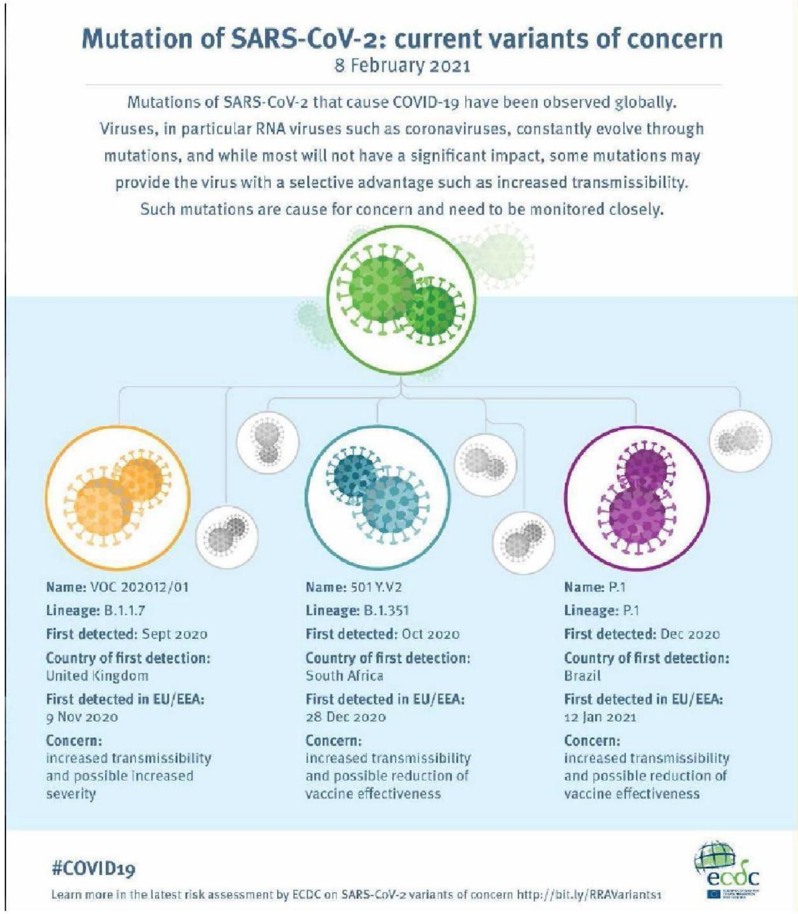


Mutation of SARS-CoV-2: current variants of concern

8 February 2021

Mutations of SARS-CoV-2 that cause COVID-19 have been observed globally. Viruses, in particular RNA viruses such as coronaviruses, constantly evolve through mutations, and while most will not have a significant impact, some mutations may provide the virus with a selective advantage such as increased transmissibility. Such mutations are cause for concern and need to be monitored closely.

Name: VOC 202012/01
Lineage: B.1.1.7
First detected: Sept 2020
Country of first detection: United Kingdom
First detected in EU/EEA: 9 Nov 2020
Concern: increased transmissibility and possible increased severity

Name: 501Y.V2
Lineage: B.1.351
First detected: Oct 2020
Country of first detection: South Africa
First detected in EU/EEA: 28 Dec 2020
Concern: increased transmissibility and possible reduction of vaccine effectiveness

Name: P.1
Lineage: P.1
First detected: Dec 2020
Country of first detection: Brazil
First detected in EU/EEA: 12 Jan 2021
Concern: increased transmissibility and possible reduction of vaccine effectiveness

#COVID19

Learn more in the latest risk assessment by ECDC on SARS-CoV-2 variants of concern http://bit.ly/RRAVariants1

Rijksinstituut voor Volksgezondheid
en Milieu
Ministerie van Volksgezondheid,
Welzijn en Sport

SARS-CoV2 Varianten

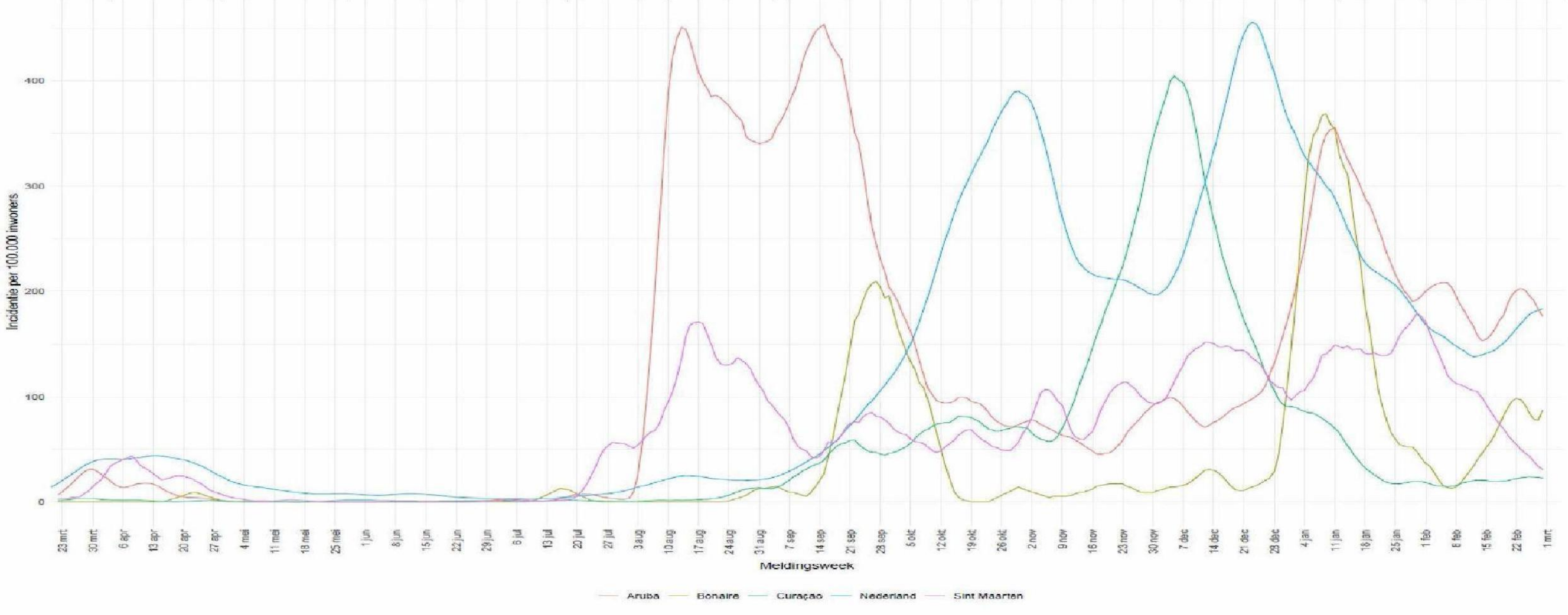
Consequenties voor Nederlandse overzeese Rijksdelen

5.1.2e 5.1.2e 5.1.2e 5.1.2e

SARS-CoV2 varianten 4-3-2021

Epidemiologie 4 landen

	Populatie	Ongeregisteerden	inw. Totaal (schatting)	aantal 17-2	aantal 24-2	aantal 3-3	Patienten laatste week	Patienten laatste 2 weken	incidentie /100.000/week	**Inc. tot. Inw./week**
Curacao	158.665	15.000	173.665	4658	4705	4740	35	82	**22,1**	**20,2**
Aruba	112.190	15.000	127.190	7513	7775	7973	198	460	**176,5**	**155,7**
Sint Maarten	41.109	15.000	56.109	2021	2050	2065	15	44	**36,5**	**26,7**
Bonaire	20.104	1.000	21.104	381	403	440	37	59	**184,0**	**175,3**
St Eustatius	3.138	0	3.138	20	20	20	0	0	**0,0**	**0,0**
Saba	1.915	0	1.915	6	6	6	0	0	**0,0**	**0,0**

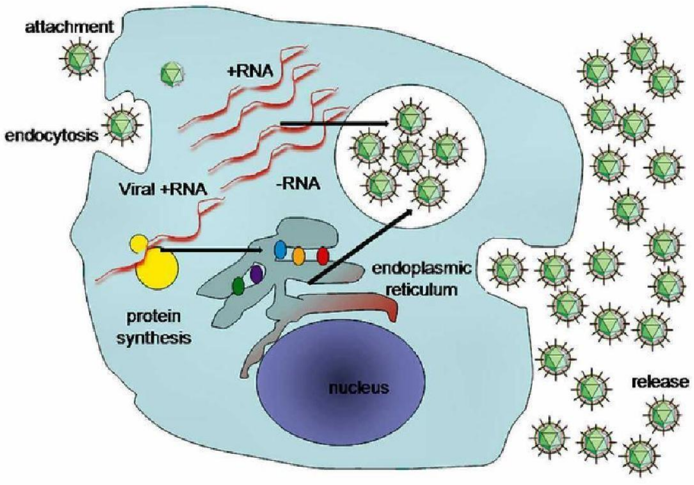


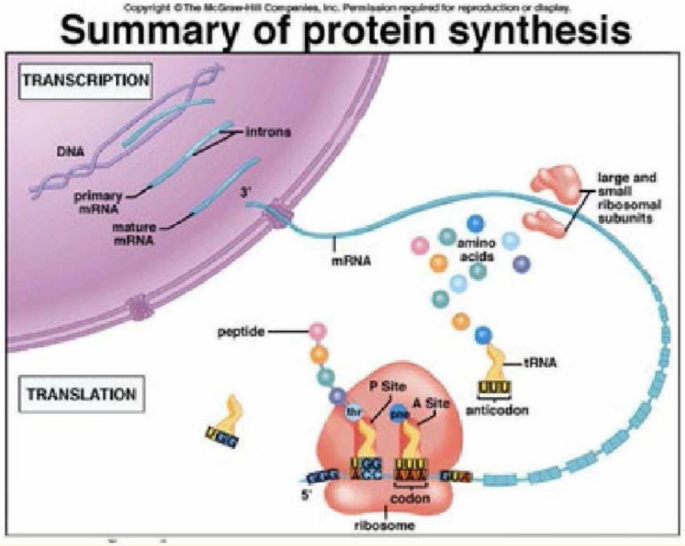
Biologie eiwitconstructie

- DNA, RNA, 4 nucleotiden (CTGA; Cytosine, Thymine, Guanine, Adenine))
- Triplets (codon) coderen voor 20 aminozuren die eiwitten vorm geven met ieder specifieke eigenschappen
- Genen, nummering nucleotiden
- Foutjes in copieren: mutaties

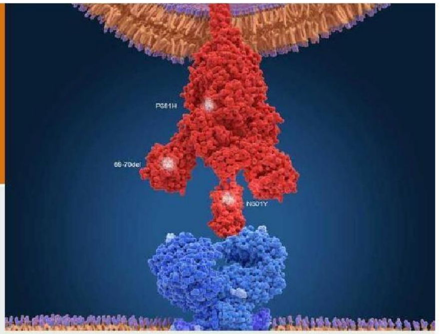
Bekende mutaties bij Sars-CoV-2:

- N501Y (Asparagine op 501 → Tyrosine)
  - Gevolg: R_t hoger, virus besmettelijker
- E484K (Glutaminezuur op 484 → Lysine)
  - Gevolg: antistoffen na natuurlijke infectie of vaccinatie minder effectief



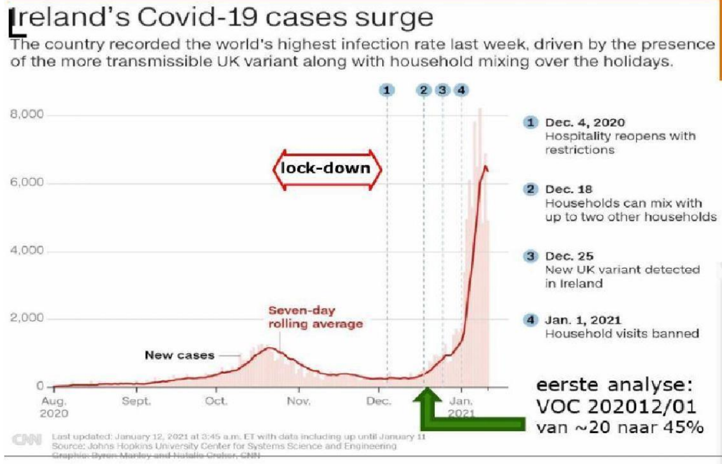


De Variants of Concern (VOC)



Variant	Weten schap pelijke naam	Rt	Reactie vaccin	Ernst beloop	Waar?	Mutaties
Britse variant	B.1.1.7	>, 1,4 x	=	>	VK, West-Europa, Noord Amerika	P681H, N501Y, 69-70del,(E484K)
Zuid Afrikaanse variant	B.1.351	> 1,5 x	<	=	Zuidelijk Afrika, Europa, UAE	K417N, E484K, N501Y
Braziliaans P1	B.1.1.28 P1	>?	<?	=	Amazonas, Manaus Peru, colombia	12, K417T, E484K, N501Y
Braziliaans P2	B.1.1.28 P2	>	<	?	Brazilië	4, E484K
Californië variant	B.1.429	>?	?	?	Z.W. VS	L452R
New York Variant	B.1.526	>?	?	?	N.O. VS	

B.1.1.7 in VK en Ierland


Ireland's Covid-19 cases surge

The country recorded the world's highest infection rate last week, driven by the presence of the more transmissible UK variant along with household mixing over the holidays.

① Dec. 4, 2020
Hospitality reopens with restrictions

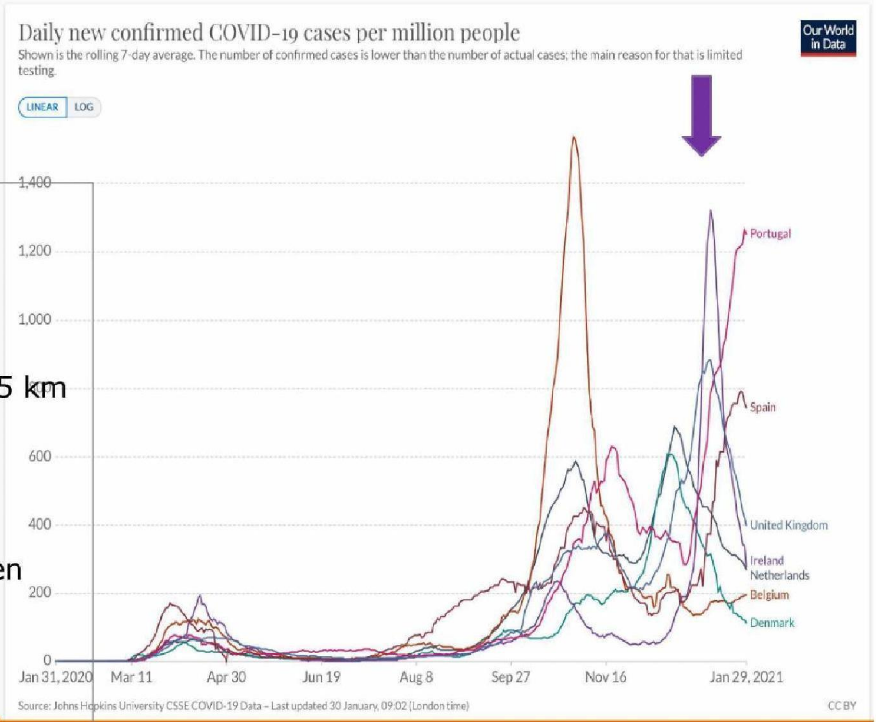
② Dec. 18
Households can mix with up to two other households

③ Dec. 25
New UK variant detected in Ireland

④ Jan. 1, 2021
Household visits banned

Last updated: January 12, 2021 at 3:45 a.m. ET with data including up until January 11
Source: Johns Hopkins University Center for Systems Science and Engineering
Graphic: Byron Manley and Natalie Croker, CNN

eerste analyse:
VOC 202012/01
van ~20 naar 45%


Daily new confirmed COVID-19 cases per million people

Shown is the rolling 7-day average. The number of confirmed cases is lower than the number of actual cases; the main reason for that is limited testing.

Source: Johns Hopkins University CSSE COVID-19 Data – Last updated 30 January, 09:02 (London time)

CC BY

Ierland – level 5

(4,9x10^6 inw.)

meer dan 50% VOC202012/01
ziekenhuisbed 2.020 (– 7132 NL)
IC-bed 221 (– 900 NL)

- blijf thuis, géén bezoek indien buiten radius 5 km
- alleenwonenden 'support bubble'
- thuiswerken tenzij essentieel beroep
- scholen gesloten, contactberoepen gesloten
- winkels muv voedsel gesloten, musea gesloten
- bouw stilgelegd, tenzij ..
- huwelijk max 6; begrafenis max 10
- kerkdiensten alleen on-line
- sportscholen gesloten

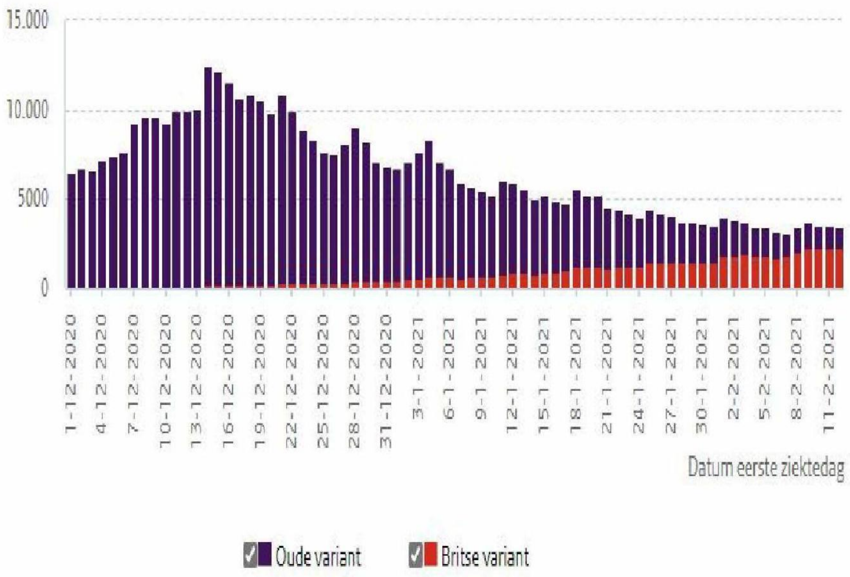
B.1.1.7 in Nederland

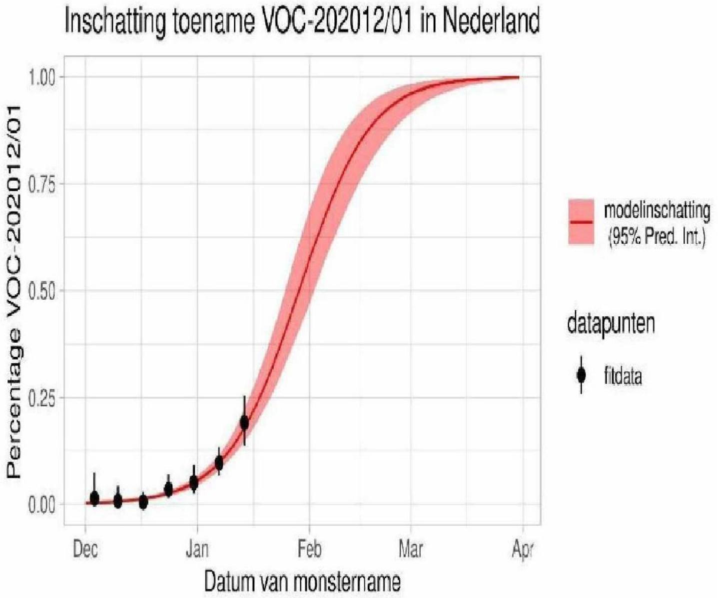
Uit analyse Nederlandse data:

- verdubbelingstijd van 6.8 dagen
- op 12 februari 67% van EZD UK variant

Rt Getal (obv 29 januari)

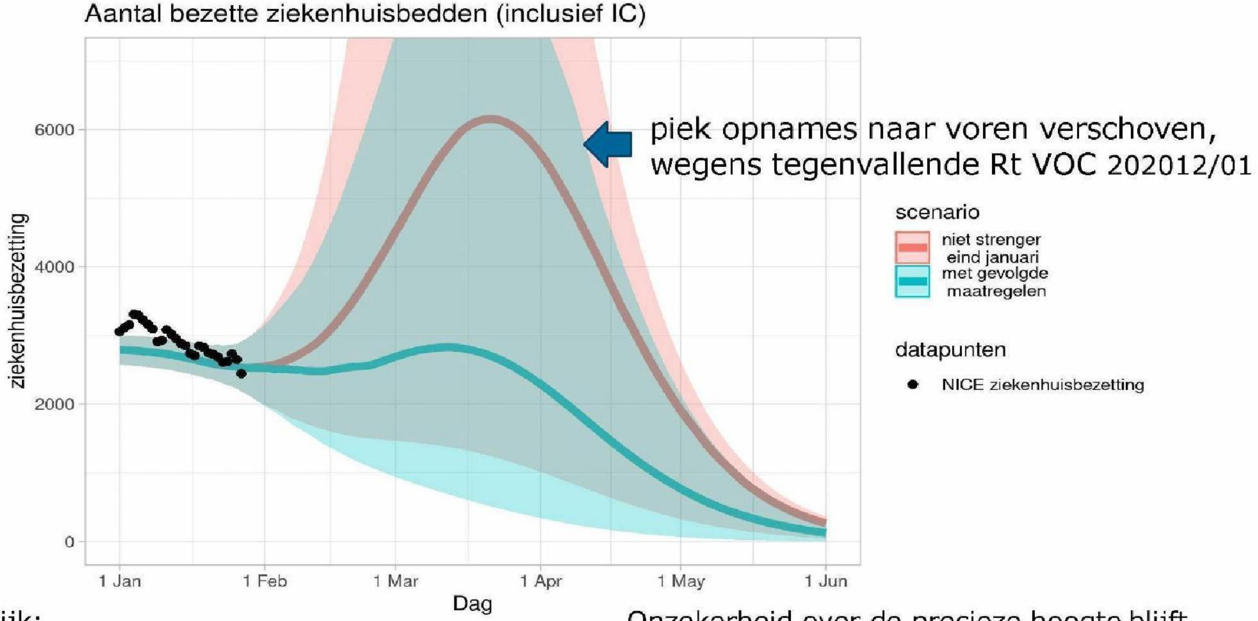
- samen: 0.96 (0.93 - 0.99)
- VOC: 1.15 (1.09 – 1.21)
- wildtype: 0.86 (0.78 – 0.92)





Modellering ziekenhuisopnamen

Bezette ziekenhuisbedden met COVID-19



piek opnames naar voren verschoven, wegens tegenvallende Rt VOC 202012/01

Belangrijk:

- dit is met vaccinatie
- dit is mét immuniteit na infectie

Onzekerheid over de precieze hoogte blijft

- hangt af van toename in Rt
- onzekere inschatting van effect strengere lockdown

B.1.1.7 in Nederland

- Grote onzekerheid – brede onzekerheidsmarges rondom mediaan
- Risico op hoge zorgpiek a.g.v. UK-variant blijft hoog zonder strenge lockdown, *ondanks* vaccinatie
- Toch: flinke reductie a.g.v. vaccinatie, *mits* transmissie voorkomen wordt dus versnellen van aanlevering vaccins mogelijk groot effect
- Huidige maatregelen inclusief vaccinatie lijken een hoge derde golf te voorkomen,
  echter
    - bij langdurig effectieve avondklok en 1 bezoeker per huishouden
    - beperkte toename bij openen primair onderwijs en kinderopvang

veel onzekerheid (ook vanwege vele variant Corona virussen)

moet nog aan model gesleuteld worden

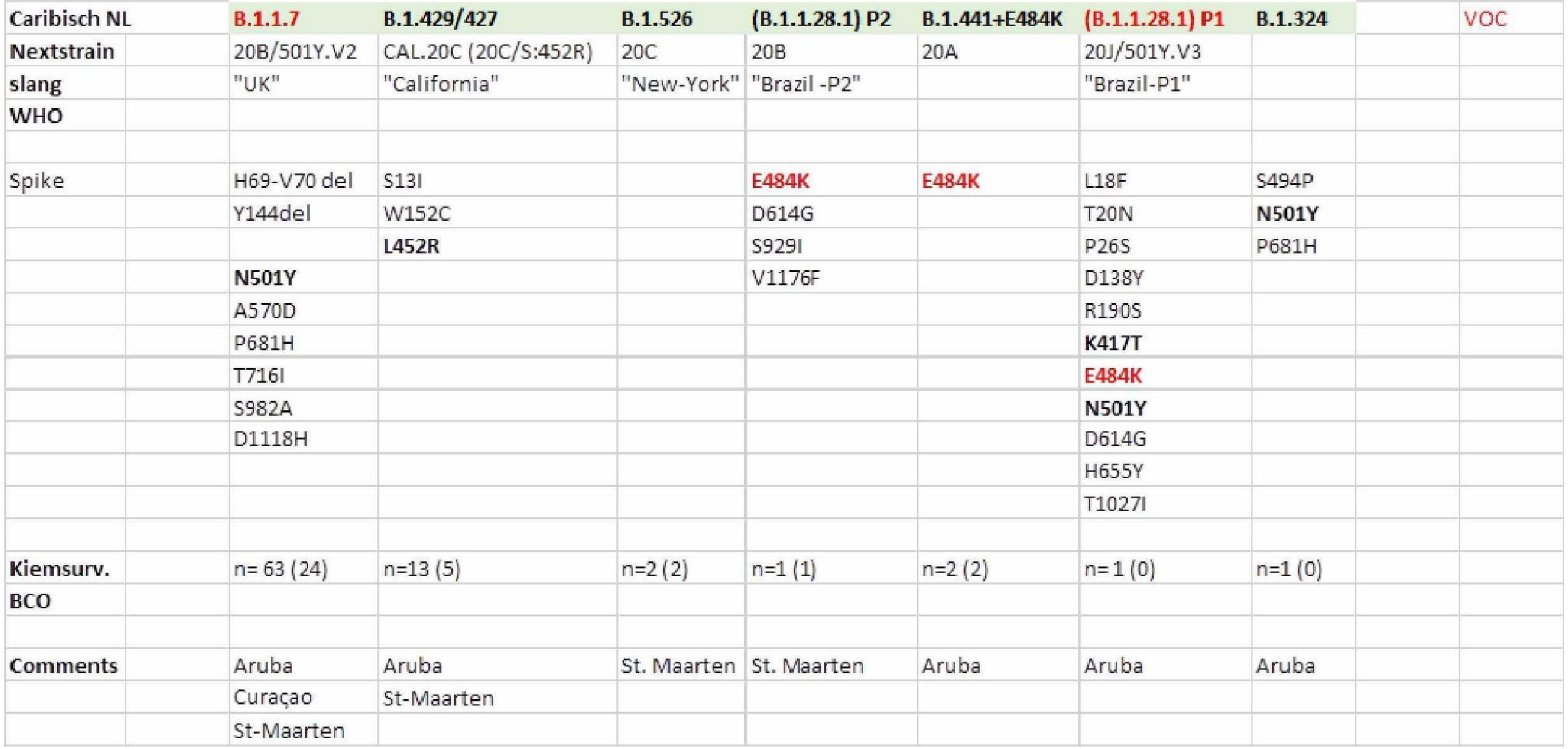
B.1.1.7 in Caribische Regio

Britse variant aangetoond op Aruba (50) en Curacao (2)
Nu snelle stijging op Aruba, laatste 2 weken ~50%.

Reden voor zorg en maatregelen:

1. Opzetten (kiem) surveillance
2. Reisbeleid aanpassen aan epidemiologie
    1. Alleen essentiele reizen tussen eilanden
    2. Testen voor / na aankomst
    3. Quarantaine en testen
    4. Complexe discussie rondom toerisme, maximaal veilig inrichten
3. Strengere maatregelen zijn nodig bij verheffingen
4. Hoge compliance voor vaccinatieprogramma noodzakelijk
5. Aandacht voor ongedocumenteerden

Varianten op de eilanden

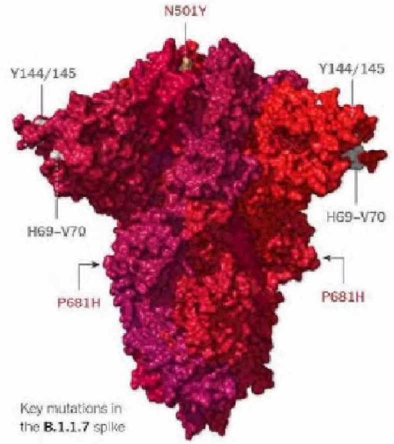


Caribisch NL	**B.1.1.7**	**B.1.429/427**	**B.1.526**	**(B.1.1.28.1) P2**	**B.1.441+E484K**	**(B.1.1.28.1) P1**	**B.1.324**		VOC
Nextstrain	20B/501Y.V2	CAL.20C (20C/S:452R)	20C	20B	20A	20J/501Y.V3			
slang	"UK"	"California"	"New-York"	"Brazil -P2"		"Brazil-P1"			
WHO									
Spike	H69-V70 del	S13I		**E484K**	**E484K**	L18F	S494P		
	Y144del	W152C		D614G		T20N	**N501Y**		
		L452R		S929I		P26S	P681H		
	N501Y			V1176F		D138Y			
	A570D					R190S			
	P681H					**K417T**			
	T716I					**E484K**			
	S982A					**N501Y**			
	D1118H					D614G			
						H655Y			
						T1027I			
Kiemsurv.	n= 63 (24)	n=13 (5)	n=2 (2)	n=1 (1)	n=2 (2)	n= 1 (0)	n=1 (0)		
BCO									
Comments	Aruba	Aruba	St. Maarten	St. Maarten	Aruba	Aruba	Aruba		
	Curaçao	St-Maarten							
	St-Maarten								

Tussenhaakjes is getal van vorige week;VOC zoals benoemd door WHO in rood.

B.1.1.7, 20I/501Y.V1, VOC202012/01

First detected by	United Kingdom
First appearance	20 September 2020
Key mutations	H69/V70 deletion; Y144 deletion; N501Y; A570D; D614G; P681H; S106/G107/F108 deletion in NSP6
Transmissibility*	Increased (43%-82%), increased secondary attack rate (10% to 13%)
Severity*	Likely associated with an increased risk of hospitalisation and death compared to infection with non-VOC viruses.
Neutralization capacity*	Slight reduction but overall neutralizing titers remained above the levels expected to confer protection
Potential impacts on vaccines*	No significant impact on Moderna, Pfizer-BioNTech, and Oxford-AstraZeneca
Potential impacts on diagnostics*	S gene target failure. No impact on Ag RDTs observed
Countries reporting cases (community transmission) as of 23 Feb	101 (45)



https://www.nytimes.com/interactive/2021/health/coronavirus-variant-tracker.html

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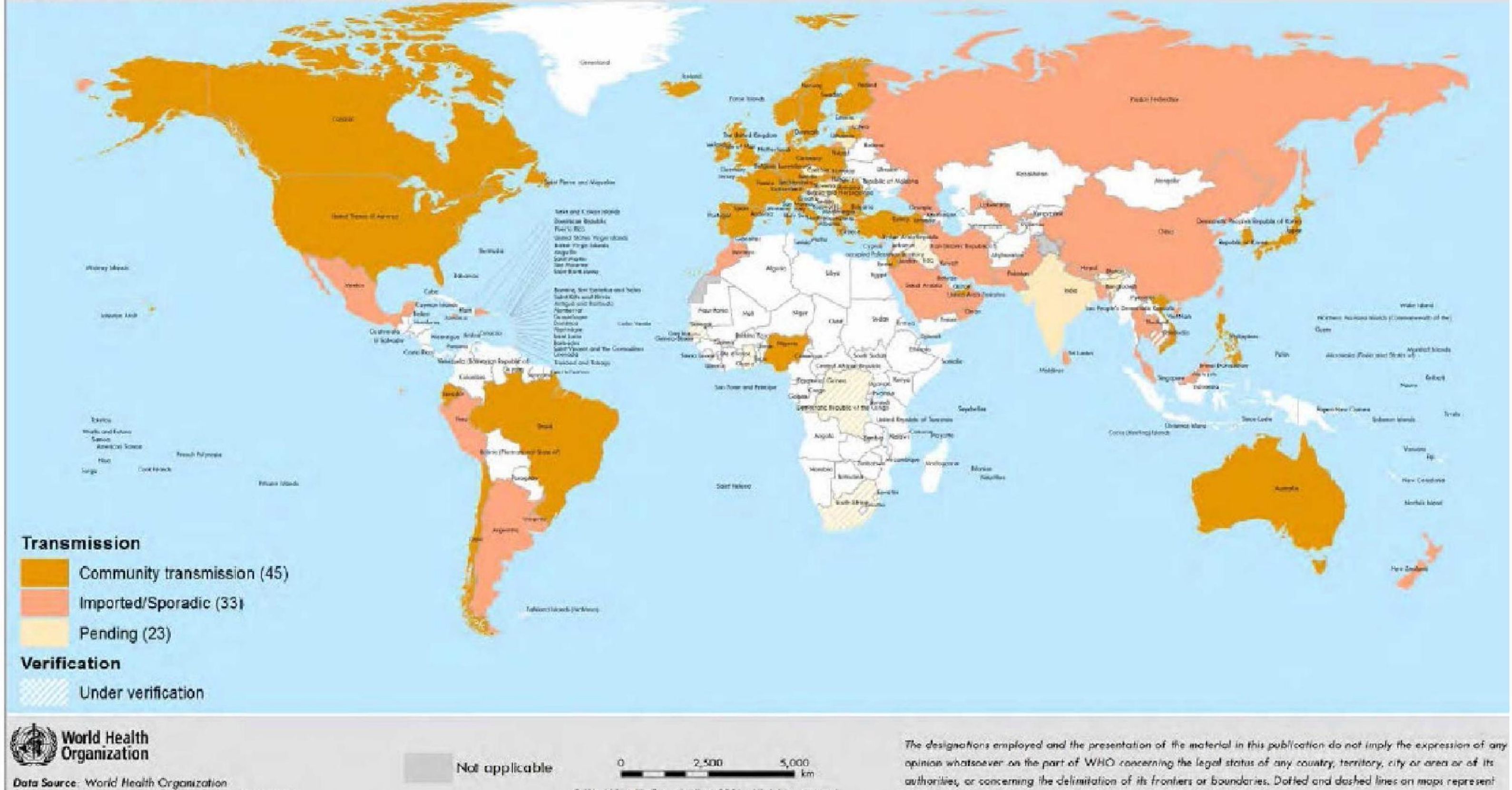
**Generalized findings as compared to non-VOC viruses. Based on emerging evidence from multiple countries, including non-peer-reviewed preprint articles and reports from public health authorities and researchers – all subject to ongoing investigation and*

Countries/territories/areas reporting lineage B.1.1.7 (situation as of 22 February 2021)



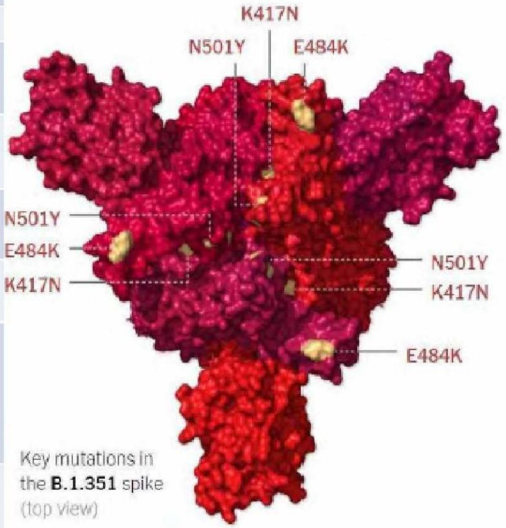
World Health Organization

Data Source: World Health Organization

Map Production: WHO Health Emergencies Programme

B.1.351, 20H/501Y.V2, VOC202012/02

First detected by	South Africa
First appearance	Early August 2020
Key mutations	L242/A243/L244 deletion; N501Y; D614G; E484K; K417N; S106/G107/F108 deletion in NSP6
Transmissibility*	Increased [1.50 (95% CI: 1.20-2.13) times more transmissible than previously circulating variants]
Severity*	No impact reported to date, no significant change in-hospital mortality
Neutralization capacity*	Decreased, suggesting potential increased risk of reinfection
Potential impacts on vaccines*	Reduction in the neutralizing activity, but impact on protection against disease or relative importance of other immune response mechanisms (e.g., T/B-cells), not fully known. Potentially decreased based on small, prelim studies.
Potential impacts on diagnostics*	None reported to date.
Countries reporting cases (community transmissions) as of 23 Feb	51 (13)



Key mutations in the **B.1.351** spike (top view)

https://www.nytimes.com/interactive/2021/health/coronavirus-variant-tracker.html

**Generalized findings as compared to non-VOC viruses. Based on emerging evidence from multiple countries, including non-peer-reviewed preprint articles and reports from public health authorities and researchers – all subject to ongoing investigation and continuous revision.*

HEALTH
EMERGENCIES
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Countries/territories/areas reporting lineage B.1.351 (situation as of 22 February 2021)

Transmission

■ Community transmission (13)

■ Imported/Sporadic (17)

■ Pending (21)

Verification

▨ Under verification

World Health Organization

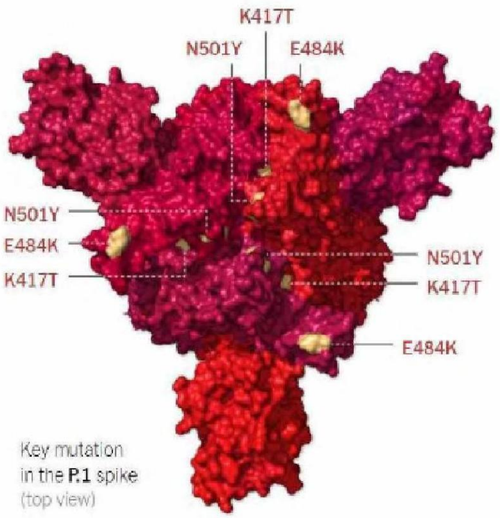
Data Source: World Health Organization
Map Production: WHO Health Emergencies Programme

■ Not applicable

0 2,500 5,000 km

B.1.128.P.1, 20J/501Y.V3

First detected by	Brazil / Japan
First appearance	December 2020
Key mutations	N501Y; D614G; E484K; K417N; S106/G107/F108 deletion in NSP6
Transmissibility*	Suggested to be increased
Severity*	Under investigation, no impact reported to date
Neutralization capacity*	Potential decrease, small number of reinfections reported
Potential impacts on vaccines*	Under investigation
Potential impacts on diagnostics*	None reported to date
Countries reporting cases (Community transmission) as of 23 Feb	29 (3)



Key mutation in the P.1 spike (top view)

https://www.nytimes.com/interactive/2021/health/coronavirus-variant-tracker.html

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Generalized findings as compared to non-VOC viruses. Based on emerging evidence from multiple countries, including non-peer-reviewed preprint articles and reports from public health authorities and researchers – all subject to ongoing investigation and continuous revision

HEALTH
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Countries/territories/areas reporting lineage P.1 (situation as of 22 February 2021)

World Health Organization

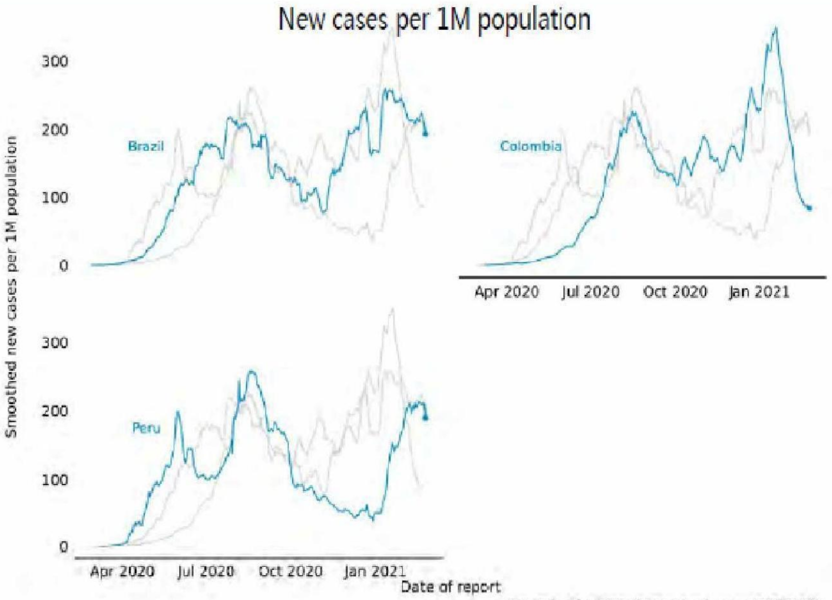
Data Source: World Health Organization
Map Production: WHO Health Emergencies Programme

Not applicable

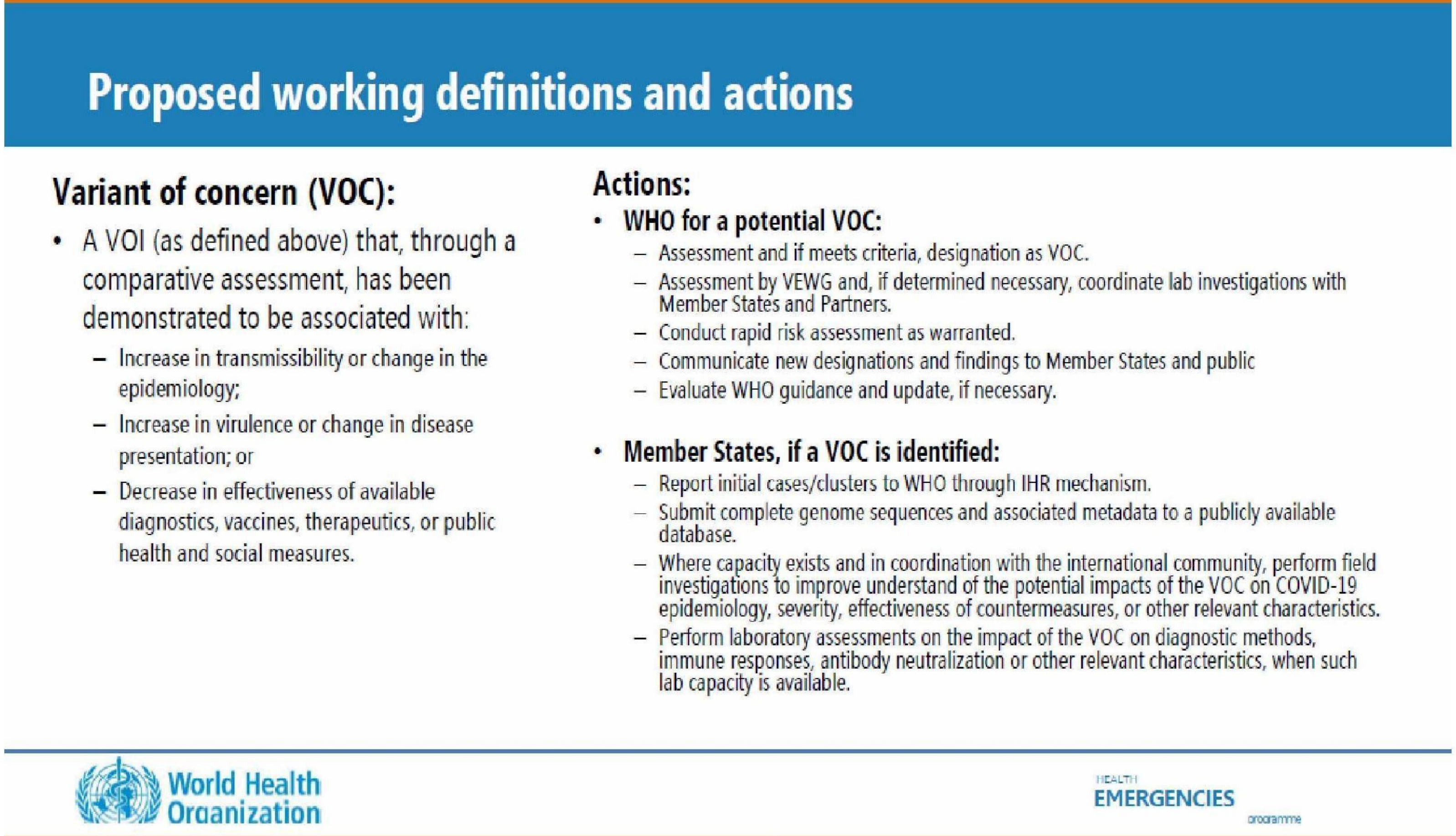
0 2,500 5,000 km

Countries reporting community transmission of variant P.1

- Incidence rates in Brazil remains elevated, and increasing in Peru
- These countries have highly heterogenous epidemiological patterns, and the relative contribution of variant P.1, as well as potential impact on the effectiveness of PHSM and countermeasures requires further investigation.



Data taken from COVID Intel database on 2021-02-25.
The lines and associated text show the trend in incidence of COVID-19 cases.



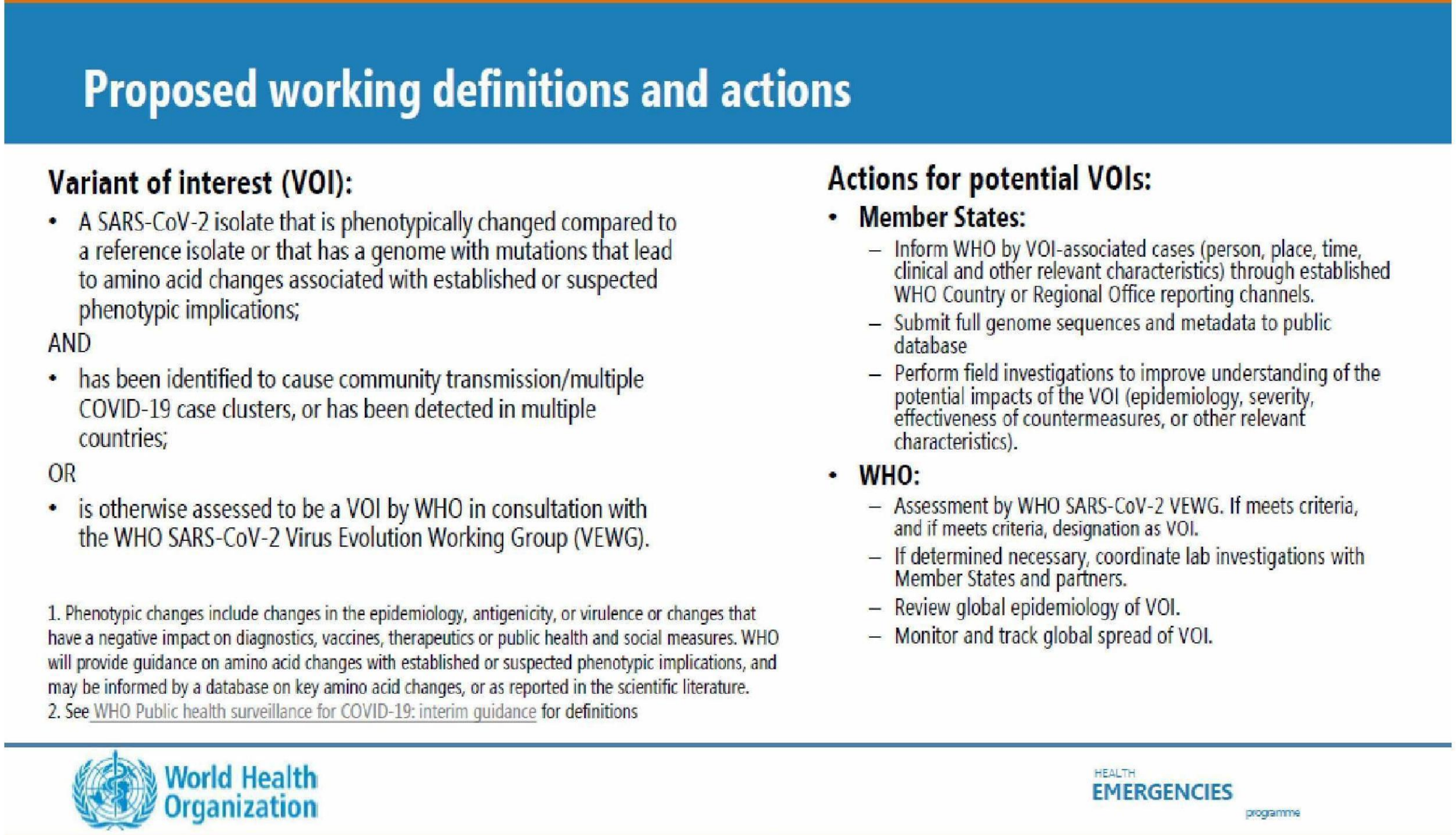
Proposed working definitions and actions

Variant of concern (VOC):

- A VOI (as defined above) that, through a comparative assessment, has been demonstrated to be associated with:
  - Increase in transmissibility or change in the epidemiology;
  - Increase in virulence or change in disease presentation; or
  - Decrease in effectiveness of available diagnostics, vaccines, therapeutics, or public health and social measures.

Actions:

- **WHO for a potential VOC:**
  - Assessment and if meets criteria, designation as VOC.
  - Assessment by VEWG and, if determined necessary, coordinate lab investigations with Member States and Partners.
  - Conduct rapid risk assessment as warranted.
  - Communicate new designations and findings to Member States and public
  - Evaluate WHO guidance and update, if necessary.
- **Member States, if a VOC is identified:**
  - Report initial cases/clusters to WHO through IHR mechanism.
  - Submit complete genome sequences and associated metadata to a publicly available database.
  - Where capacity exists and in coordination with the international community, perform field investigations to improve understand of the potential impacts of the VOC on COVID-19 epidemiology, severity, effectiveness of countermeasures, or other relevant characteristics.
  - Perform laboratory assessments on the impact of the VOC on diagnostic methods, immune responses, antibody neutralization or other relevant characteristics, when such lab capacity is available.



Proposed working definitions and actions

Variant of interest (VOI):

- A SARS-CoV-2 isolate that is phenotypically changed compared to a reference isolate or that has a genome with mutations that lead to amino acid changes associated with established or suspected phenotypic implications;

AND

- has been identified to cause community transmission/multiple COVID-19 case clusters, or has been detected in multiple countries;

OR

- is otherwise assessed to be a VOI by WHO in consultation with the WHO SARS-CoV-2 Virus Evolution Working Group (VEWG).

Actions for potential VOIs:

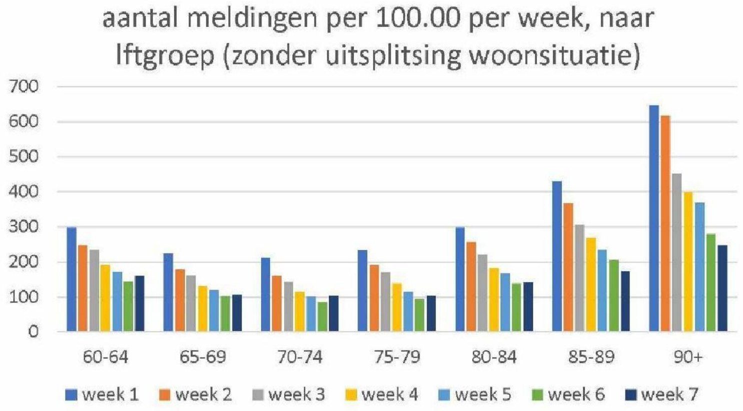
- **Member States:**
  - Inform WHO by VOI-associated cases (person, place, time, clinical and other relevant characteristics) through established WHO Country or Regional Office reporting channels.
  - Submit full genome sequences and metadata to public database
  - Perform field investigations to improve understanding of the potential impacts of the VOI (epidemiology, severity, effectiveness of countermeasures, or other relevant characteristics).
- **WHO:**
  - Assessment by WHO SARS-CoV-2 VEWG. If meets criteria, and if meets criteria, designation as VOI.
  - If determined necessary, coordinate lab investigations with Member States and partners.
  - Review global epidemiology of VOI.
  - Monitor and track global spread of VOI.

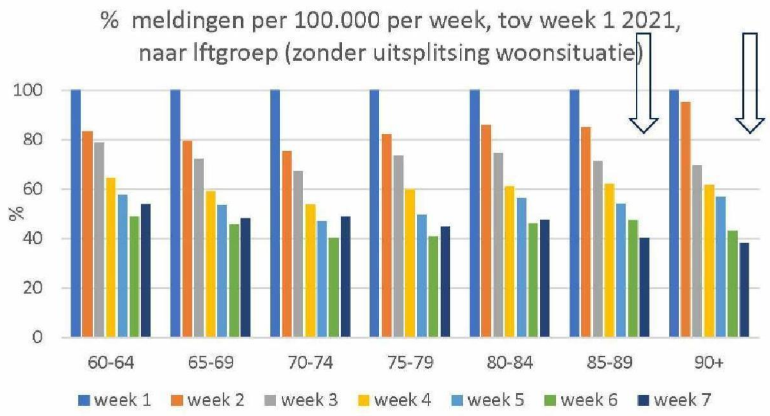
1. Phenotypic changes include changes in the epidemiology, antigenicity, or virulence or changes that have a negative impact on diagnostics, vaccines, therapeutics or public health and social measures. WHO will provide guidance on amino acid changes with established or suspected phenotypic implications, and may be informed by a database on key amino acid changes, or as reported in the scientific literature.
2. See WHO Public health surveillance for COVID-19: interim guidance for definitions

Meldingen per leeftijdsgroep vanaf 60 jaar, zonder uitsplitsing naar woonsituatie

Week 3: start vaccinatie verpleeghuisbewoners
week 4: start vaccinatie thuiswonende 85+ jr (± 60% ≥ 1 dosis)
Week 5: start vaccinatie thuiswonende 80-84 jr (± 27% ≥ 1 dosis)
Week 7: start vaccinatie thuiswonende 6-64 jr

Mogelijk eerste effecten vaccinatie in oudste leeftijdsgroepen, die als eerste gevaccineerd zijn


aantal meldingen per 100.00 per week, naar lftgroep (zonder uitsplitsing woonsituatie)


% meldingen per 100.000 per week, tov week 1 2021, naar lftgroep (zonder uitsplitsing woonsituatie)