVID-19 condition, cognitive symptoms were associated with greater levels of depressive symptoms, greater reported functional impairment, and lesser likelihood of full-time employment.

Meaning The findings of this study suggest that self-reported cognitive symptoms are prevalent in post–COVID-19 condition, often co-occur with depressive symptoms, and are associated with functional impairment.

+ Supplemental content

Author affiliations and article information are listed at the end of this article.

How are post–COVID-19 condition self-reported cognitive symptoms associated with employment status, functional outcomes, and mood?

In those with post–COVID-19 condition, **cognitive symptoms were associated with greater levels of depressive symptoms, greater reported functional impairment**, and lesser likelihood of full-time employment

Self-reported cognitive symptoms are prevalent in post–COVID-19 condition, often co-occur with depressive symptoms, and are associated with functional impairment.

GLOBAL HEALTH PRESS

Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™
EMERGING INFECTIOUS DISEASES®
Volume 30, Number 3—March 2024
Research

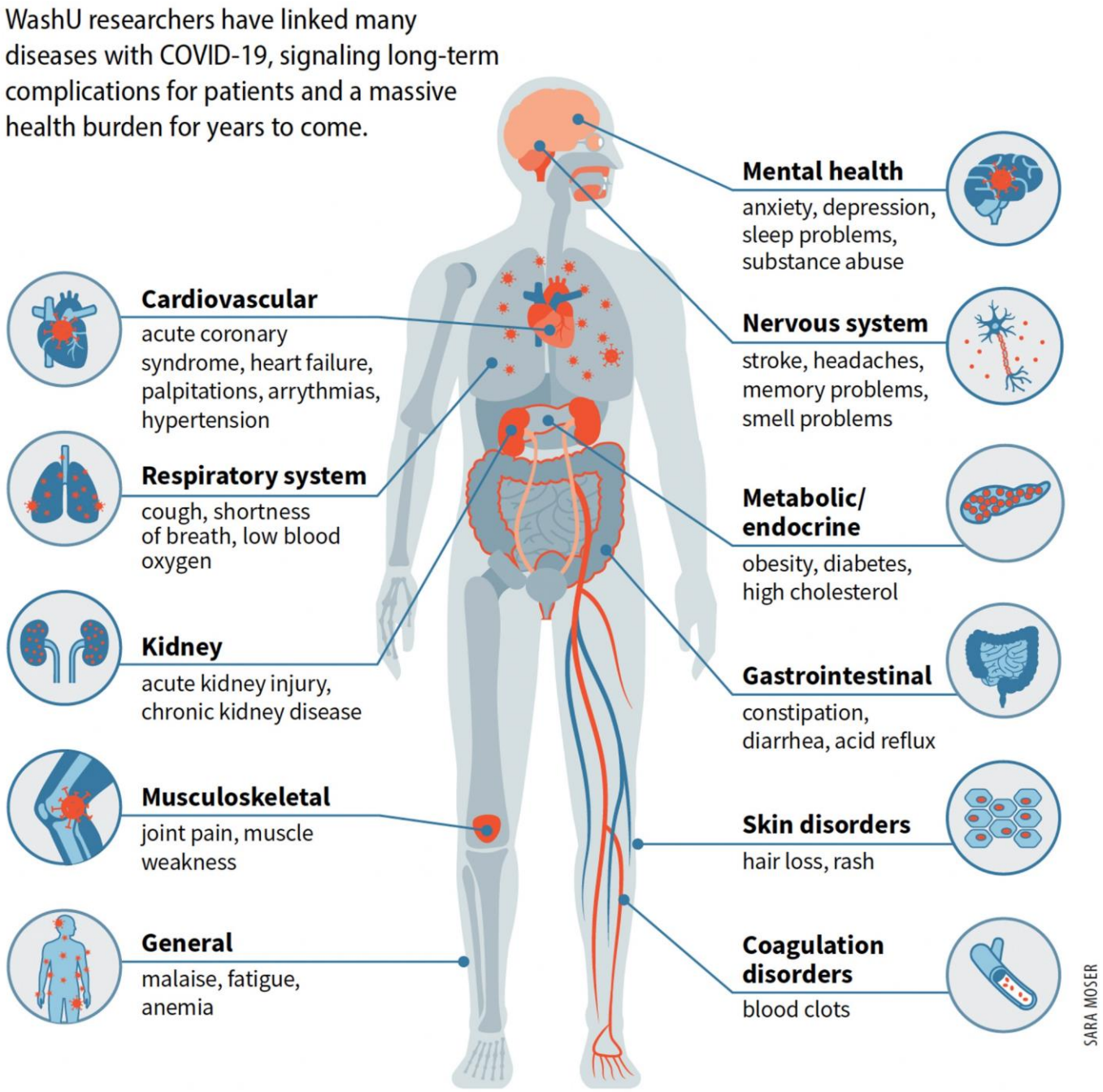
Estimates of Incidence & Predictors of Fatiguing Illness after SARS-CoV-2 Infection

Quan M. Vu, Annette L. Fitzpatrick, Jennifer R. Cope, Jeanne Bertolli, Nona Sotoodehnia, T. Eoin West, Nikki Gentile, and Elizabeth R. Unger

Abstract

This study aimed to estimate the incidence rates of post–COVID-19 fatigue and chronic fatigue and to quantify the additional incident fatigue caused by COVID-19. We analyzed electronic health records data of 4,589 patients with confirmed COVID-19 during February 2020–February 2021 who were followed for a median of 11.4 (interquartile range 7.8–15.5) months and compared them to data from 9,022 propensity score–matched non–COVID-19 controls. **Among COVID-19 patients (15% hospitalized for acute COVID-19), the incidence rate of fatigue was 10.2/100 person-years and the rate of chronic fatigue was 1.8/100 person-years.** Compared with non–COVID-19 controls, the hazard ratios were 1.68 (95% CI 1.48–1.92) for fatigue and 4.32 (95% CI 2.90–6.43) for chronic fatigue. **The observed association between COVID-19 and the significant increase in the incidence of fatigue and chronic fatigue reinforces the need for public health actions to prevent SARS-CoV-2 infections.**

Post COVID-19 condition *(Long COVID)*



Definition

It is defined as the **continuation** or **development of new symptoms 3 months after the initial SARS-CoV-2 infection**, with these symptoms lasting for at least 2 months with no other explanation.

Symptoms

While common symptoms of long COVID can include fatigue, shortness of breath and cognitive dysfunction over 200 different symptoms have been reported that can have an impact on everyday functioning.

GLOBAL HEALTH PRESS

https://www.who.int/europe/news-room/fact-sheets/item/post-covid-19-condition

id-ea.org

thebmj Visual abstract

Effect of exercise for depression

A systematic review and network meta-analysis of randomised controlled trials

Summary

For treating depression, various exercise modalities are well tolerated and effective, particularly walking or jogging, yoga, and strength training. Effects were comparable to psychotherapy and pharmacotherapy. Exercise worked better when more intense

Population

14 170 participants | Participants with depression (ie, meeting clinical thresholds or diagnosed by a clinician) | No other exclusion criteria, so participants are from any age, and with any comorbidities

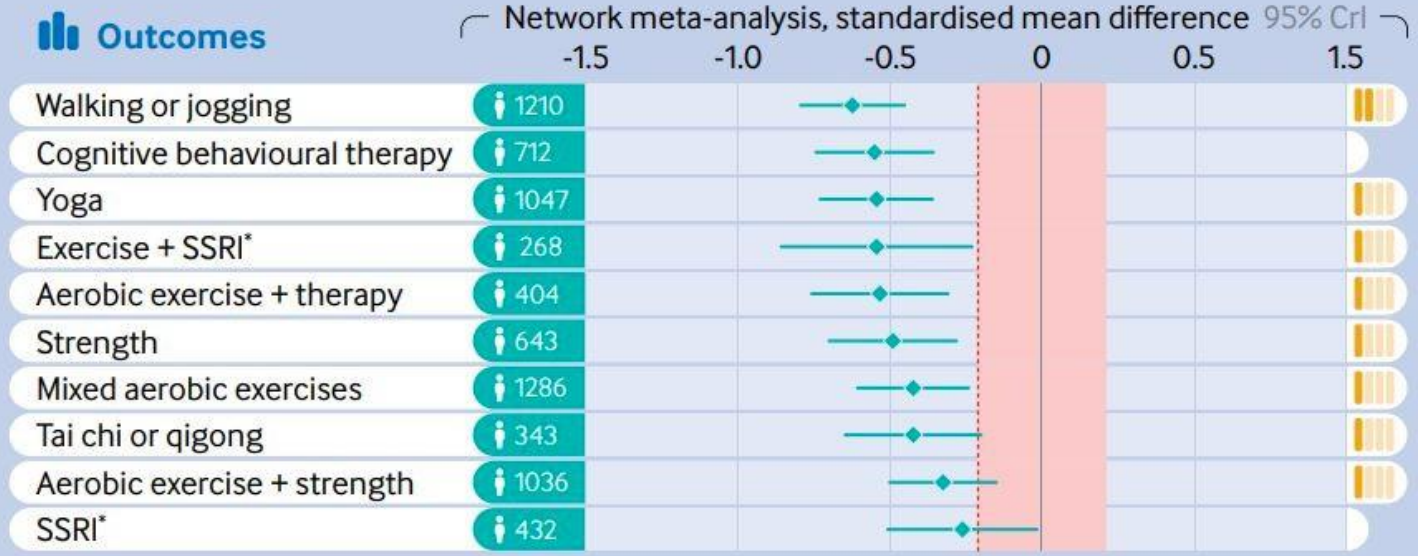
Study design

218 studies | 495 unique arms

Comparison

Different forms of exercise compared with other common treatments for depression. All results are presented as 'compared with active controls.'

Outcomes



https://bit.ly/BMJ-exedep

Effect of exercise for depression: systematic review and network meta-analysis of randomised controlled trials

Objective To identify the optimal dose and modality of exercise for treating major depressive disorder, compared with psychotherapy, antidepressants, and control conditions.

The **effects of exercise were proportional to the intensity prescribed**. Strength training and yoga appeared to be the most acceptable modalities. Results appeared robust to publication bias, but only one study met the Cochrane criteria for low risk of bias. As a result, confidence in accordance with CINeMA was low for walking or jogging and very low for other treatments.

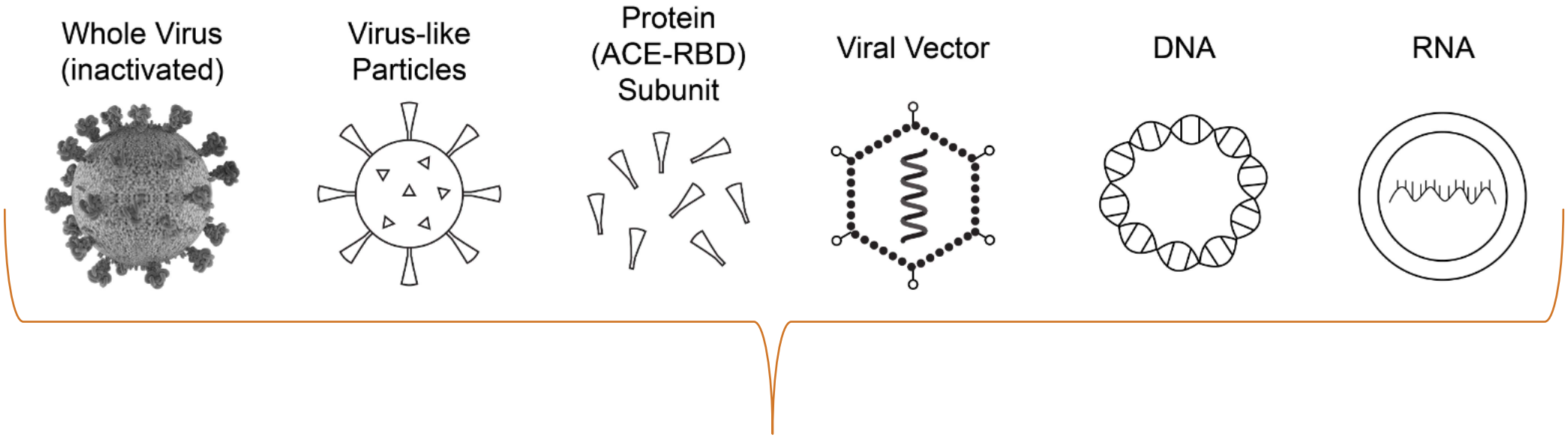
https://www.bmj.com/content/384/bmj-2023-075847

Types of Side Effects of Vaccines

1. Reactogenicity
2. Anaphylaxis
3. Technical errors
4. Vaccine-specific side effects

SARS-CoV-2 Vaccine platforms: Vaccine-specific AE

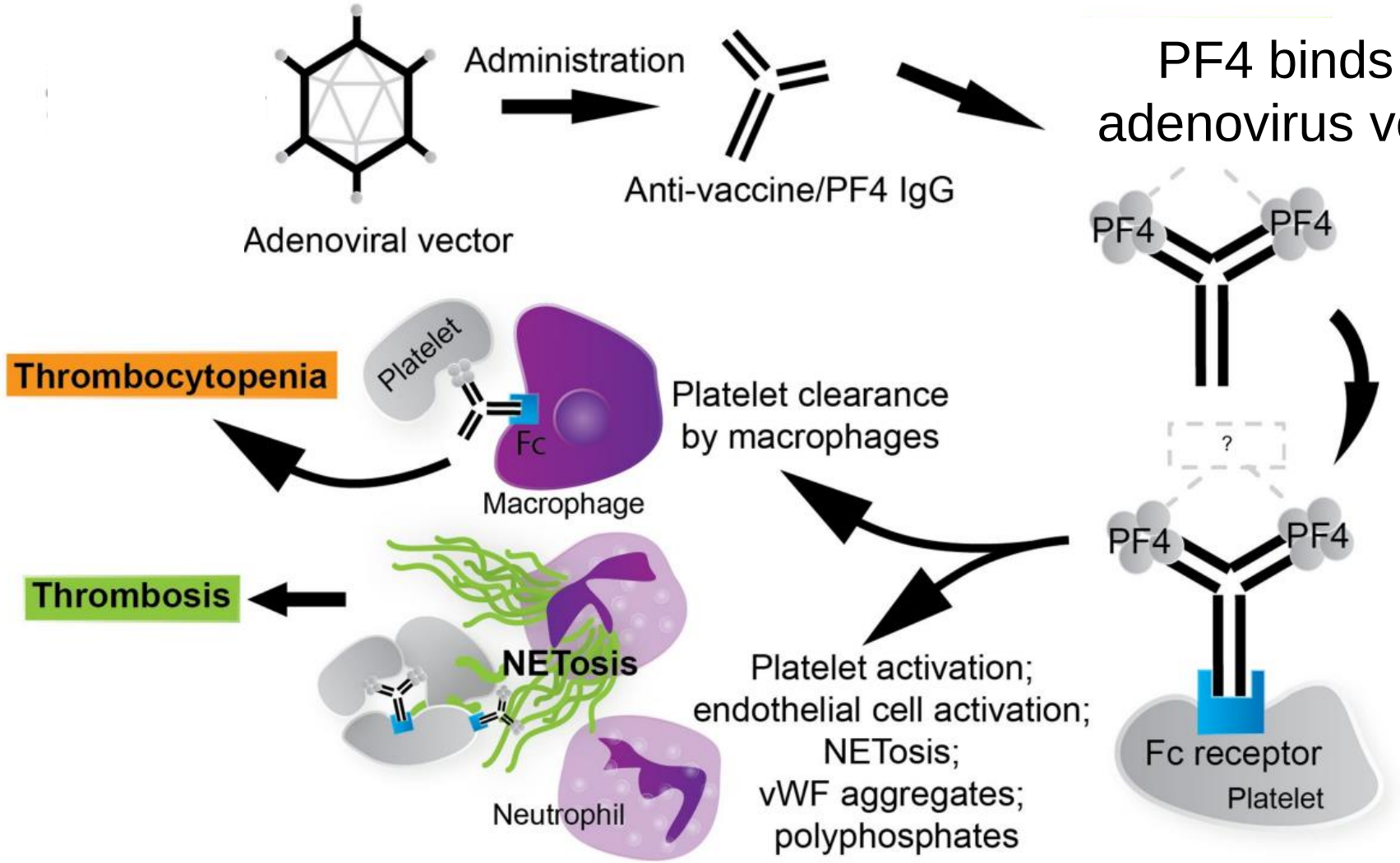
Coincidental or Causal association? Frequency?



?

1. Facial Paralysis: causal relation, but protection by vaccine
2. **Vaccine Induced Thrombocytopenia and Thrombosis (VITT)**
3. Myocarditis

Pathogenesis of VITT



Frequency of VITT by Vaccine

Manufacturer	Vaccine name	Vaccine type	Vaccine efficacy	VITT Incidence, as of Q1 2022	VITT mortality rate, as of Q1 2022	Total # of vaccines administered in the USA or EU (in millions) (5)
Oxford/AstraZeneca	ChAdOx1 nCoV-19	Adenoviral vector (Y25)	63% (6)	1/64,000 (7), 1/125,000 (8)	18% (7)	67
Johnson & Johnson/Janssen	Ad26.COV2.S	Adenoviral vector (Ad26)	67% (9)	1/310,000 (7), 1/200,000 (8)	15% (7, 10)	37
Gamaleya Research Institute of Epidemiology and Microbiology	Sputnik V	Adenoviral vector (Ad26 and Ad5)	91% (6)	Low (11)	n/a	1.8
CanSino Biologics	Ad5-nCoV-S	Adenoviral vector (Ad5)	58% (12)	n/a	n/a	n/a

On HIT and VITT

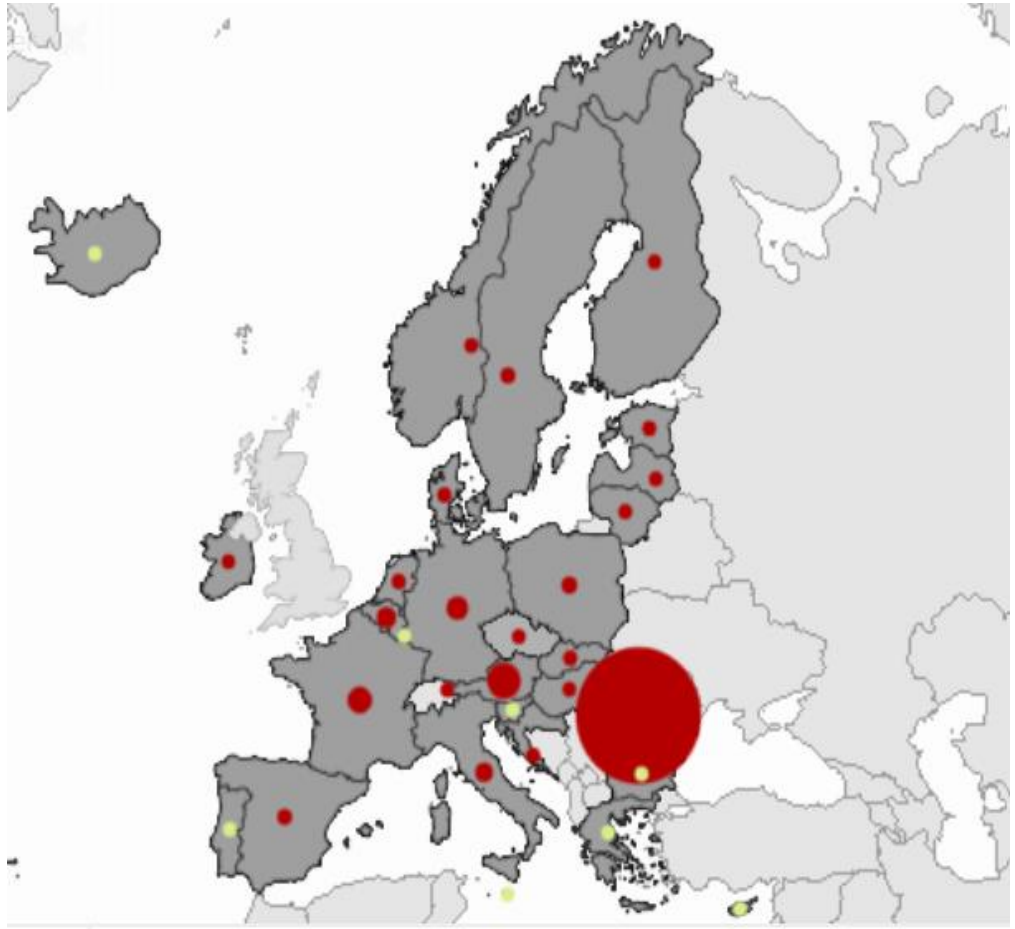
- **Only (?) adenoviral vector-based COVID19 vaccines may cause**
  - Vaccine-induced immune thrombocytopenia and thrombosis (VITT)
  - Seen in ~1 in 100,000 vaccinees (??)
  - VITT is diagnosed 5–30 days post-vaccination
  - Clinically: thrombocytopenia, elevated D-dimers, platelet-activating anti-platelet factor 4 (PF4) antibodies, thrombosis - especially at atypical sites (e.g. cerebral venous sinus and/or splanchnic veins)
  - Very similar to heparin-induced thrombocytopenia (**HIT**).
  - Both: caused by anti-PF4 antibodies with platelet and leukocyte activation resulting in massive thrombo-inflammation.
  - Trigger: adenovirus vector

GLOBAL HEALTH PRESS

Measles – Europe (ECDC) February 10th, 2024

Ending the COVID19-gap?

EU/EEA (without UK)	1607
EU/EEA (with UK until 2019)	1607
Austria	186
Belgium	52
Bulgaria	0
Croatia	3
Cyprus	0
Czechia	1
Denmark	5
Estonia	4
Finland	1
France	101
Germany	73



HEV increase in Europe

- Hepatitis E virus (HEV) infections have been noted in the EU/EEA with **520 cases reported in ten countries in January 2024**
- An unusual increase is reported in **Belgium, Czechia and Finland (vs.** 2023)
- Belgium: **sub-genotype 3c** was most frequently identified
- **In Finland, 21/24** interviewed cases reported consuming **mettwurst or salami of various brands** during the incubation period, thus raising a hypothesis of these type of meat products as possible vehicles of infection.
- Cases of hepatitis E are likely to continue to be reported in the EU/EEA.

10 Year Efficacy of HEV-Vaccine (Hecolin®, China)

	Vaccine group (n=56 302)		Placebo group (n=56 302)		External control* (n=178 236)		Vaccine *vs* placebo, vaccine efficacy, % (95% CI)	Vaccine *vs* external control	
	Number of patients with hepatitis E	Incidence (per 10 000 person-years)	Number of patients with hepatitis E	Incidence (per 10 000 person-years)	Number of patients with hepatitis E	Incidence (per 10 000 person-years)		Unstandardised vaccine efficacy, % (95% CI)	Standardised vaccine efficacy,† % (95% CI)
Modified intention to treat									
0–66 months	7	0·2	60	1·9	207	2·1	88·3% (74·5 to 95·5)	89·3% (77·5 to 95·7)	88·4% (75·7 to 95·4)
0–78 months	8	0·2	66	1·8	239	2·1	87·9% (74·7 to 95·0)	89·4% (78·8 to 95·5)	88·8% (77·6 to 95·2)
0–90 months	9	0·2	70	1·7	267	2·0	87·1% (74·2 to 94·4)	89·3% (79·4 to 95·2)	89·4% (79·5 to 95·2)
0–102 months	11	0·2	74	1·5	288	1·9	85·1% (71·8 to 92·9)	87·9% (78·0 to 94·0)	88·1% (78·4 to 94·1)
0–120 months	13	0·2	77	1·4	325	1·8	83·1% (69·4 to 91·4)	87·3% (78·0 to 93·3)	88·0% (79·1 to 93·7)
Per protocol									
7–66 months	3	0·1	51	2·1	186	2·1	94·1% (81·8 to 98·8)	94·1% (82·5 to 98·8)	93·9% (81·9 to 98·8)
7–78 months	4	0·1	57	2·0	218	2·1	93·0% (81·0 to 98·2)	93·3% (82·6 to 98·2)	93·5% (83·1 to 98·2)
7–90 months	5	0·1	60	1·8	246	2·0	91·7% (79·5 to 97·4)	92·6% (82·4 to 97·6)	93·4% (84·4 to 97·9)
7–102 months	7	0·2	64	1·7	267	1·9	89·1% (76·2 to 95·8)	90·4% (80·0 to 96·2)	91·4% (82·0 to 96·6)
7–120 months	9	0·2	67	1·5	304	1·8	86·6% (73·0 to 94·1)	89·2% (79·2 to 95·1)	90·6% (81·9 to 95·7)
First two doses subset									
1·5–30 months	0	0·0	6	2·3	85	2·0	100·0% (15·4 to 100·0)	100·0% (29·6 to 100·0)	100·0% (31·1 to 100·0)
1·5–54 months	1	0·3	6	1·8	167	2·1	83·4% (–36·7 to 99·6)	86·2% (21·9 to 99·7)	85·7% (19·1 to 99·6)
1·5–78 months	1	0·2	6	1·5	238	2·0	83·4% (–36·5 to 99·6)	88·3% (34·2 to 99·7)	88·1% (32·8 to 99·7)
1·5–102 months	1	0·2	7	1·5	287	1·9	85·8% (–10·4 to 99·7)	89·1% (39·0 to 99·7)	89·1% (39·0 to 99·7)
1·5–120 months	1	0·2	7	1·3	324	1·8	85·8% (–10·4 to 99·7)	89·8% (42·7 to 99·7)	89·9% (43·4 to 99·7)

What is Hecolin®?

- **Hecolin® is a recombinant vaccine** used for prevention of hepatitis E
- Contains hepatitis E virus **(HEV)-like particles** using recombinant *Escherichia coli* expression system.
- Approved for use in China in people aged 16 and above.
- Recommended for individuals at high risk of HEV infection.
- Main adverse events associated with its use have been local reactions at the injection site, no safety concerns
- Schedule with 3 doses administered in a 0, 1 and 6 months
- Limited data: two doses (at 0 and 6 months, or at 0 and 1 month) lead to a high rate of seroconversion though the antibody titers are lower.
- **Very high efficacy rate, primarily applicable to genotype 4 disease; data on disease caused by other genotypes are either too limited (genotype 1) or are not available (genotype 2 and 3).**
- **Vaccine lowers, but does not eliminate, the risk of asymptomatic infection.**
- **Also, there are no data on protection against severe forms of disease, namely acute liver failure, which is particularly frequent in pregnant women.**
- **Some limited available data suggest that the vaccine is safe in pregnant women**

What we talked about today

- Older adults who exercised before the pandemic were at lower risk of COVID infection and hospitalization
- Cognitive issues and depression in those with long COVID
- COVID infection linked to fatigue
- Even low intensity activities (walking/yoga) help with depression
- Vaccine induced thrombocytopenia and thrombosis (VITT)
- Measles in Europe – more to come after the COVID19-gap?
- Hepatitis E in Europe – vaccination useful?