

Immediate seizure worsening and 6-month outcomes following first and second SARS-CoV2 mRNA vaccinations: a multicenter study with a nationwide survey

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Japan Epilepsy Society

Disclosure of conflict of interest

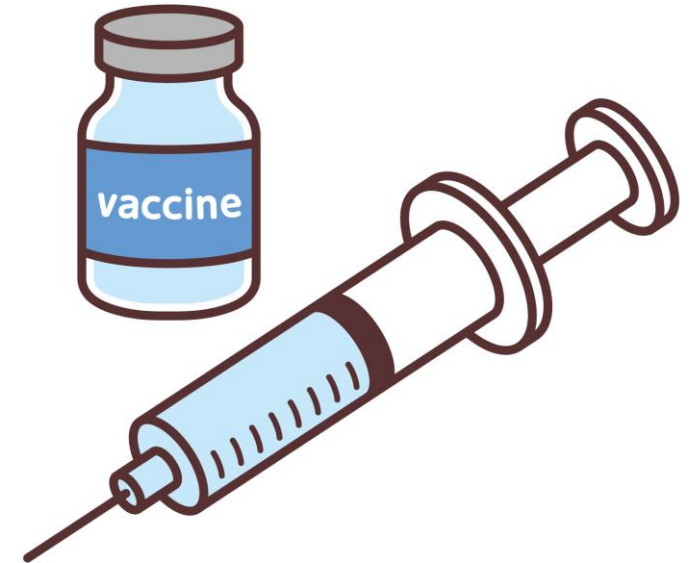
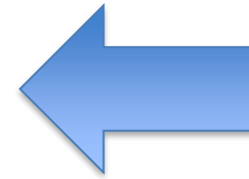
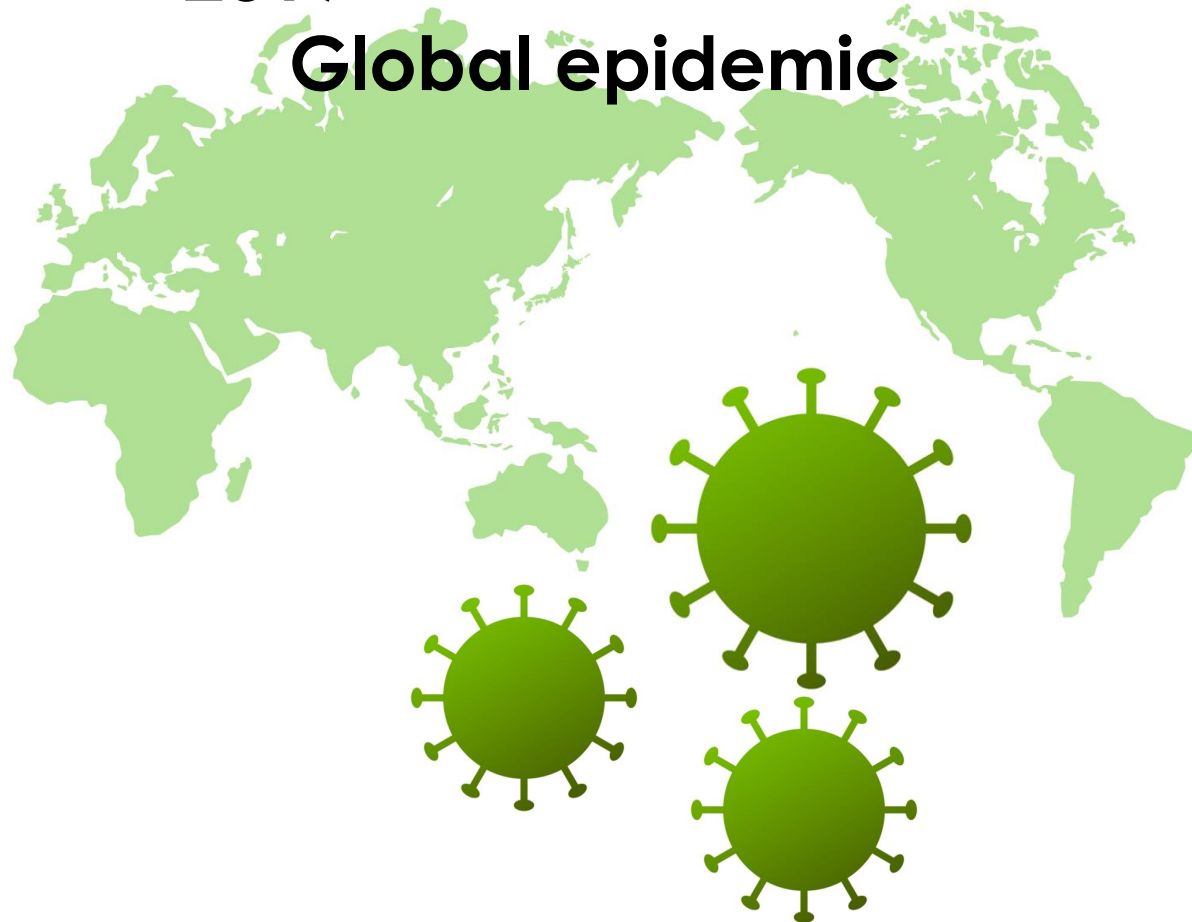
Name of presenter: Megumi Nonaka

This presentation is not related to any company with a conflict of interest that should be disclosed

The novel coronavirus disease 2019 (COVID-19)

2019~

Global epidemic



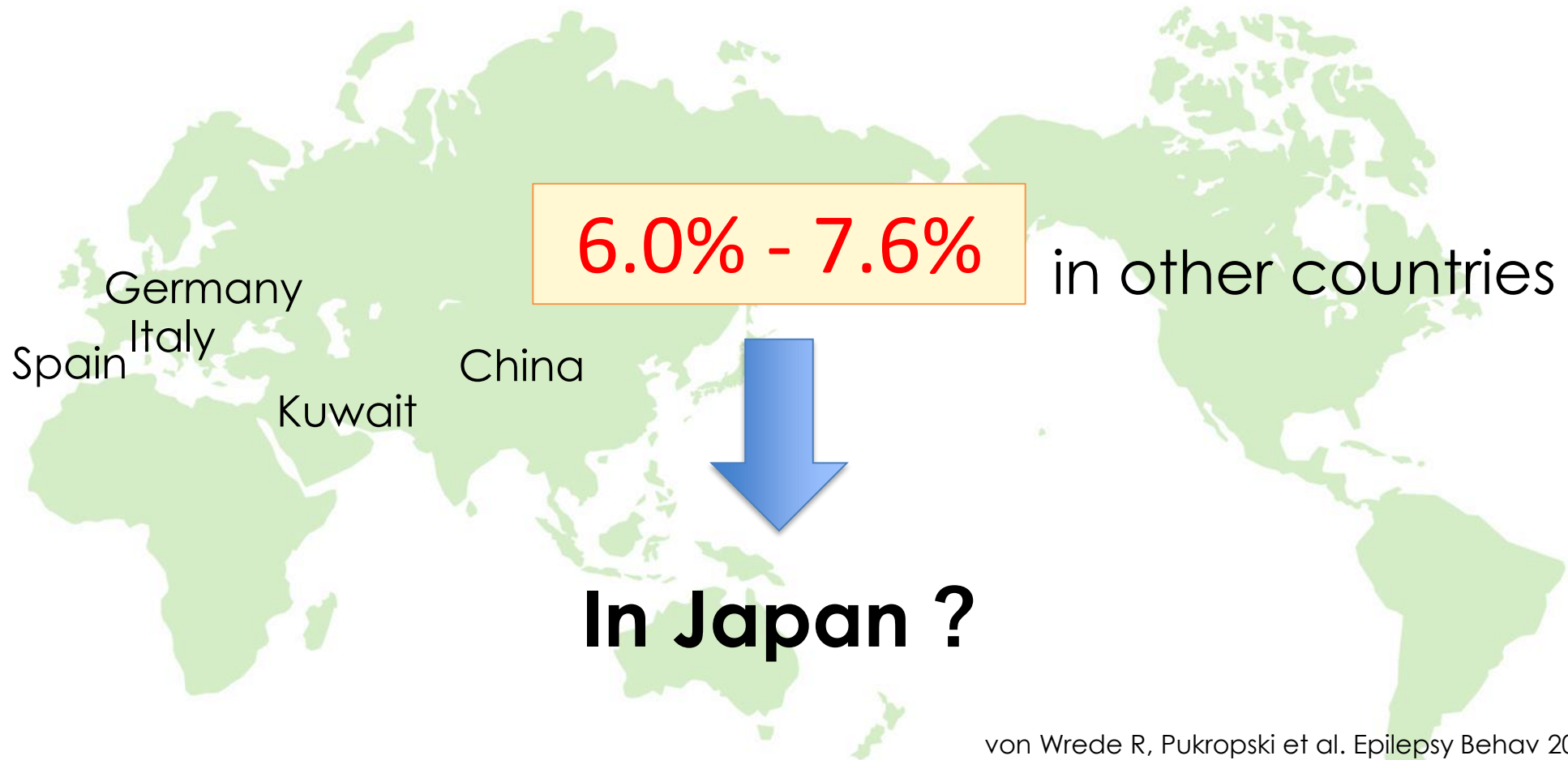
Safe in people with epilepsy ?

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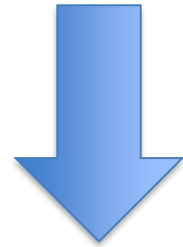
Seizure worsening rate in PWE after SARS-CoV2 vaccination



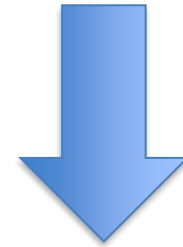
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Objective

To investigate the real world data of seizure worsening after SARS-CoV2 vaccination in Japan



① Multicenter study at four tertiary hospitals in Hiroshima

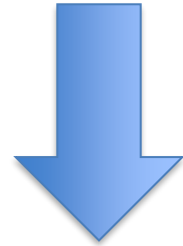


② Nationwide questionnaire in Japan

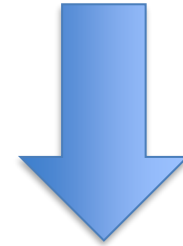


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Method

① Multicenter study at four tertiary hospitals in Hiroshima



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2021

Apr.

May.

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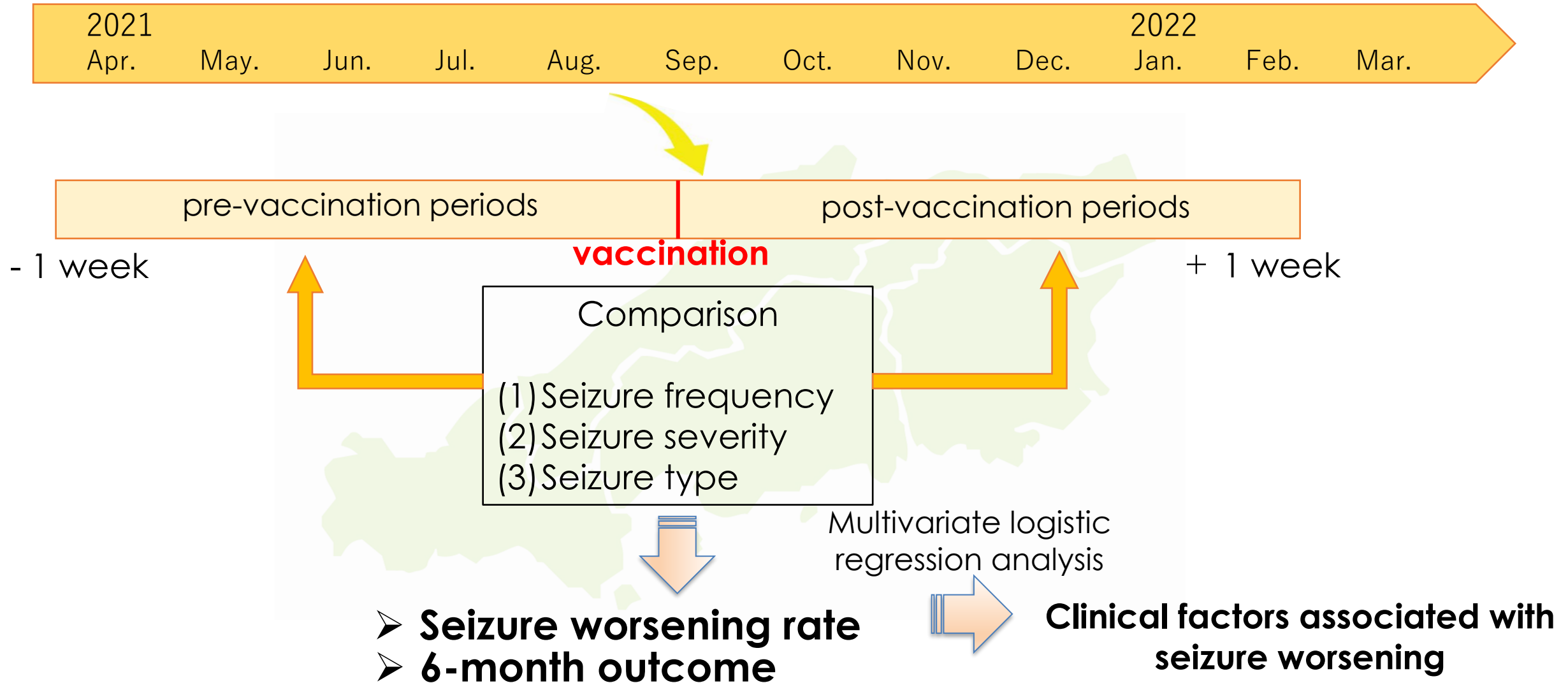
Feb.

Mar.

- Who: 332 PWEs
- When: April 2021 - March 2022
- Where: 4 tertiary hospitals in Hiroshima
- What: seizure worsening and 6-month outcomes
- How: observational study

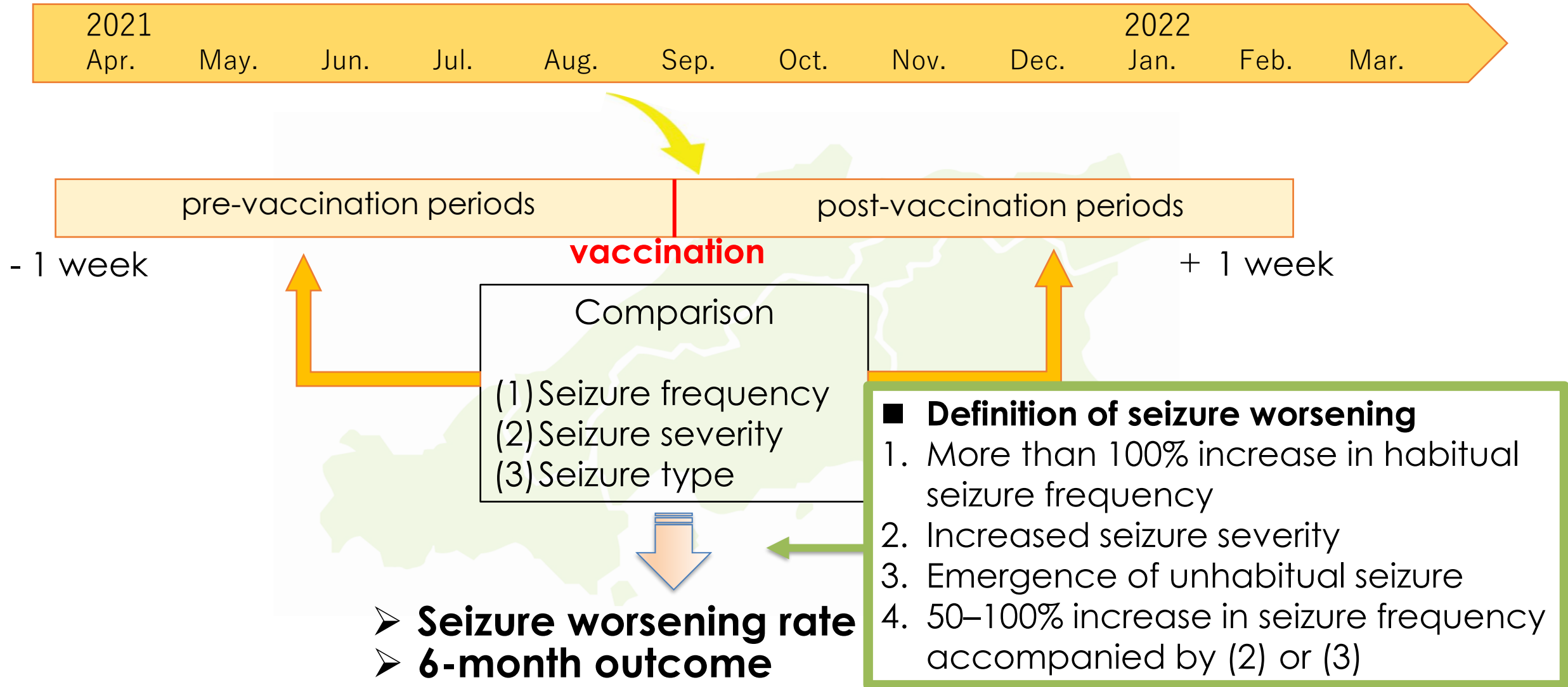
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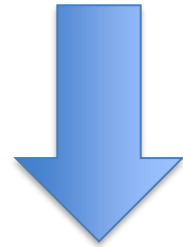
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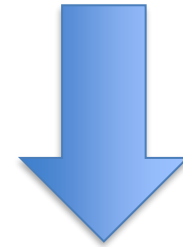


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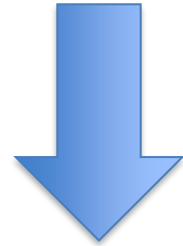


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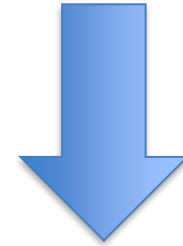


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- Who: 261 clinicians
- When: April 2021- March 2022
- Where: 99 institutes in Japan
- What: **self-reported** seizure worsening
- How: retrospective observational study

This study was not official survey and approved by the Ethics Committee of Hiroshima University Hospital (No. E-2812).

We

Questions via e-mail

- Total number of PWE followed by clinicians
- Total number of PWE with seizure worsening

261 clinicians

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We thank all the physicians who contributed to our nationwide questionnaire.

Result 1 Clinical characteristics in multicenter study

PWE (n = 332)

Age, years (mean ± SD)	36.4 ±17.2
Onset age, years (mean ± SD)	23.9 ±18.5
Disease duration (mean ± SD)	12.2 ±12.3
Gender, male (n, %)	168 (51.2)
Epilepsy classification (n, %)	
- Generalized epilepsy	81 (24.4)
- Focal epilepsy	200 (60.2)
-Temporal lobe epilepsy	82 (24.7)
-Frontal lobe epilepsy	51 (15.4)
-Unclassified	51 (15.4)
Comorbidity (n, %)	
-ADHD/ASD	13 (3.9)
-Intellectual disability	66 (20.6)

Seizure type (n, %)	
- FAS	68 (20.5)
- FIAS	142 (42.8)
- Myoclonus	41 (12.3)
- FBTCS	125 (37.7)
- BTCS	95 (28.6)
- PNES	20 (6.0)
Seizure frequency (n, %)	
- Weekly or more	60 (18.1)
- Monthly	96 (28.9)
- Yearly or less	158 (47.6)
Drug-resistant epilepsy (n, %)	101 (30.4)
Number of ASMs (mean ± SD)	1.8 ±1.2

Drug-resistant epilepsy: PWE taking 2 or more ASMs with seizures monthly or more

Result 2 Vaccination rate in multicenter study

Vaccination rate

84.9% in our study



80% : BNT162b2 (Pfizer-BioNTech)
20% : mRNA-1273 (Moderna)

PWE who were vaccinated (n = 282)

Adverse reaction	
Adverse reaction, yes (n, %)	146 (51.8)
- Yes, after the first dose	63 (22.3)
- Yes, after the second dose	137 (48.6)
- Fever (over 37.0°C), yes (n, %)	123 (43.6)

Result 3 Seizure worsening rate in multicenter study

Seizure worsening rate

5.7%

(By closed question)



➤ 6-month outcome
All cases returned to the baseline

Details of seizure worsening

Definite seizure worsening	16	(5.7)
– Increased habitual seizure frequency	12	(4.3)
– increase by >100%	10	(3.5)
– increase by 50–100%	2	(0.7)
– Increased seizure severity	6	(2.1)
– Unhabitual seizure emergence	3	(1.1)
– Seizures on the day of vaccination	4	(1.4)
– Seizure relapse in several years	3	(1.1)
– Hospitalized for seizure	5	(1.8)
– Status epilepticus	4	(1.4)

Result 4 Differences in clinical characteristics between PWE with or without seizure worsening following the vaccination

	Seizure worsening (n=18)	Without Seizure worsening (n=263)	P value
Age, years (mean \pm SD)	39.3 (17.1)	37.6 (17.7)	0.71
Sex, male (n, %)	8 (50.0)	136 (51.7)	0.89
Seizure frequency, monthly or more (n, %)	12 (75.0)	124 (46.6)	0.025
Drug-resistant epilepsy (n, %)	10 (62.5)	76 (28.6)	0.007
Febrile seizure, yes (n, %)	2 (12.5)	31(11.7)	0.92
EEG, spike (n, %)	7 (43.8)	124 (51.0)	0.57
MRI, hippocampal sclerosis (n, %)	2 (12.5)	21 (7.9)	0.54
Type of vaccine , BNT162b2 (n, %)	14 (87.5)	208 (78.2)	0.35
Adverse reaction, yes (n, %)	10 (62.5)	136 (51.1)	0.37
-fever, yes (n, %)	10 (62.5)	113 (42.5)	0.12

Result 4 Differences in clinical characteristics between PWE with or without seizure worsening following the vaccination

	Seizure worsening (n=18)	Without Seizure worsening (n=263)	P value
Epilepsy classification (n, %)			
– Generalized epilepsy	3 (18.8)	59 (22.2)	0.74
– Focal epilepsy	13 (81.3)	166(62.4)	0.11
– Temporal lobe epilepsy	6 (37.5)	69 (25.9)	0.33
– Frontal lobe epilepsy	1 (6.3)	46 (17.3)	0.20
Seizure type (n, %)			
– FAS	6 (37.5)	52 (19.6)	0.11
– FIAS	14 (87.5)	114 (42.9)	<0.001
– Myoclonic seizure	1 (6.3)	30 (11.3)	0.50
– FBTCS	8 (50.0)	99 (37.2)	0.31

Result 5 Multivariate analysis of factors associated with seizure worsening

	OR	95%CI	P value
FIAS	7.0	1.50–32.77	0.014
Drug-resistant epilepsy	2.5	0.84-7.43	0.10

FIAS and drug-resistant epilepsy were selected for logistic regression analysis (force entry).

FIAS was independently associated with worsening

Result 6 Seizure worsening rate in nationwide questionnaire in Japan

261 clinicians (99 institutes)

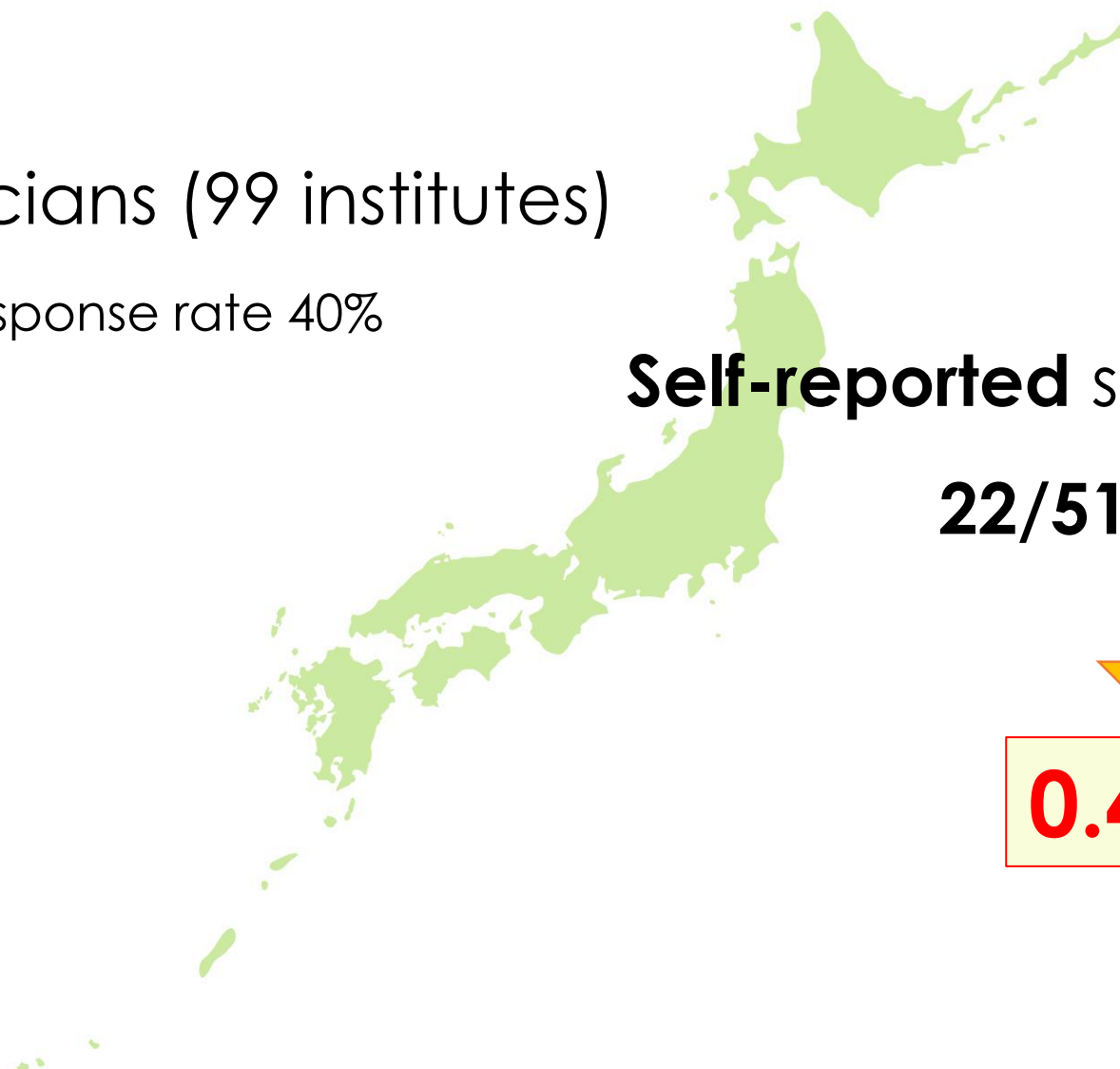
response rate 40%

Self-reported seizure worsening

22/5156 PWE



0.43%



Discussion 1 Seizure worsening and 6-month outcomes

Seizure worsening rate in multicenter study



**All worsening events were transient.
There were no cases with poor outcomes.**

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**All worsening events were transient.
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Self-reported
seizure worsening
0.43%



Unreported seizure worsening
which had little or no real-life effect.

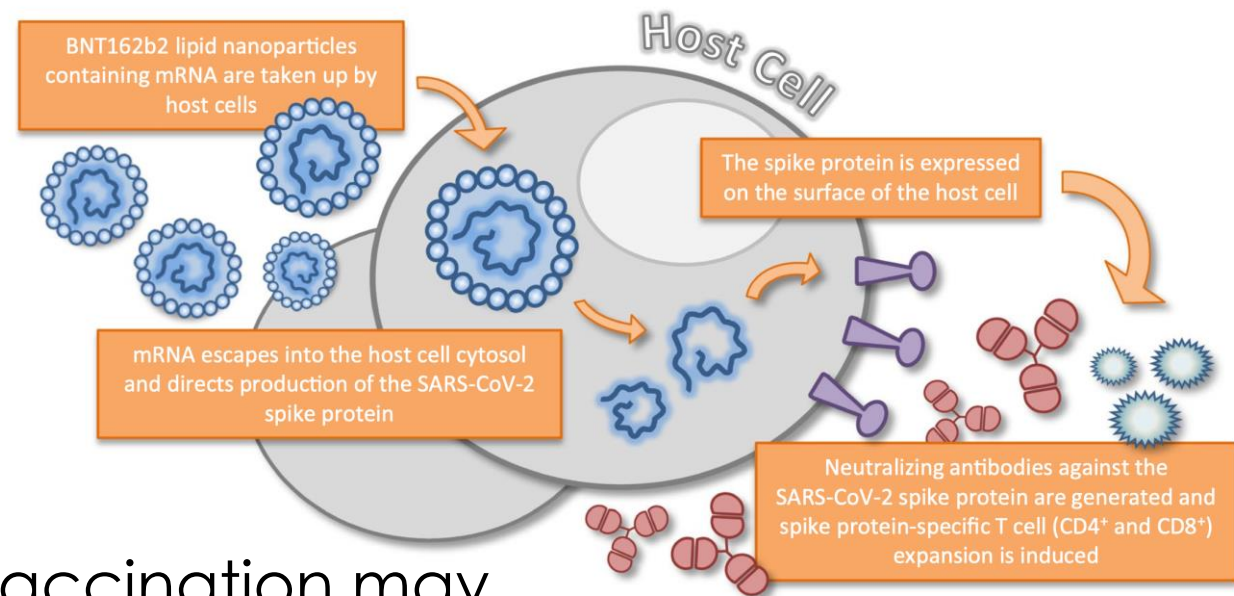
Discussion 2 Potential mechanism of seizure worsening

Risk factor of seizure worsening

FIAS



Inflammation produced by vaccination may have an effect on the **limbic system** ?



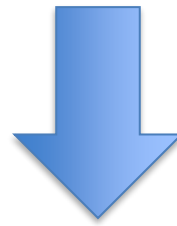
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Garrido I, Lopes S, Simões MS, et al. *J Autoimmun* 2021;125:102741.

Conclusion

- Some PWE, particularly with FIAS, exhibited seizure worsening.
- Seizure worsening was a monophasic course and there were no cases with poor outcomes after 6 months of follow-up.



- There is little evidence that worsening seizures discourage current and future vaccinations.

This study is in submission.