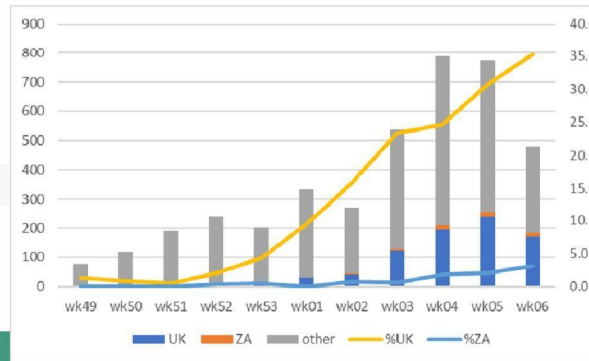


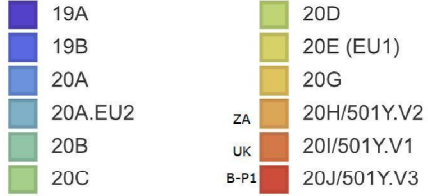
Variant



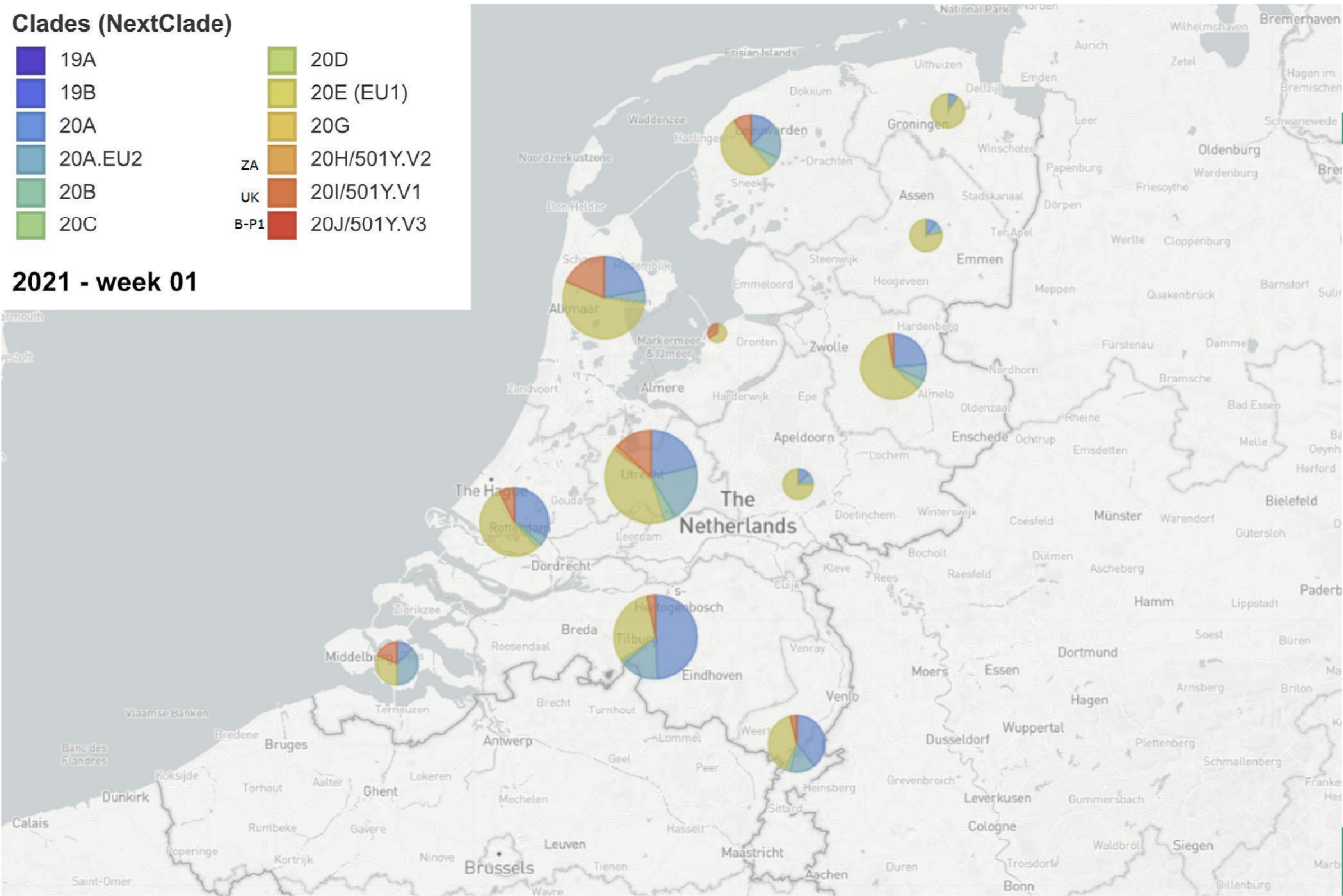
| wk# | UK | ZA | other | %UK | %ZA | total |
|------|-----|----|-------|------|-----|-------|
| wk49 | 1 | 0 | 76 | 1.3 | 0.0 | 77 |
| wk50 | 1 | 0 | 117 | 0.8 | 0.0 | 118 |
| wk51 | 1 | 0 | 189 | 0.5 | 0.0 | 190 |
| wk52 | 5 | 1 | 232 | 2.1 | 0.4 | 238 |
| wk53 | 9 | 1 | 194 | 4.4 | 0.5 | 204 |
| wk01 | 32 | 0 | 302 | 9.6 | 0.0 | 334 |
| wk02 | 43 | 2 | 225 | 15.9 | 0.7 | 270 |
| wk03 | 125 | 3 | 408 | 23.3 | 0.6 | 536 |
| wk04 | 194 | 14 | 578 | 24.7 | 1.8 | 786 |
| wk05 | 238 | 16 | 520 | 30.7 | 2.1 | 774 |
| wk06 | 169 | 15 | 295 | 35.3 | 3.1 | 479 |



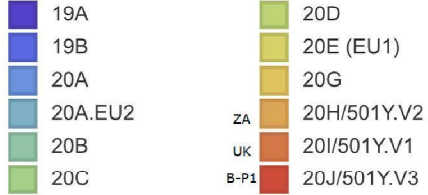
Clades (NextClade)



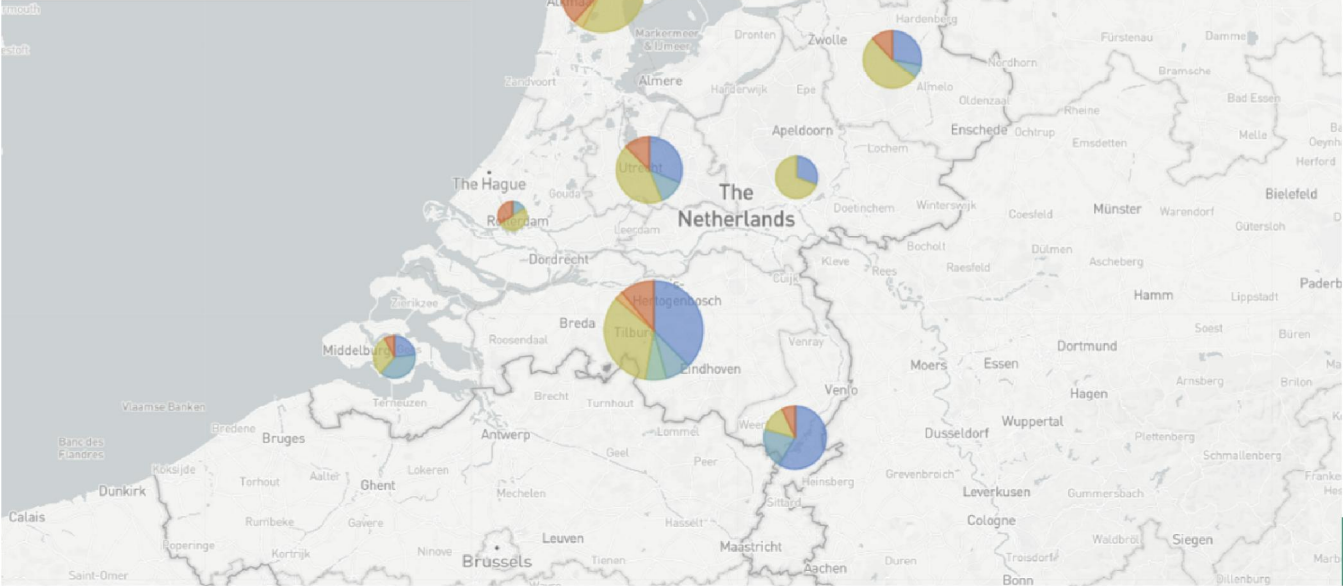
2021 - week 01



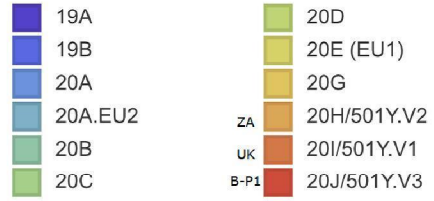
Clades (NextClade)



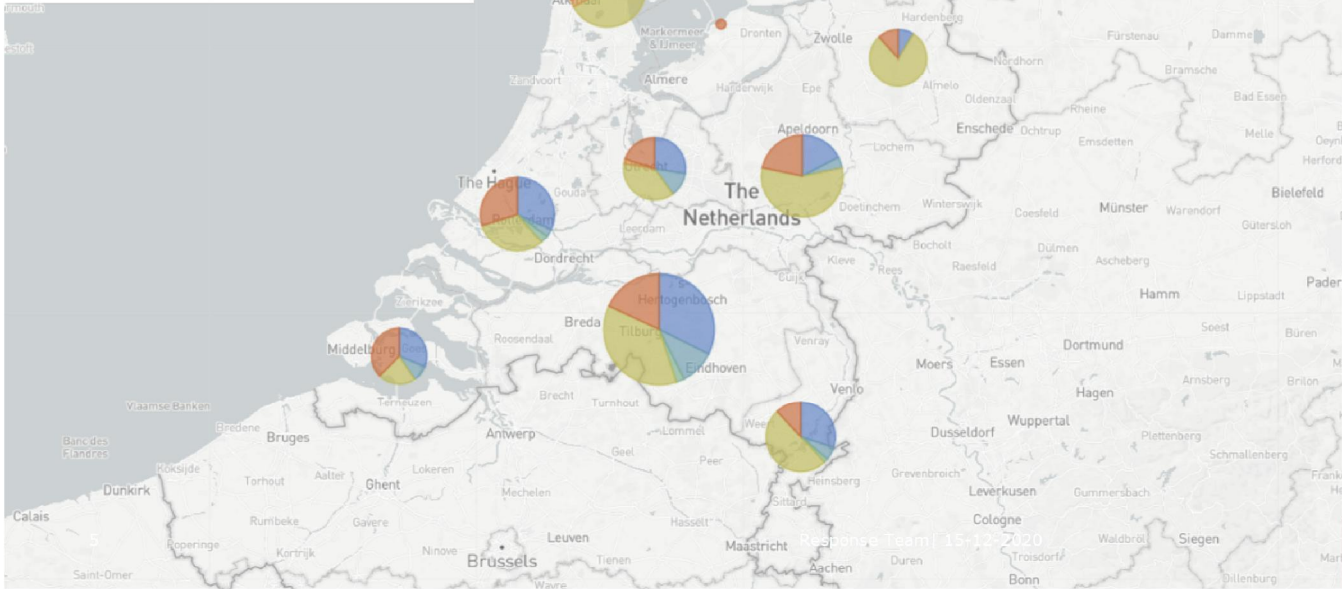
2021 - week 02



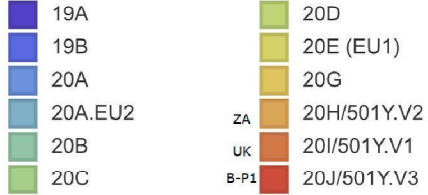
Clades (NextClade)



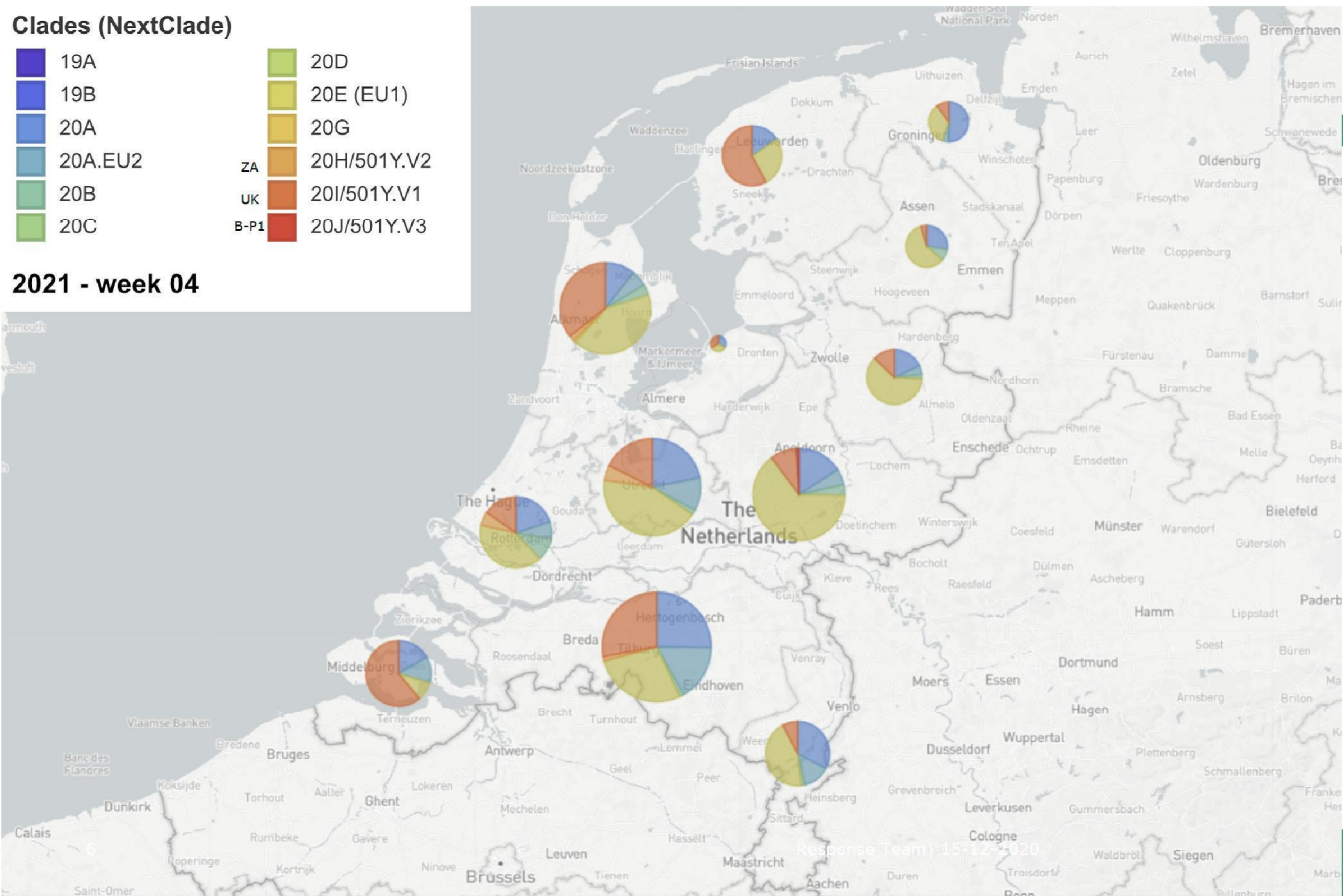
2021 - week 03



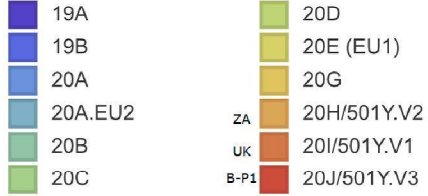
Clades (NextClade)



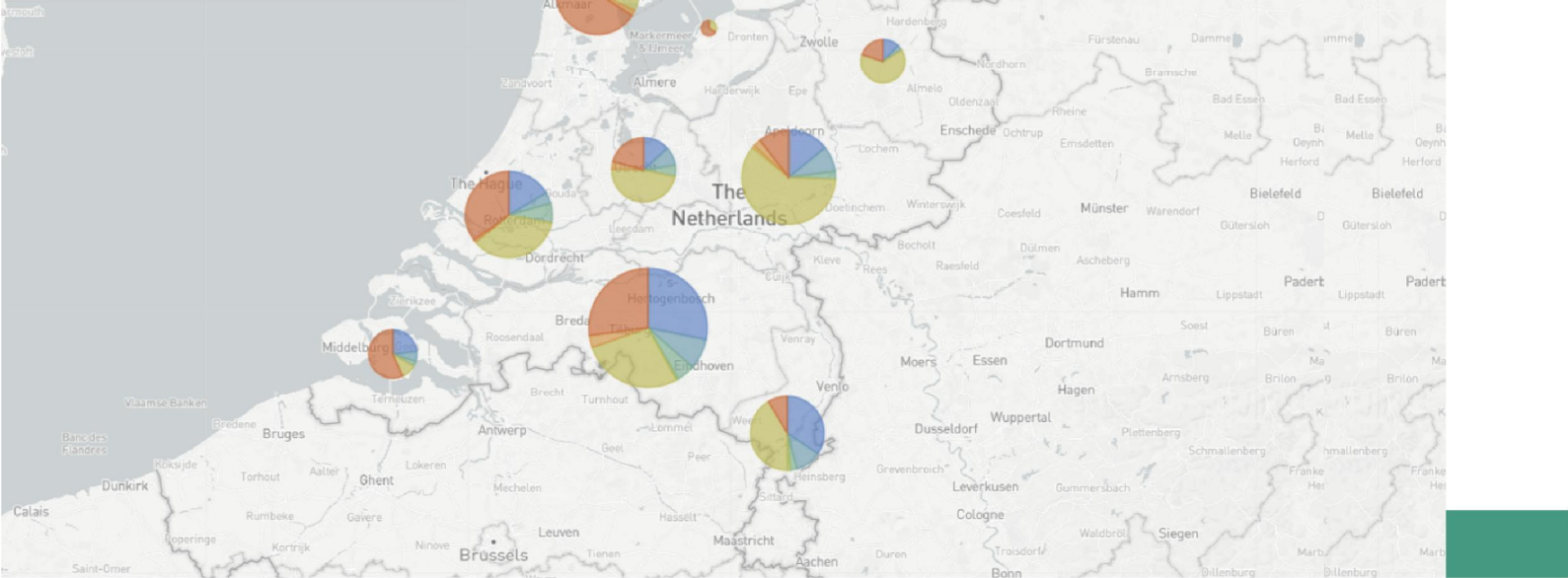
2021 - week 04



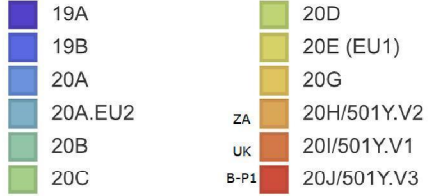
Clades (NextClade)



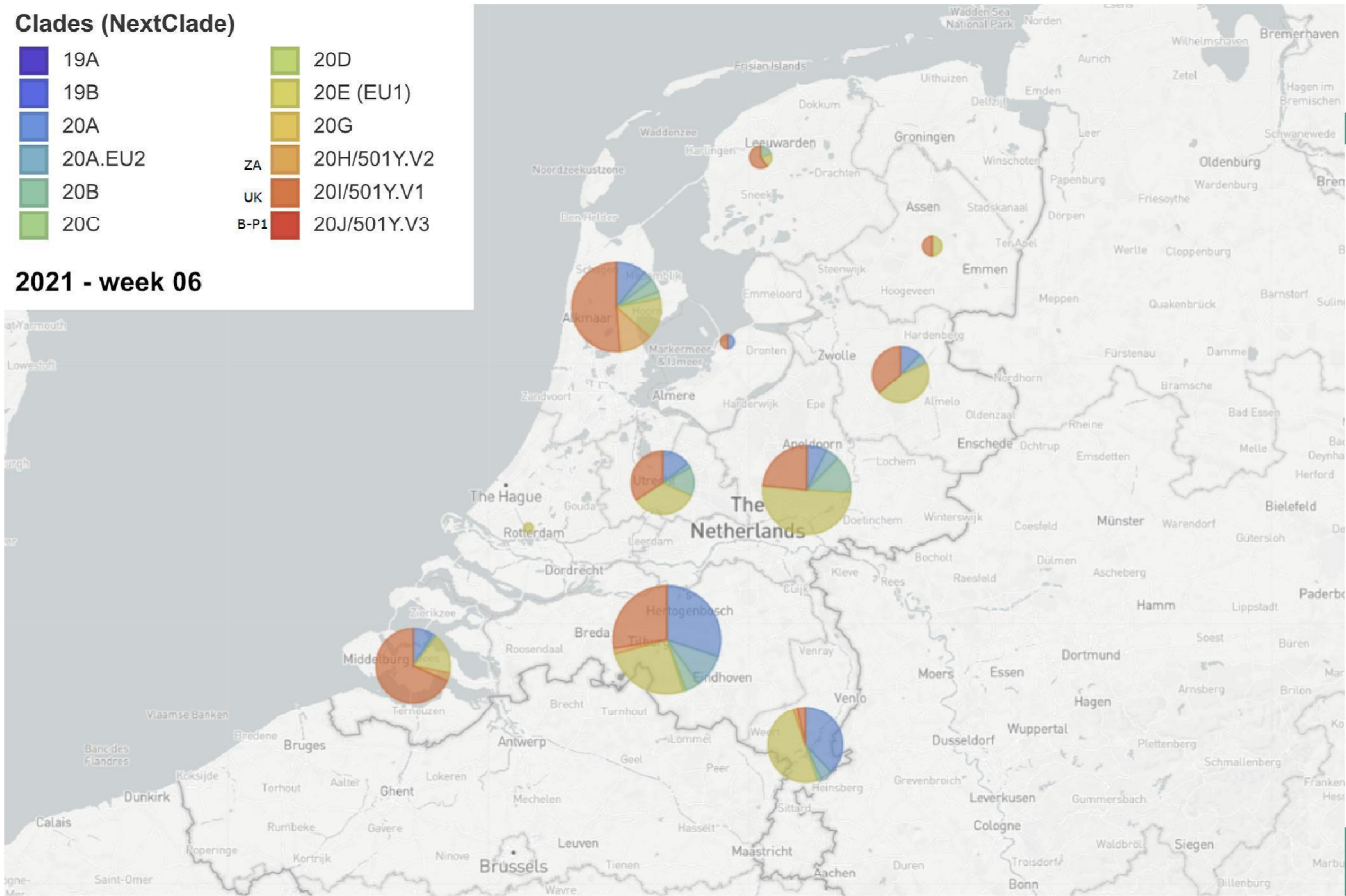
2021 - week 05



Clades (NextClade)



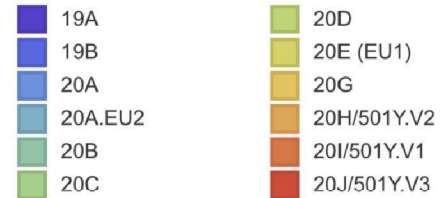
2021 - week 06



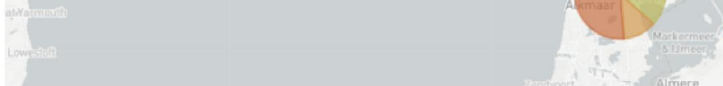
Monitoring 20I/501Y



Clades (NextClade)



2021 - week 06



AMS-SLA (s-drop out):

| | | |
|-------|-------|-----------|
| Wk 52 | 5.2% | (21/407) |
| Wk 1 | 9.3% | (31/334) |
| Wk 2 | 20.0% | (83/414) |
| Wk 3 | 31.4% | (170/542) |
| Wk 4 | 39.1% | (144/368) |
| Wk 5 | 47.5% | (145/266) |
| Wk 6 | 54.5% | (177/373) |
| Wk 7 | 61.7% | (140/227) |

Confirmatory seq:

| | |
|-------|-----------------|
| Wk 52 | 17/17 |
| Wk 1 | 16/17 (B.1.258) |
| Wk 2 | 12/12 |
| Wk 3 | 10/10 |
| Wk 4 | ongoing |
| Wk 5 | 7/7 |
| Wk 6 | 10/10 |
| Wk 7 | ongoing |

Variant



| | B.1.1.7 | B.1.1.7+E484K | B.1.351 | B.1.525+E484K+F888L | (B.1.1.28.1) P1 | (B.1.1.28.1) P2 | A.23.1+E484K | B.1.177 | B.1.160+E484K | B.1.313+E484K | B.1.1.316+E484K | B.1.1.7+S494P | B.1.1.318 | A.27 |
|-------------------|---|--|---|---------------------------------|--|---|---|---------|--------------------------|---------------|-----------------|--|--|----------|
| Pangolin | 20I/501Y.V1 | 20I/501Y.V1+E484K | 20I/501Y.V2 | 20A | 20I/501Y.V3 | "Brazil-P2" | | 20E.EU1 | 20A.EU2 | 20A | 20B | 20B/501Y.V2+S494P | | |
| Nextstrain | "UK" | "UK+E484K" | "South-Africa" | | "Brazil-P1" | | | | | | | "UK+S494P" | | "France" |
| WHO | | | | | | | | | | | | | | |
| Spike | H69-V70 del Y144del N501Y A570D P681H T716I S982A D1118H | H69-V70 del Y144del E484K N501Y A570D P681H T716I S982A D1118H | D80A D215G L242-A243-L244 del K417N E484K N501Y A701V | Q25R E484K Q677H F888L | L18F T20N P26S D138Y R190S K417T N501Y D614G H655Y T1027I | E484K D614G S929I V1176F Q613H P681R | F157L V367F E484K Q613H P681R | E484K | S477N E484K E1202Q | E484K | E484K | H69-V70 del Y144del S494P N501Y A570D P681H T716I S982A D1118H | Y144del E484K P681H D796H T95I | |
| Kiemsurv. | n=818 | n=1 | n=52 | n=5 | n=1 | n=4 | n=1 | n=1 | n=5 | n=1 | n=9 | n=1 | 0 | 0 |
| BCO | n.a. | 0 | n=35; stop | ongoing | n=5 | n=15 | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | | |



- culture & serum collection => antigenic characterization, (inter)national strain sharing
- Wekelijks opload GISAID; 26/2/2021: 5774 (total NL 10.992); incl Caribisch NL: 6100
- Dubbel-infecties? (oa casus Nijmegen)
- Eerste gevaccineerden in data sets; casus : 2x Pfizer shot. Geïnfectederd met ZA-variant



Distribution of variants among sequenced samples during week 2021-01 to 2021-05

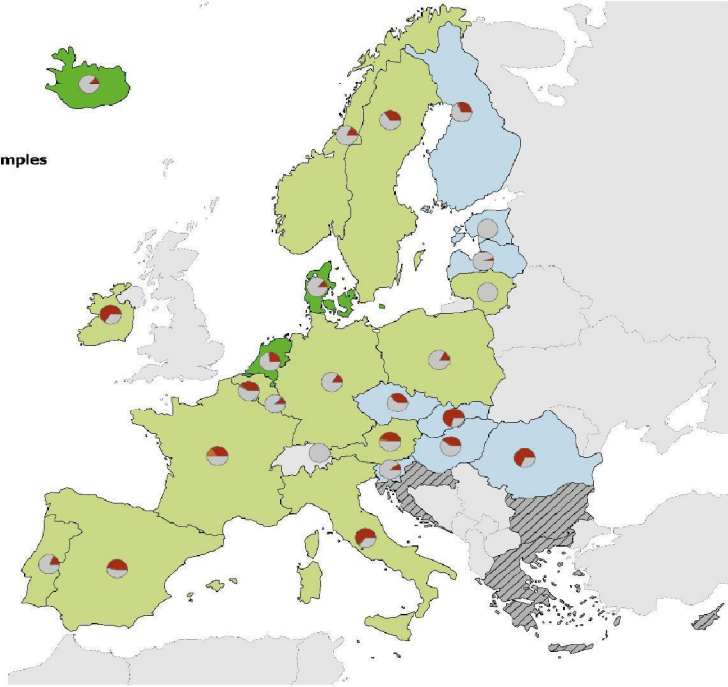
- B.1.1.7
- B.1.351
- P.1
- Other variants

Weekly average of samples collected with a published sequence during week 2021-01 to 2021-05

- <60
- 60 - 499
- ≥500 or ≥10% of total samples
- No data reported
- Not included

Countries not visible in the main map extent

- Malta
- Liechtenstein
- Luxembourg



Source: GISAI3D EpiCoV data™. Administrative boundaries: © EuroGeographics
 The boundaries and names shown on this map do not imply official endorsement or acceptance by the European Union, ECDC. Map produced on: 24 Feb 2021
 webinar WHO | 16-09-2020



Bonaire)

| | B.1.1.7 | B.1.429/427 | B.1.526 | (B.1.1.28.1) P2 | B.1.441+E484K |
|------------------|---|------------------------|-------------|-----------------------------------|---------------|
| Pangolin | 20B/501Y.V2 | CAL.20C (20C/S:452R) | 20C | 20B | 20A |
| Nextstrain | "UK" | "California" | "New-York" | "Brazil -P2" | |
| slang | | | | | |
| WHO | | | | | |
| Spike | H69-V70 del Y144del N501Y A570D P681H T716I S982A D1118H | S13I W152C L452R | | E484K D614G S929I V1176F | E484K |
| Kiemsurv. BCO | n=24 | n=5 | n=2 | n=1 | n=2 |
| Comments | Aruba Curaçao St-Maarten | Aruba St-Maarten | St. Maarten | St. Maarten | Aruba |

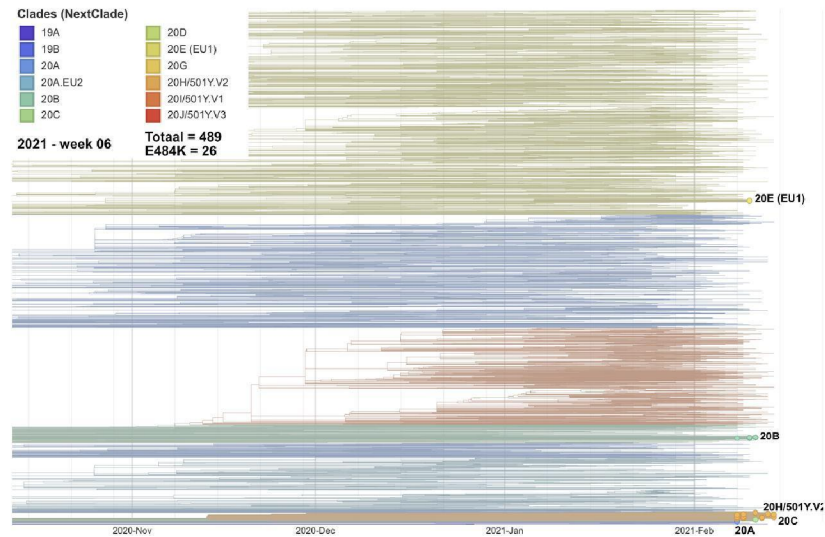
culture & serum collection

Variant



| weeknummer | Totaal | E484K | % |
|------------|--------|-------|------|
| 2020_52 | 238 | 1 | 0.42 |
| 2020_53 | 204 | 1 | 0.49 |
| 2021_01 | 334 | 0 | 0.00 |
| 2021_02 | 270 | 6 | 2.22 |
| 2021_03 | 536 | 3 | 0.56 |
| 2021_04 | 786 | 19 | 2.42 |
| 2021_05 | 774 | 18 | 2.33 |
| 2021_06 | 489 | 26 | 5.32 |

Lijkt in mate toe te nemen (ZA)
In NL in 10 verschillende backbones



WHO

Proposed working definitions for Variants of Interest and Variants of Concern – 25 February 2021



- Variants of Interest (VOI):
 - low threshold to guarantee sensitive surveillance
 - changed phenotype* or a.a.r changes with established/suspected phenotypic implications

and

- community transmission/multiple cases/clusters or detected in multiple countries

or

- defined by international WHO working group

*
Antigenicity
Virulence
Epidemiology

Negative impact on:
diagnostics
Vaccines
Therapeutics
PHSM



WHO

Proposed work
Interest and Variants of Concern – 25 February 2021



- Variants of Concern (VOC):
 - high threshold to focus (limited) resources to variants with highest public health impact
 - VOI -> VOC if based on comparative assessment:
 - increase in transmissibility or detrimental change in COVID-19 epidemiology;
or
 - increase in virulence or change in clinical disease presentation;
or
 - decrease in effectiveness of PHSM or available diagnostics, vaccines, therapeutics.
or
 - assessed to be a VOC by WHO



Table 3: Overview of emerging information on key variants of concern, as of 23 February 2021*

| Nextstrain clade | 20I/S01Y.V1 | 20H/S01Y.V2 [†] | 20I/S01Y.V3 |
|--|---|---|--|
| Pango lineage | B.1.1.7 | B.1.351 | B.1.1.28.1 |
| GISAID clade | GR | GH | GR |
| Alternate names | VOC 202012/01 [†] | VOC 202012/02 | P.1 [†] |
| First detected by | United Kingdom | South Africa | Brazil / Japan |
| First appearance | 20 September 2020 | Early August 2020 | December 2020 |
| Key spike mutations | H69/V70 deletion; Y144 deletion; N501Y; A570D; D614G; and P681H | L242/A243/L244 deletion; N501Y; D614G; E484K; and K417N | N501Y; D614G; E484K; and K417N |
| Key mutation in common | S106/G107/F108 deletion in Non-Structural Protein 6 (NSP6) | | |
| Transmissibility* | Increased ¹ (36%-75%); ² increased secondary attack rate ³ (10% to 13%) | Increased [1.50 (95% CI: 1.20-2.13) times more transmissible than previously circulating variants] ^{4,5} | Suggested to be increased |
| Severity* | Possible increased severity and mortality ⁴ | No impact reported to date ^{4,5} , no significant change in-hospital mortality ⁶ | Under investigation, no impact reported to date |
| Neutralization capacity* | Slight reduction but overall neutralizing titers still remained above the levels expected to confer protection ⁸ | Decreased, suggesting potential increased risk of reinfection ^{9,10} | Potential decrease, small number of reinfections reported ^{11,12} |
| Potential impacts on vaccines* | No significant impact on Moderna, Pfizer-BioNTech, and Oxford-AstraZeneca vaccines ^{13,14} | Moderna and Pfizer-BioNTech: Reduction in the neutralizing activity, but impact on protection against disease not known. ^{15,16} Novavax and Johnson & Johnson: Lower vaccine efficacy in South Africa compared to settings without the variant (press release data only). Moderate-severe disease were assessed. Serologic neutralization results pending. ^{17,18} Oxford/AstraZeneca: Limited vaccine efficacy against mild-moderate COVID-19 disease, with wide confidence intervals, impact on severe disease undetermined. Serologic neutralization substantially reduced compared with original strains, based on small number of samples analyzed ^{19,20} | Under investigation |
| Potential impacts on diagnostics* | S gene target failure (SGTF) ¹⁸ No impact on Ag RDTs observed ²¹ | None reported to date | None reported to date |
| Countries reporting cases (newly reported in last week)** | 101 (7) | 51 (5) | 29 (8) |

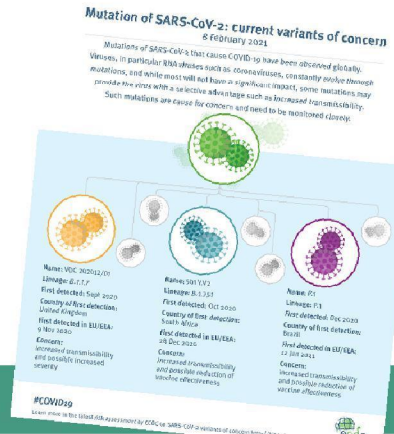
*While work is ongoing to establish standardized nomenclature for key variants, these are the names by which WHO will refer to them in this publication.
[†]Generalized findings as compared to non-VOC viruses. Based on emerging evidence from multiple countries, including non-peer-reviewed preprint articles and reports from public health authorities and researchers – all subject to ongoing investigation and continuous revision.
^{**}Includes official and unofficial reports of VOCs detections in countries among either travellers (imported cases only) or community samples (local transmission).



WHO

VOC: B.1.1.7; B.1.351; B.1.1.28 P1

VOI: B.1.525+E484K+Q677H+F888L; B.1.1.7+E484K





Openstaande vragen

- A. Criteria voor instellen BCO nav varianten?
- B. Melden varianten internationaal (EWRS) (naast routinematige upload in GISAID)?
- C. Melden variant tellingen in weekberichten RIVM
- D. ?

Uitgangspunt classificatie van WHO/ECDC aangevuld met intern monitoren van lit, rapportages, vanuit diverse internationale werkgroepen/overleggen (schaduwlijst).

- A+B Bij WHO-officiële VOI, VOC waar nog geen brede community transmissie is waargenomen => data kiemsurveillance? drempelwaarde?
- A. Bij VOI intern vastgesteld waar nog geen brede community transmissie is waargenomen? Alleen bij reizigers? vs Kiemsurv (vertraging)?
 - B. Als reactie op EWRS berichten aangaande specifieke varianten
 - C. Voorstel alleen de WHO/ECDC VOI en VOC en alleen bij afwezigheid community transmissie ook de getallen uit BCO. (vaststellen drempelwaarde)



| Variant | NSP | S1: NTD | S1:RBD | S1/S2 | S2 | Methods | Reporting |
|---------------------|-----------------|--|---|---------------------------|----------------------------|---|--|
| B.1.1.7 (+E484K) | Δ106-108 | Δ69-70 Δ144 | N501Y, (E484K) | A570D, D614G, P681H | T716I, S982A, D1118H | 1)S-gene dropout screening 2)Specific RT-PCRs to detect characteristic mutations 3)Sequencing at least the entire N-terminal and receptor binding domain (RBD) (amino acid 1-541, 1 623 bp) | 1)S-gene drop out variable/coded value 2)If only 1 PCR- based assay for E484K or N501Y or Orf1a del (Δ3675-3677) used/is positive: report the respective variable/coded value or Wild_Type (if negative) If several SNP assays/SGTF used/are positive: report based on your interpretation* the closest that describes your finding** (either one of the single mutations if you cannot distinguish the lineage or B.1.1.7 or B.1.1.7+E484K) 3)B.1.1.7 or B.1.1.7+E484K |
| B.1.351 | Δ106-108 | D80A, D215G | K417N, E484K, N501Y | D614G | A701V | 1)Specific RT-PCRs to detect characteristic mutations 2) Sequencing at least 69-70 (no deletion), D80A, D215G, E484K, N501Y, A701V | 1)If only 1 PCR-based assay for E484K or N501Y or Orf1a del (Δ3675-3677) used/is positive: report the respective variable/coded value or Wild_Type (if negative) If several SNP assays used/are positive: report based on your interpretation* the closest that describes your finding** (either one of the single mutations if you cannot distinguish the lineage or B.1.351) 2) B.1.351 |
| P.1 | Δ106-108 | L18F, T20N, P26S, D138Y, R190S | K417T, E484K, N501Y | D614G, H655Y | T1027I, V1176F | 1)Specific RT-PCRs to detect characteristic mutations 2) Sequencing at least 69-70 (no deletion), D80A, D215G, E484K, N501Y, A701V | 1)If only 1 PCR-based assay for E484K or N501Y or Orf1a del (Δ3675-3677) used/is positive/are positive: report the respective variable/coded value or Wild_Type (if negative) If several SNP assays used/are positive: report based on your interpretation* the closest that describes your finding** (either one of the single mutations if you cannot distinguish the lineage or P.1) 2) P.1 |