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IWA TASK FORCE ON COVID-19

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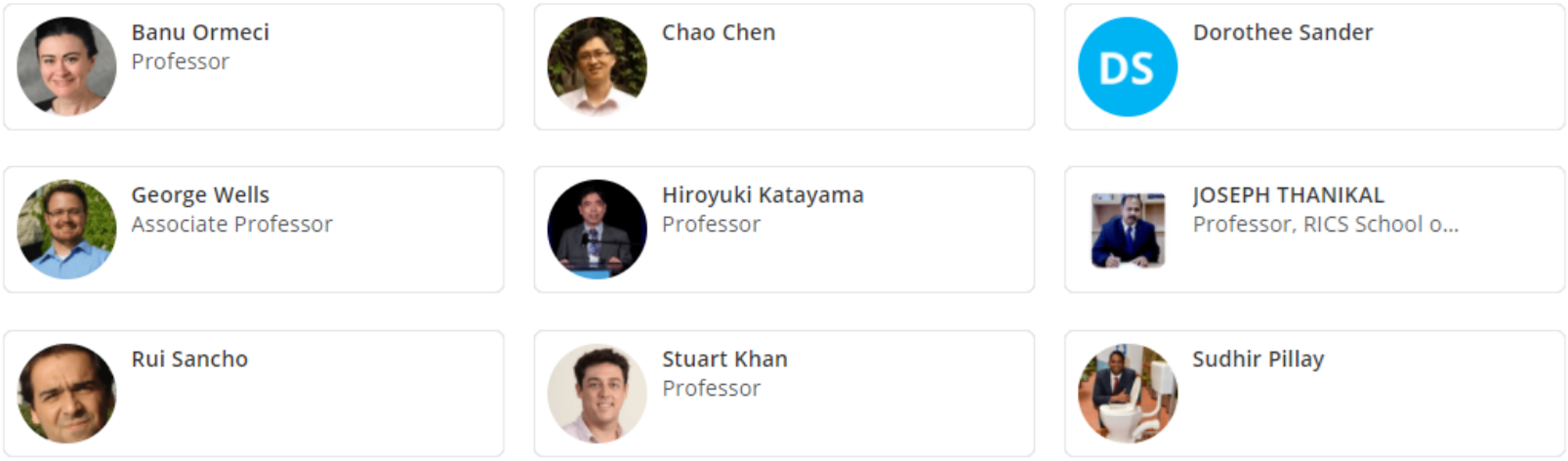
IWA convened the Task Force on COVID-19, from amongst its membership, to provide the sector with an **authoritative reference point** regarding both the **relevant science** and **operational matters** relating to the SARS-CoV-2 virus.



IWA COVID-19 Task Force

Join **the IWA COVID-19 Task Force Interest Group** on IWA Connect!

https://iwa-connect.org/group/iwa-covid-19-task-force-interest-group/timeline

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Gertjan Medema

KWR
Netherlands

Tamar Kohn

Swiss Federal Institute of Technology in Lausanne
Switzerland

Niko Beerenwinkel

Department of Biosystems Science and Engineering, ETH Zurich
Switzerland

Giuseppina La Rosa

Istituto Superiore di Sanità
Italy

Elisabetta Suffredini

Istituto Superiore di Sanità
Italy

Joan Rose

Michigan State University
USA

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AGENDA

- **Introduction**
  Banu Örmeci | *Joan Rose*
- **Using wastewater to monitor the emergence of variants of concern**
  Gertjan Medema
- **Detection and surveillance of SARS-CoV-2 genomic variants in Swiss wastewater**
  Tamar Kohn | *Niko Beerenwinkel*
- **SARS-CoV-2 Variants of Concern in urban sewage in Italy identified by Nested RT-PCR**
  Giuseppina La Rosa | *Elisabetta Suffredini*
- **Q&A Panel Discussion**

Using wastewater to monitor the emergence of variants of concern

GERTJAN MEDEMA
KWR, NETHERLANDS

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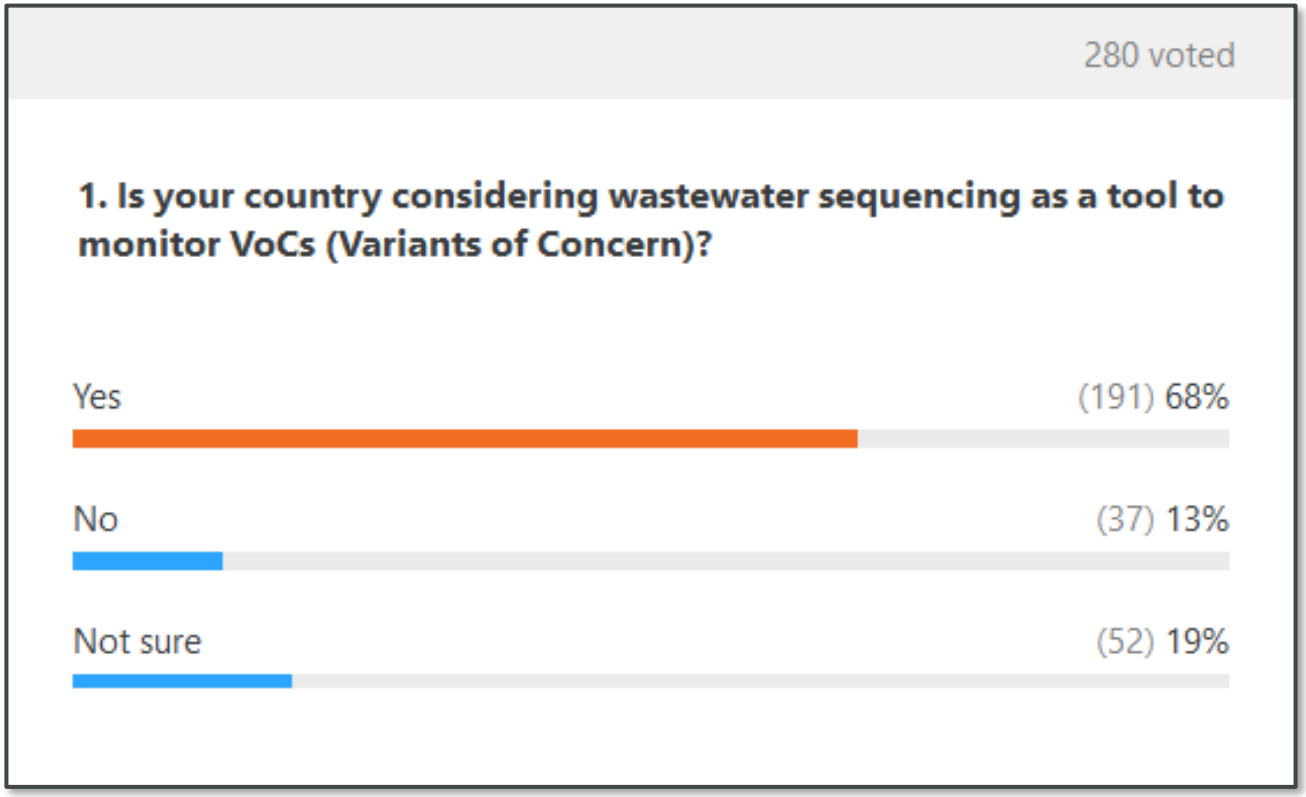
POLL 1: WASTEWATER SEQUENCING

Single choice

1. Is your country considering wastewater sequencing as a tool to monitor VoCs (Variants of Concern)?

- Yes
- No
- Not sure

POLL 1: WASTEWATER SEQUENCING

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Erasmus MC
KWR
Hoogheemraadschap van Schieland en de Krimpenerwaard
Hoogheemraadschap van Delfland
stowa
GGD Rotterdam-Rijnmond
HOOGHEEMRAADSCHAP DE STICHTSE RIJNLANDEN
Royal HaskoningDHV
Enhancing Society Together
waterschap Hollandse Delta
Rijksinstituut voor Volksgezondheid en Milieu
Ministerie van Volksgezondheid, Welzijn en Sport
PARTNERS4URBANWATER
onderzoek & advies
waternet

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EMC-department of Virology
EMC-department of general practice
EMC-department Medical Microbiology
EMC-department of Medical informatics
RIVM – national institute for public health – epidemiology
GGD- Municipal Health Services
Danish Technical University

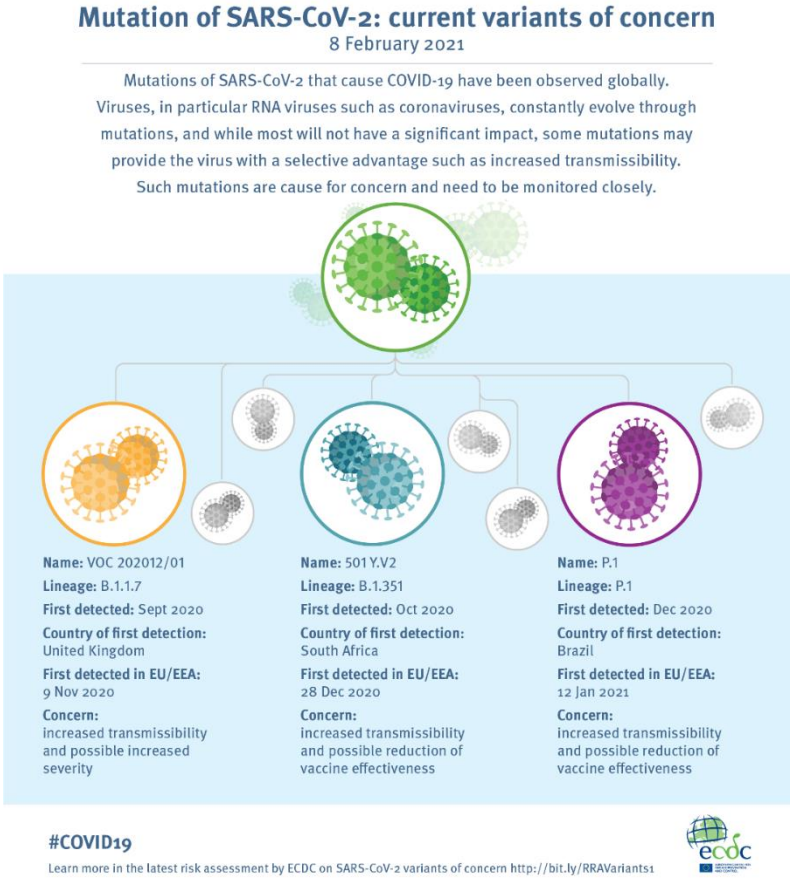
KWR water research institute
Partners4UrbanWater
STOWA Foundation for applied water research
Waterbeheer
Waterschap Hollandse Delta
Hoogheemraadschap van Schieland en de Krimpenerwaard
Hoogheemraadschap van Delfland
Royal Haskoning DHV
IMD
Aquon

Izquierdo Lara
Evelien de Schepper
Goffe Elsinga
Christian Carrizosa Balmont
Leo Heijnen
Claudia Schapendonk
Patrick Bindels
Johan van der Lei
Margreet Vos
Eelco Franz
Roan Pijnacker
Frederic Béen
Stefanie Stubbé
Richard Molenkamp
Remy Schilperoort
Johan post
Frank Aarestrup
Ewout Fanoy
Jeroen Langeveld
Marion Koopmans
Miranda de Graaf
Gertjan Medema

SARS-COV-2 VARIANTS OF CONCERN

- Why concern?

- Impact on diagnostics (drop-out PCR)
- Increased transmissibility
- Increased disease severity
- Reduction of therapy effectiveness
- Reduction of immunity/vaccination effectiveness



CONCERN

More difficult to control transmission

Tougher, longer lockdowns to reduce transmission

- Immunity/vaccination less effective
  - Reinfection and illness
  - Reinfection and transmission
  - Re-vaccination

ROLE OF SURVEILLANCE

Observe emergence/circulation of new VoC

Understand disease, transmission dynamics

Observe vaccination efficacy to VoC

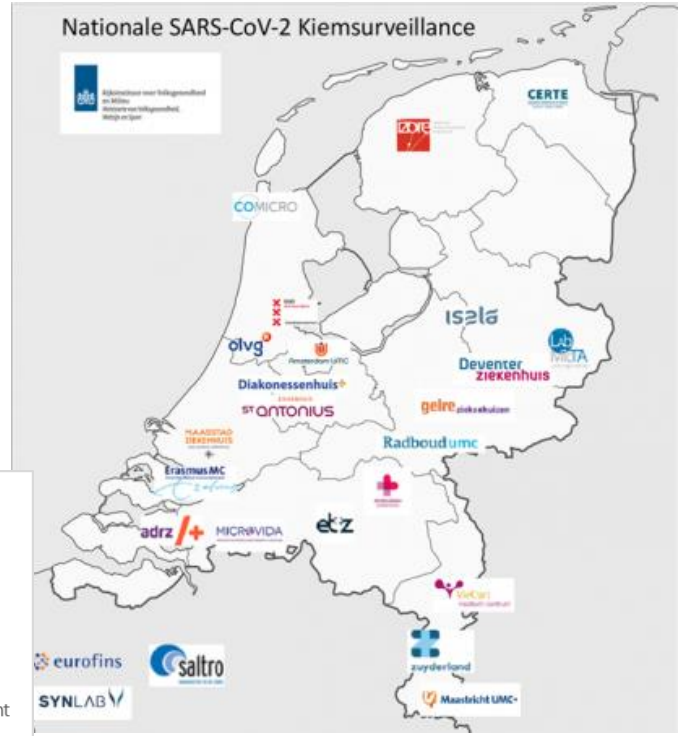
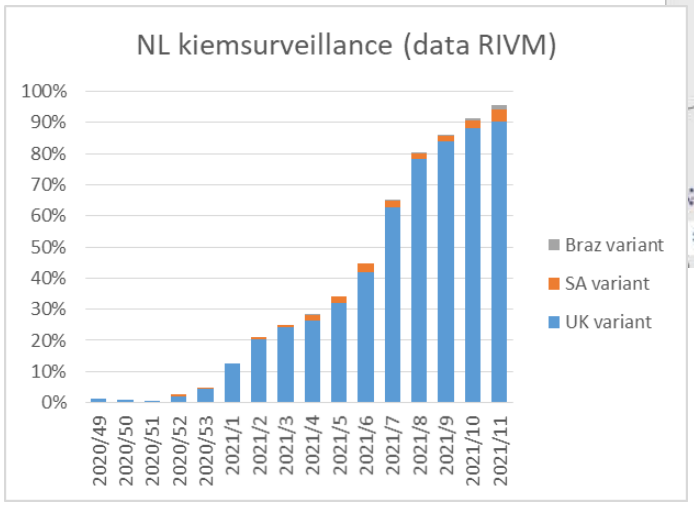


Image: RIVM



THE USE CASE OF SURVEILLANCE: TRENDS IN SARS-COV-2 VOC

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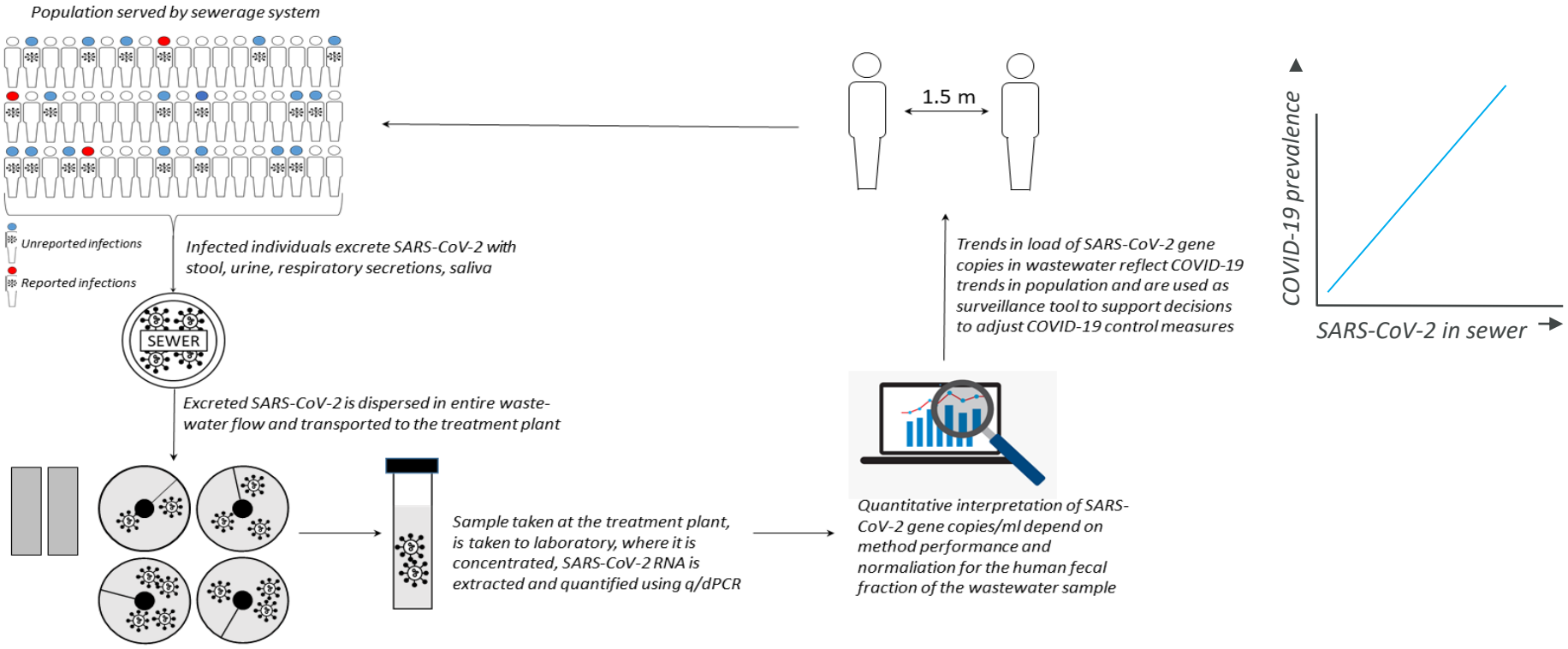

Image: Medema et al., COESH 2021

DETECTION OF VARIANTS OF CONCERN IN WASTEWATER

- VoC do not affect the ability to detect SARS-CoV-2 in current surveillance studies
- Wastewater is a mixture of variants from multiple cases: more complex methods/bioinformatics needed than for clinical samples
- Next generation sequencing of wastewater with bioinformatics to analyse SARS-CoV-2 genomic information
- Digital droplet PCR of ‘signature mutations’ of variants of concern

NGS FOR VARIANT CIRCULATION IN WASTEWATER

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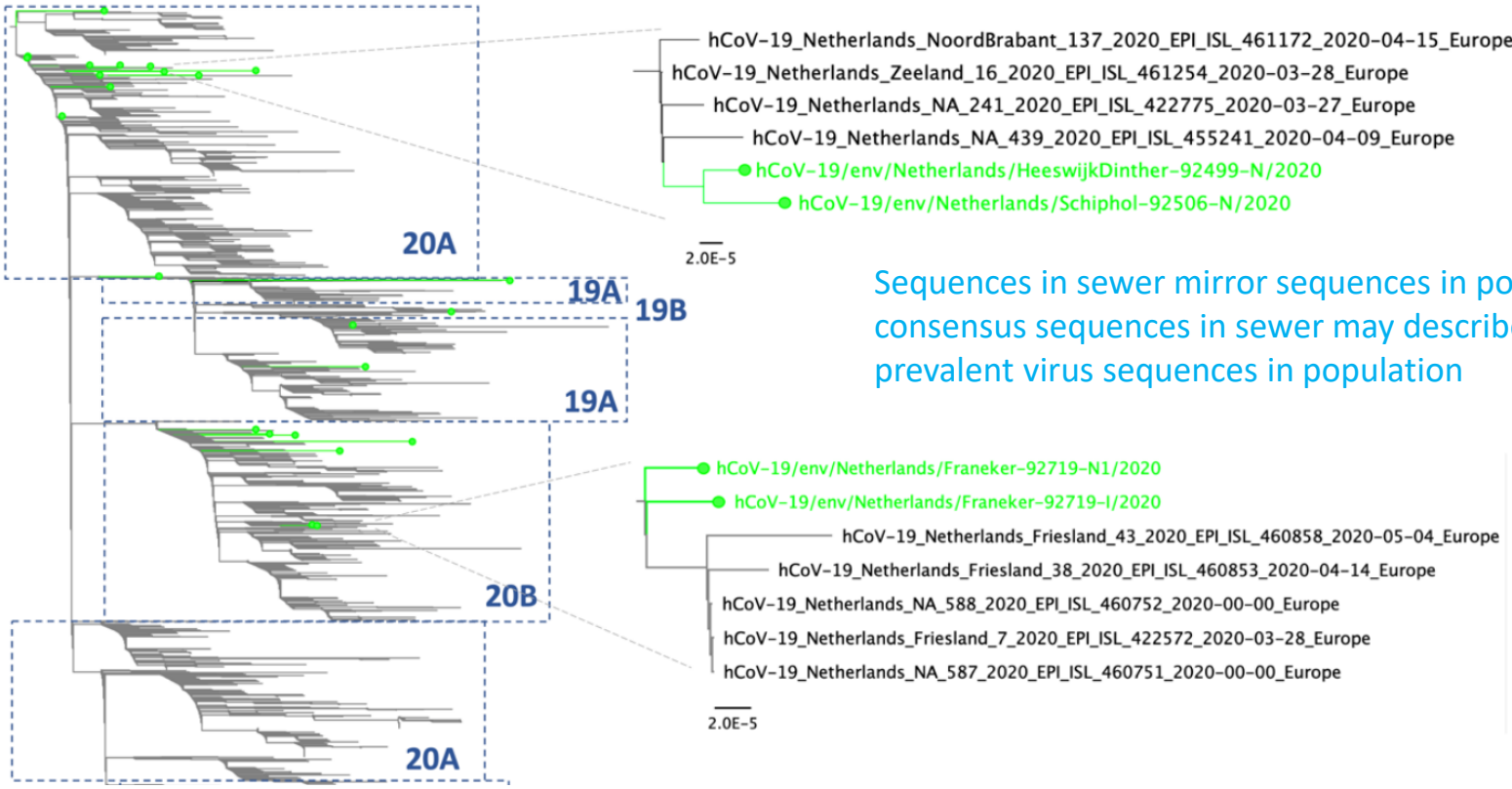
Erasmus MC

Conducted by Viroscience at Erasmus Medical Centre

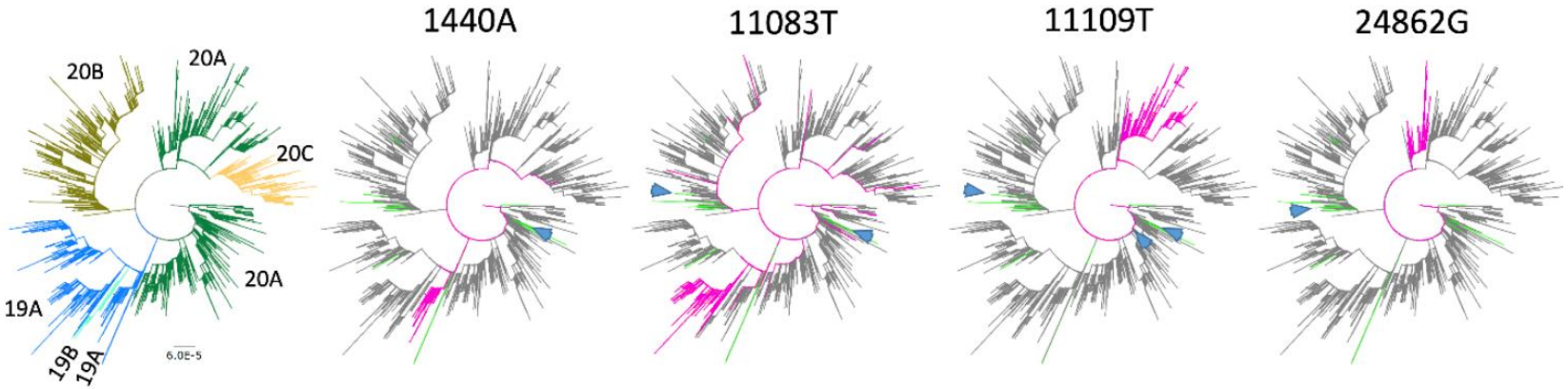


Sequences in sewer mirror sequences in population: consensus sequences in sewer may describe most prevalent virus sequences in population

Lara et al, 2021, EM INF DIS

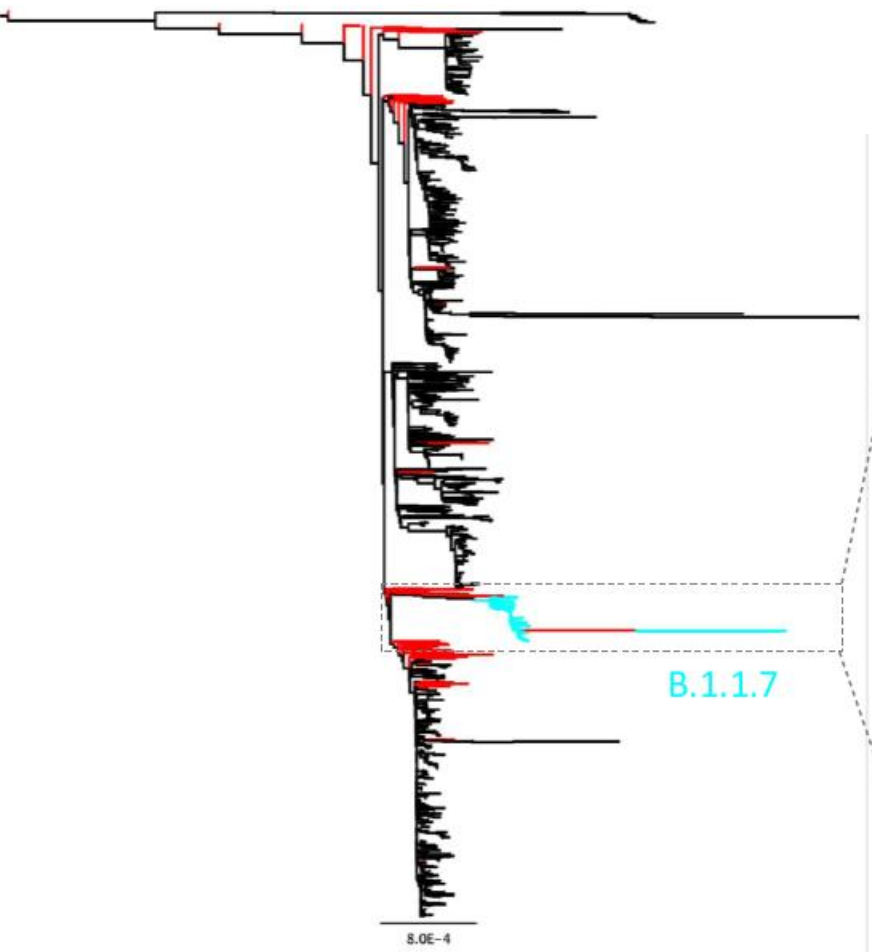
NGS OF SARS-COV-2 MUTATIONS IN SEWAGE

Conducted by Viroscience at Erasmus Medical Centre



Detection of novel mutations in the virus genome that are not seen in patients

UK VARIANT IN ROTTERDAM WASTEWATER



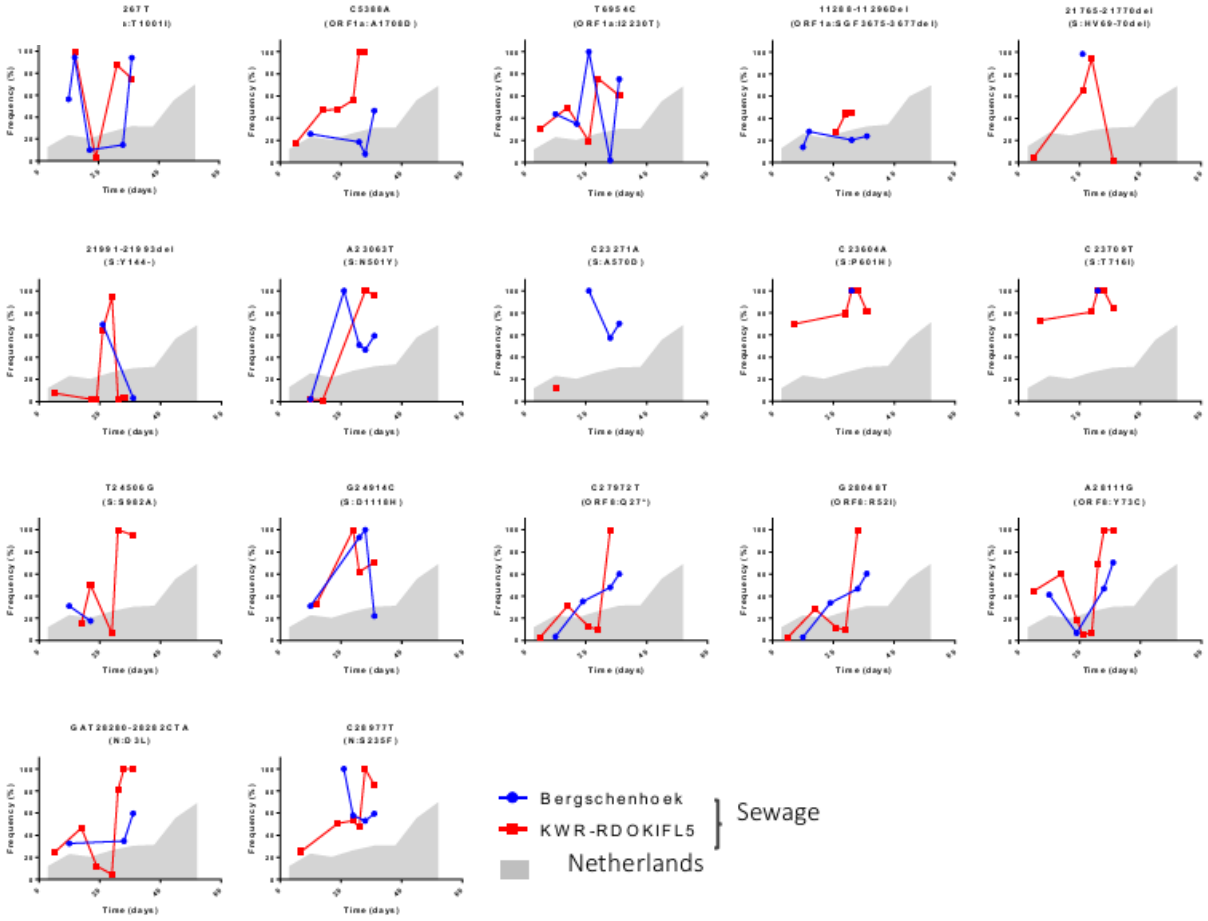
Versatile Emerging Infectious Disease Observatory

This work is supported by European Union"s Horizaon 2020 research and innovation programme under Grant No.874735 (VEO).

UK VARIANT MUTATIONS/DELETIONS IN ROTTERDAM WASTEWATER

gene	nucleotide	amino acid
ORF1ab	C3267T	T1001I
	C5388A	A1708D
	T6954C	I2230T
	11288-11296 deletion	SGF 3675-3677 deletion
spike	21765-21770 deletion	HV 69-70 deletion
	21991-21993 deletion	Y144 deletion
	A23063T	N501Y
	C23271A	A570D
	C23604A	P681H
	C23709T	T716I
	T24506G	S982A
	G24914C	D1118H
Orf8	C27972T	Q27stop
	G28048T	R52I
	A28111G	Y73C
N	28280 GAT->CTA	D3L
	C28977T	S235F

Vanaf 01-01-2021



Versatile Emerging Infectious Disease Observatory

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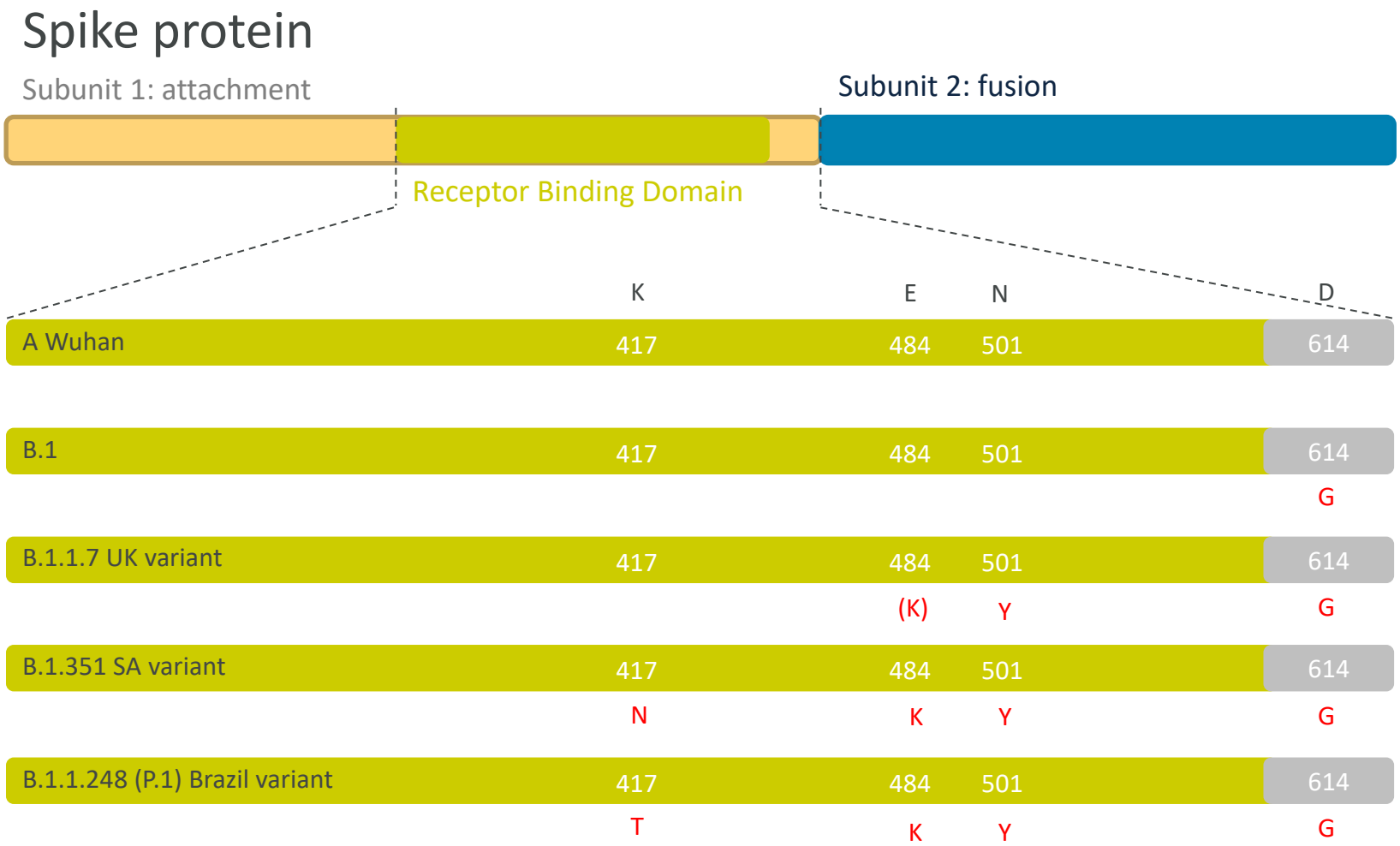
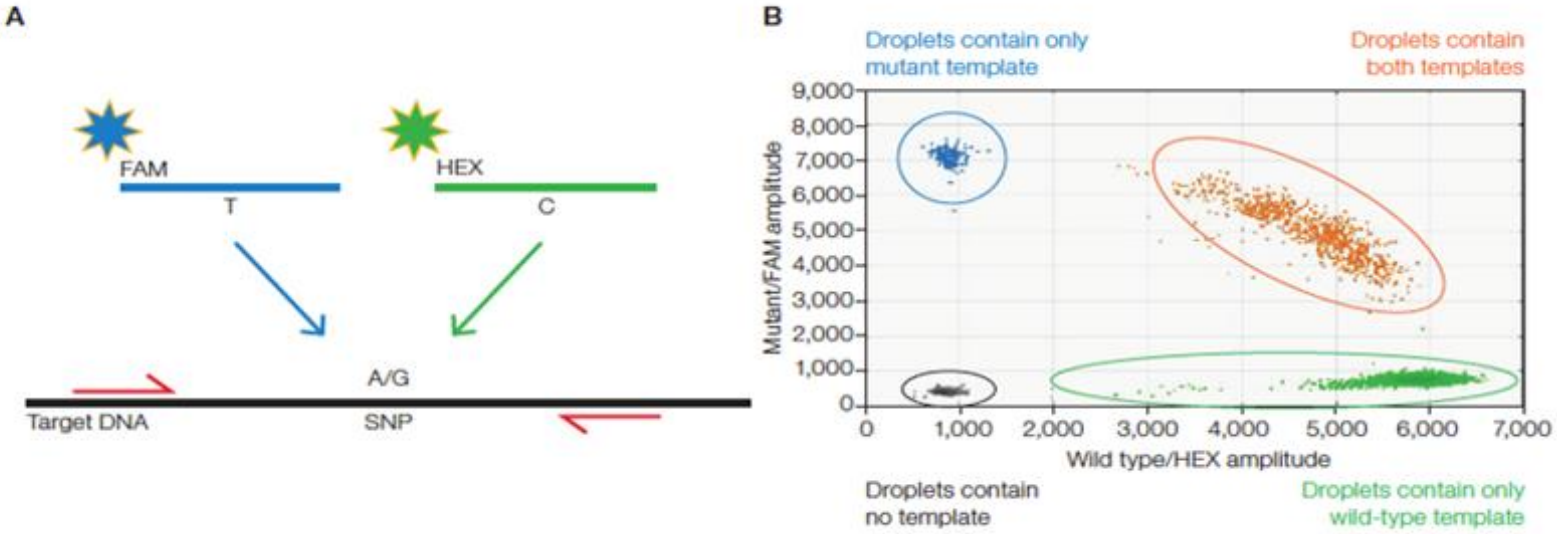
VARIANTS OF CONCERN: SIGNATURE MUTATIONS



DDPCR TO DETECT (RARE) SINGLE NUCLEOTIDE MUTATION

Rare Mutation Detection (RMD) refers to the detection of a sequence variant that is present at a very low frequency in a pool of wild-type background copies.

The challenge for RMD is the discrimination between two highly similar sequences, one of which is significantly more abundant than the other.



BioRad, 2021

SIMULTANEOUS DETECTION OF N501Y AND WILD TYPE WITH MULTIPLEX DDPCR

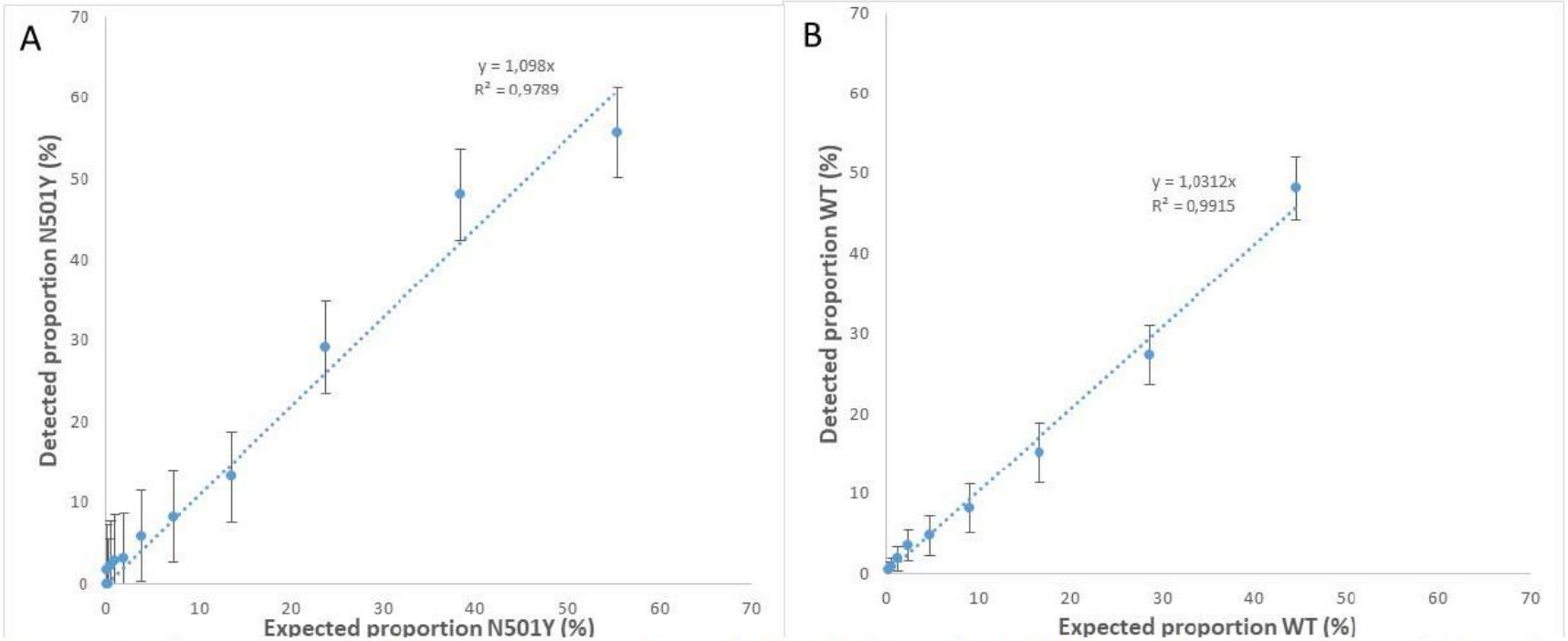


Figure 3. The expected and detected proportion of N501Y (A) and WT (B) in artificial mixtures of WT and lineage B.1.351 as detected by ddPCR.

Heijnen et al, 2021 medxriv

USE CASE: VARIANTS OF CONCERN INTRODUCTION N501Y MUTATION VS 'WILD TYPE' BY DDPCR

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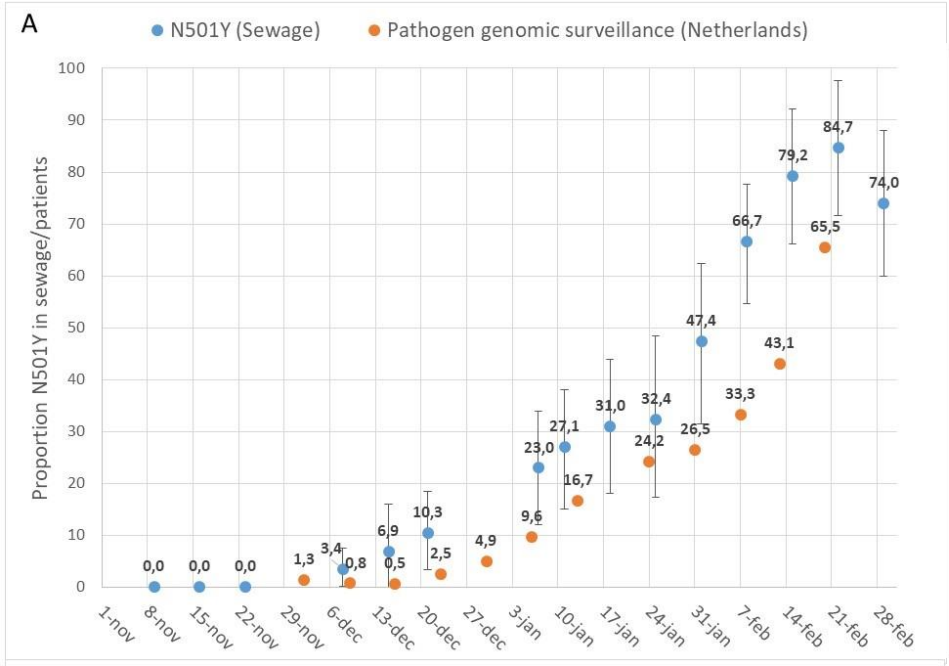
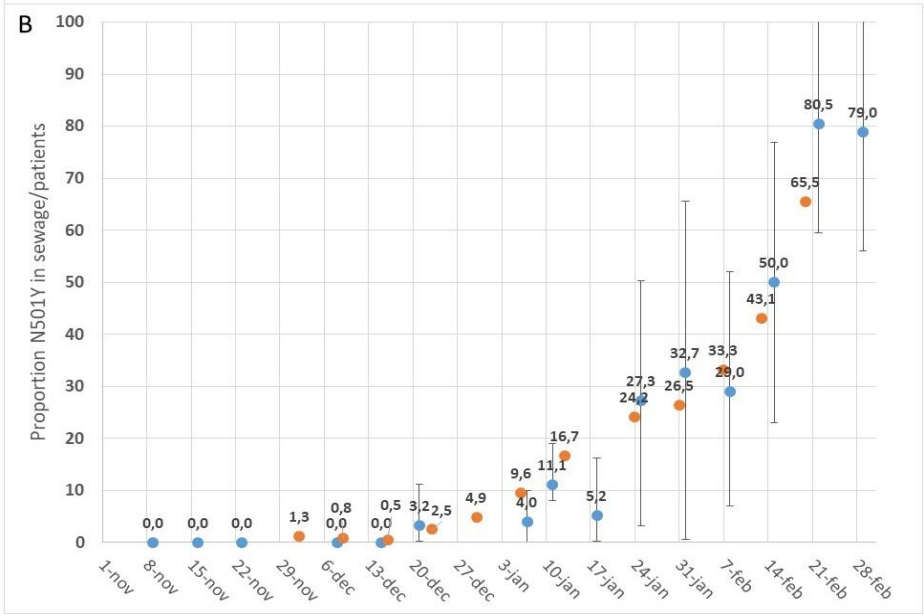


Amsterdam



Utrecht

WASTEWATER SURVEILLANCE IS OF ADDED VALUE FOR VOC SURVEILLANCE

- Feasible for emergence of (signature mutations of) VoC
- Fast (with ddPCR within days, compared to 3-4 weeks for clinical surveillance with NGS)
- Efficient: on population sample, allowing high resolution surveillance
- EU HERA incubator: recommendation to Member States to apply wastewater surveillance of variants of concern

THANK YOU FOR YOUR ATTENTION

the international water association

Bridging Science to Practice

Towards a Water-wise World

the international water association

Detection and surveillance of SARS-CoV-2 genomic variants in Swiss wastewater

TAMAR KOHN
EPFL,
SWITZERLAND

NIKO BEERENWINKEL
ETHZ,
SWITZERLAND

EPFL
eawag aquatic research
ETH zürich

Aerial view of STEP de Vidy *© Jean-Christophe Bott / Keystone*

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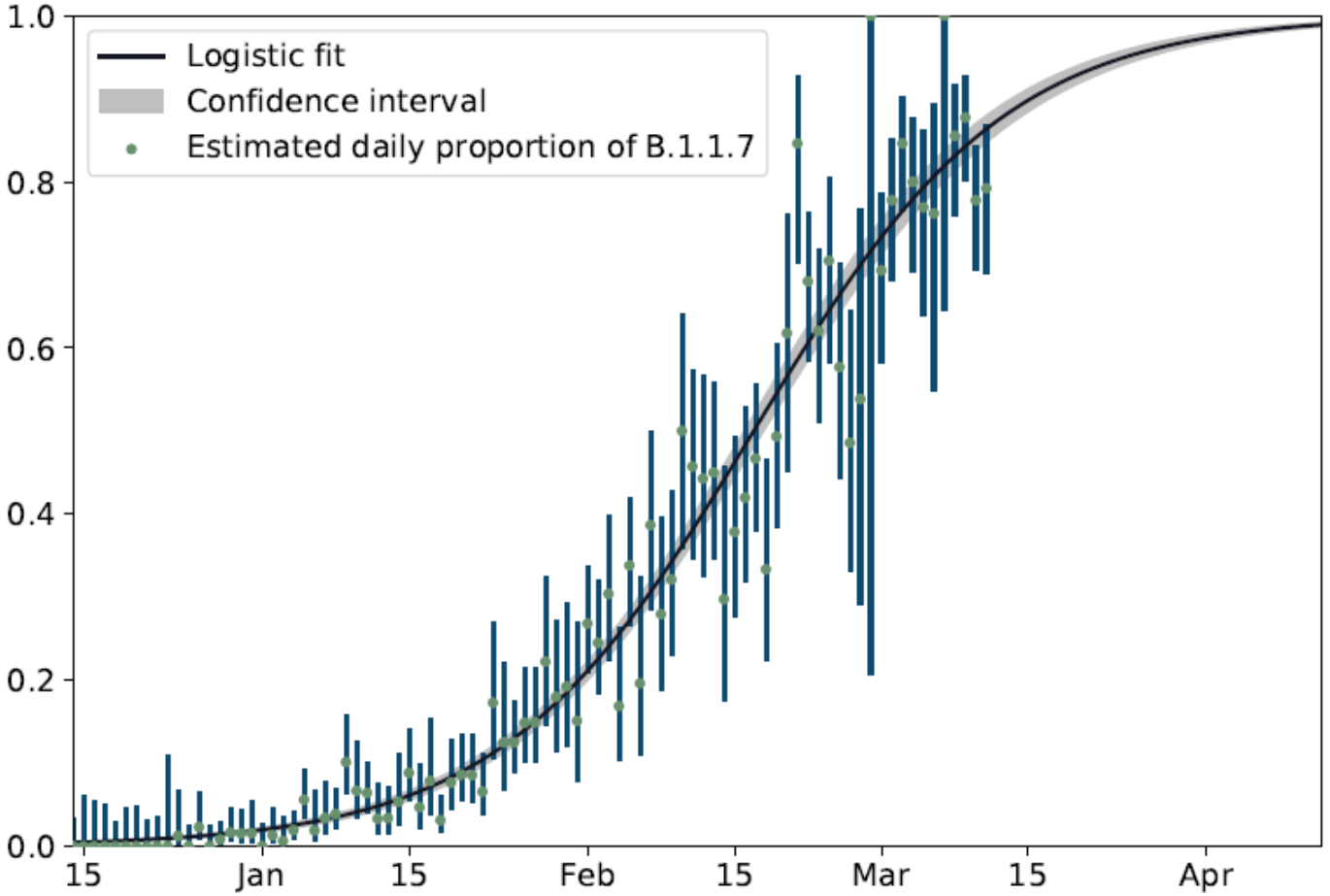
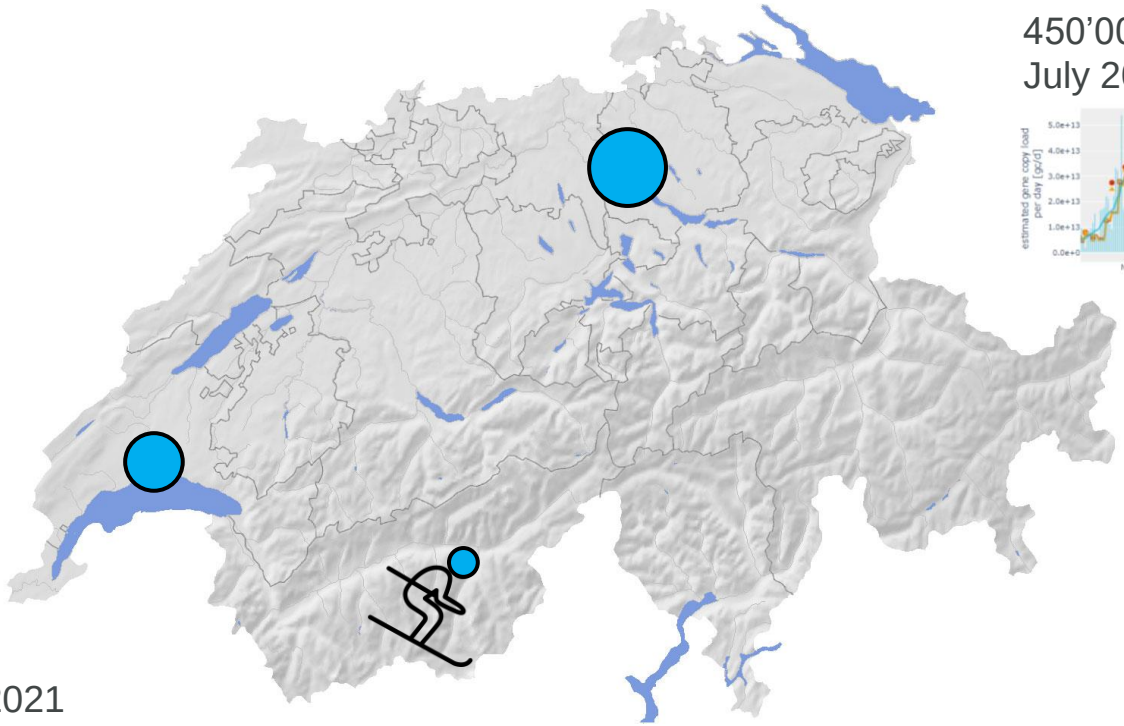
VARIANTS OF CONCERN IN SWITZERLAND

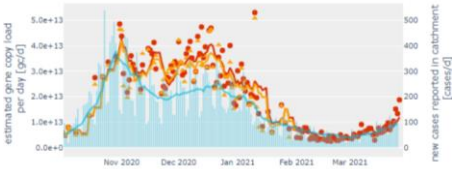


Chen et al. 2021, https://doi.org/10.1101/2021.03.05.21252520

WASTEWATER SAMPLING CAMPAIGN



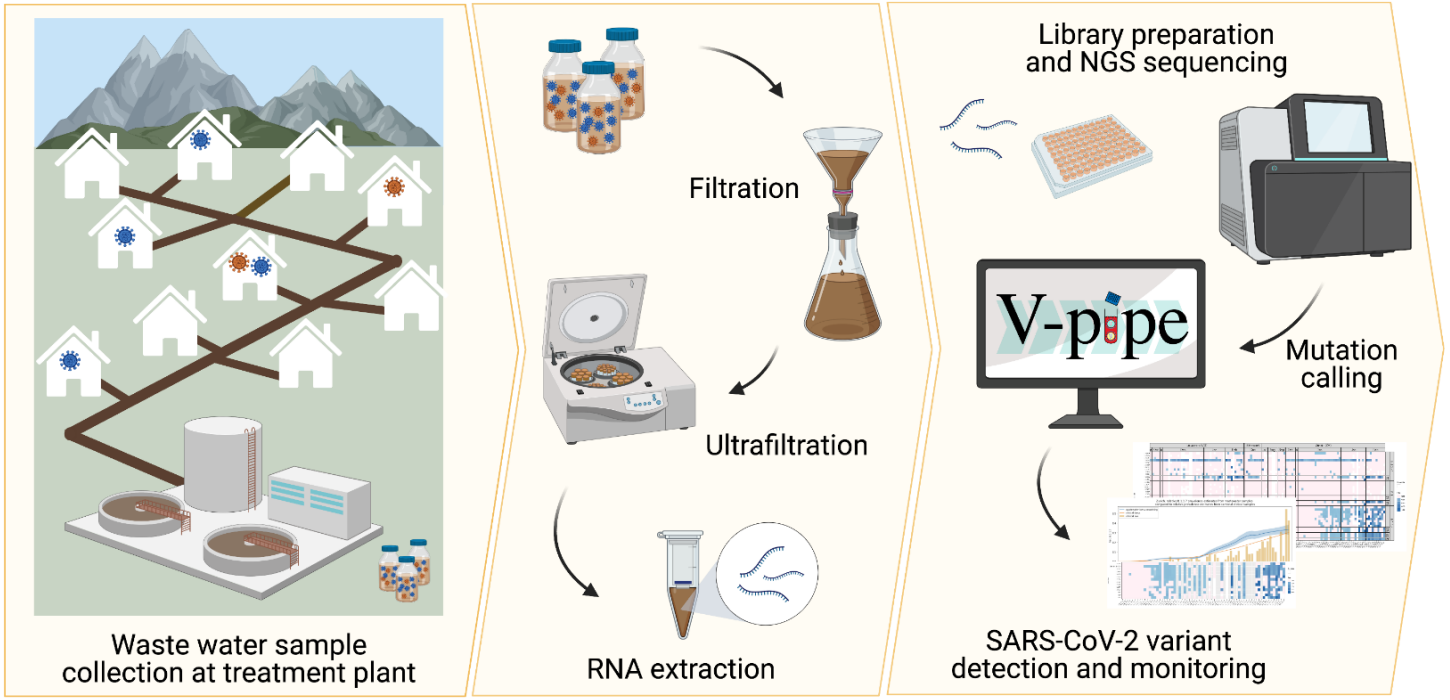
Zurich
450’000 p.e.
July 2020 – Feb 2021



Lausanne
240’000 p.e.
Sept 2020 – Feb 2021

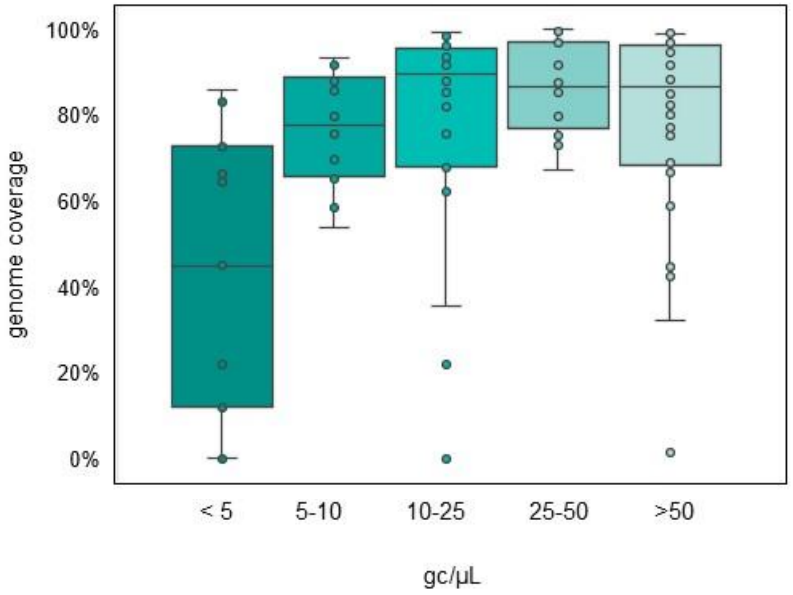
Alpine ski resort
< 10’000 p.e.
December 2020

METHODOLOGY



DATA QUALITY: COVERAGE

- Could sequence samples > 5 genome copies / µL extract (≈ 8 gc/mL ww) or less
- No consistent differences in normalized coverage between clinical and ww samples
- > 1 M aligned reads per sample
- Low-frequency (1/3000) mutation calling possible in most samples



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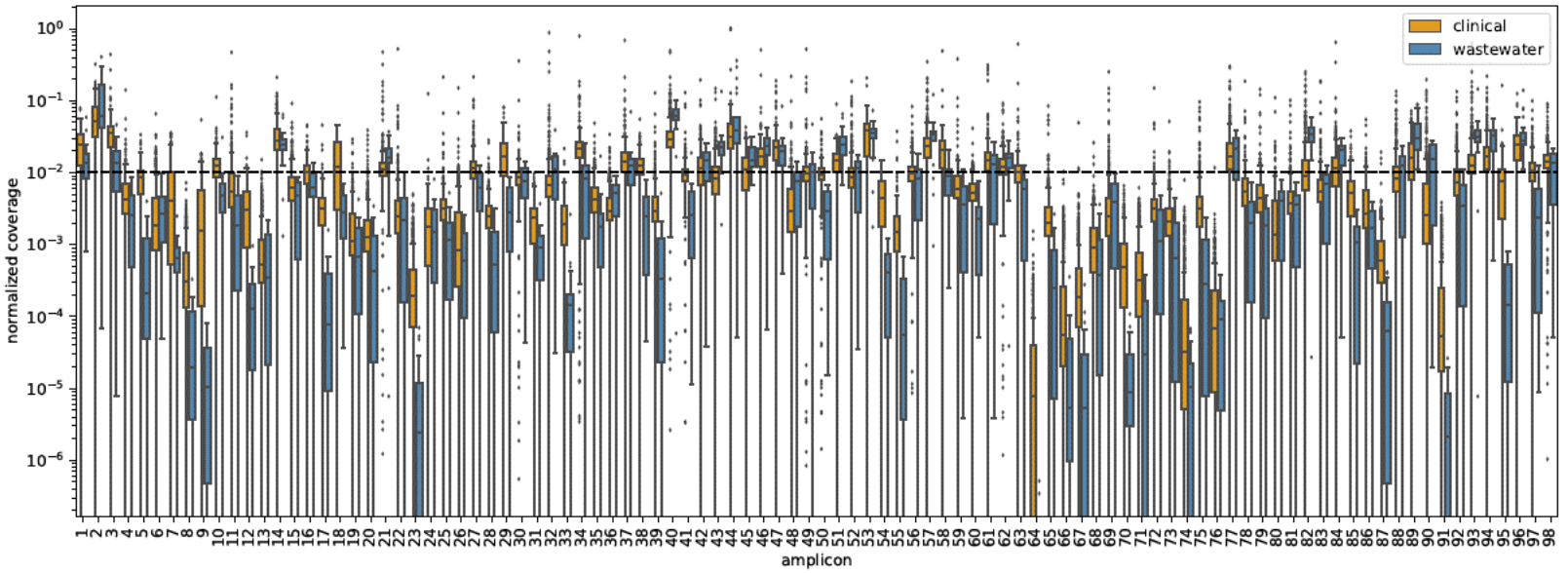


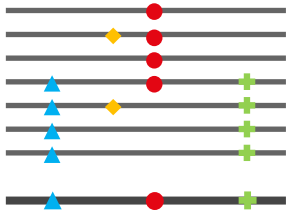
V-PIPE: A BIOINFORMATICS PIPELINE FOR MIXED VIRUS SAMPLES

the international water association

Read data

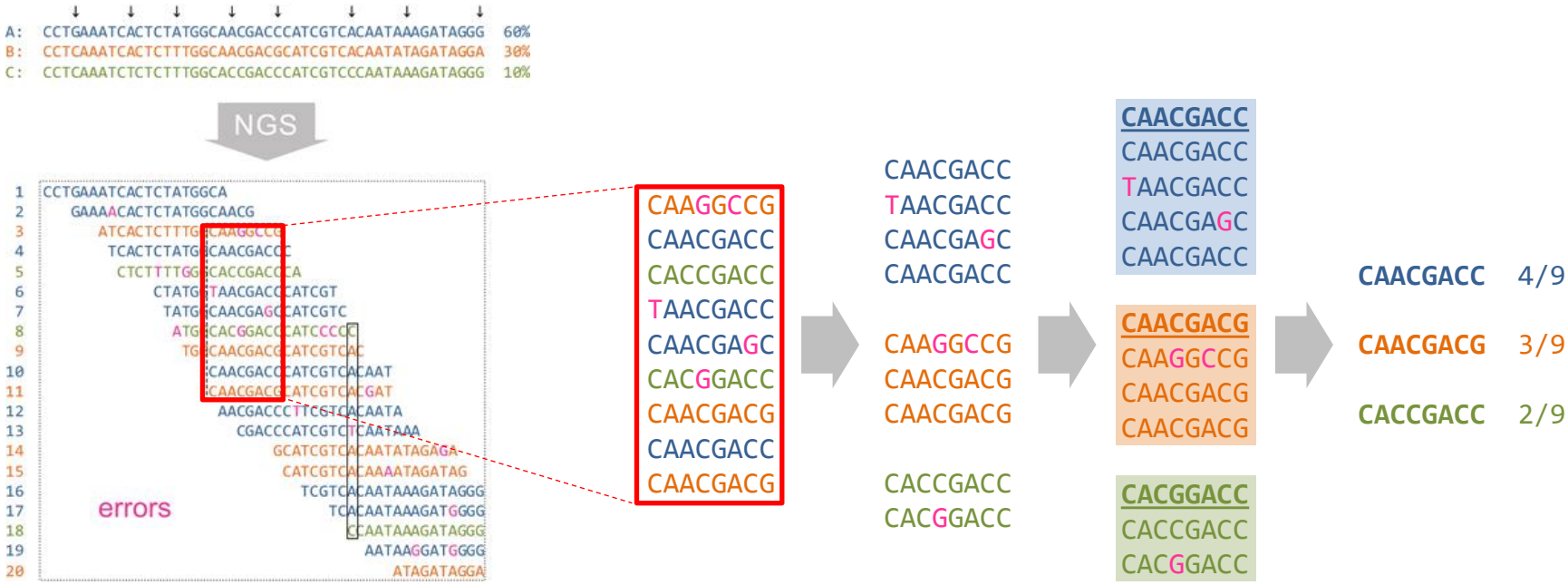
V-pipe

SNVs and SNV frequencies

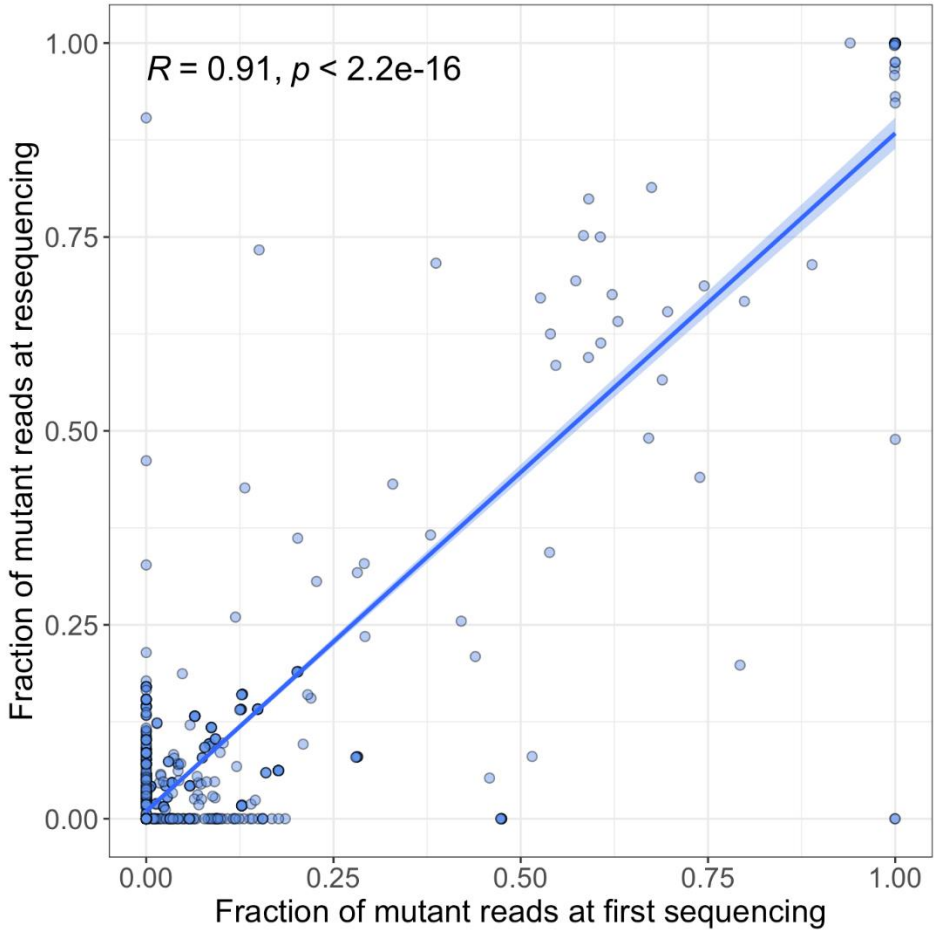


Posada et al., Bioinformatics, 2021

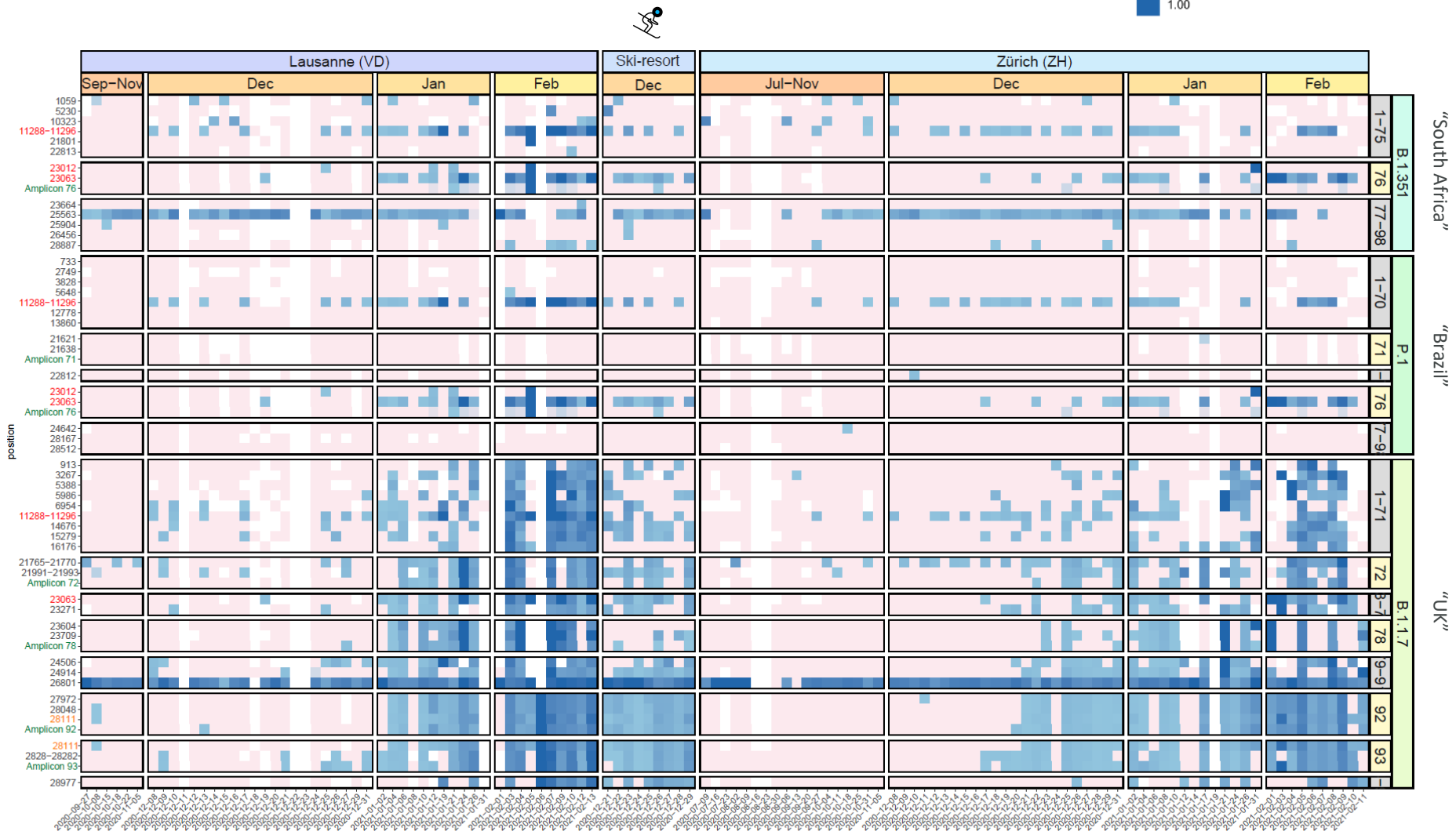
V-PIPE: MUTATION CALLING



FRACTION OF MUTANT READS



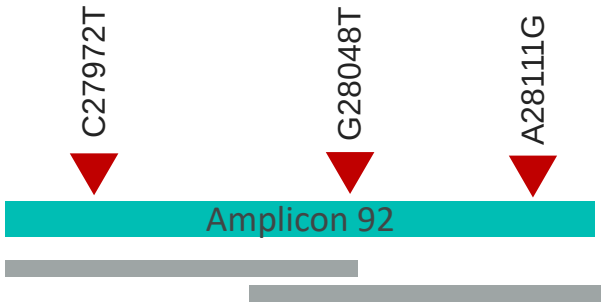
VARIANTS OF CONCERN



Jahn et al. 2021, https://doi.org/10.1101/2021.01.08.21249379

MUTATION CO-OCCURRENCE

- Artic v3 protocol:
  ~ 400 bp amplicons

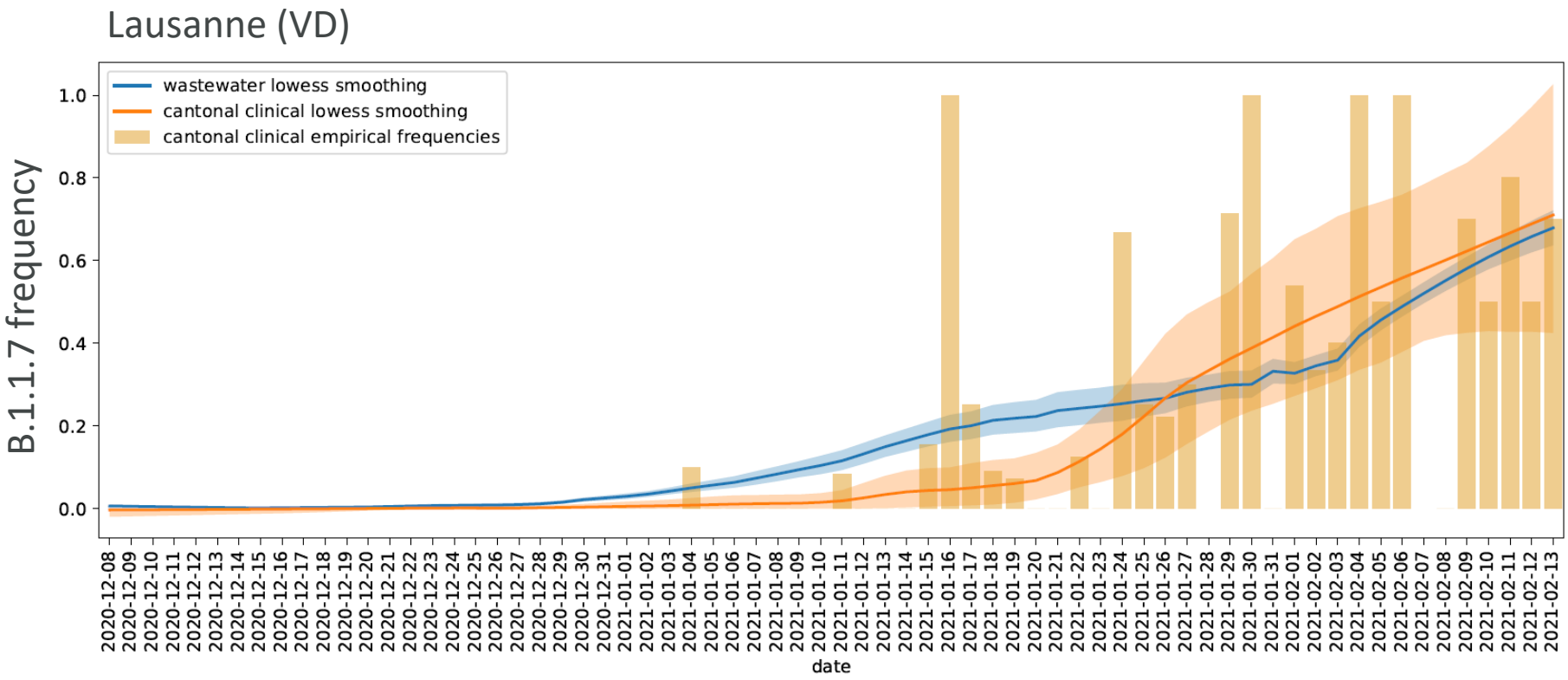


Paired-end 250 bp reads

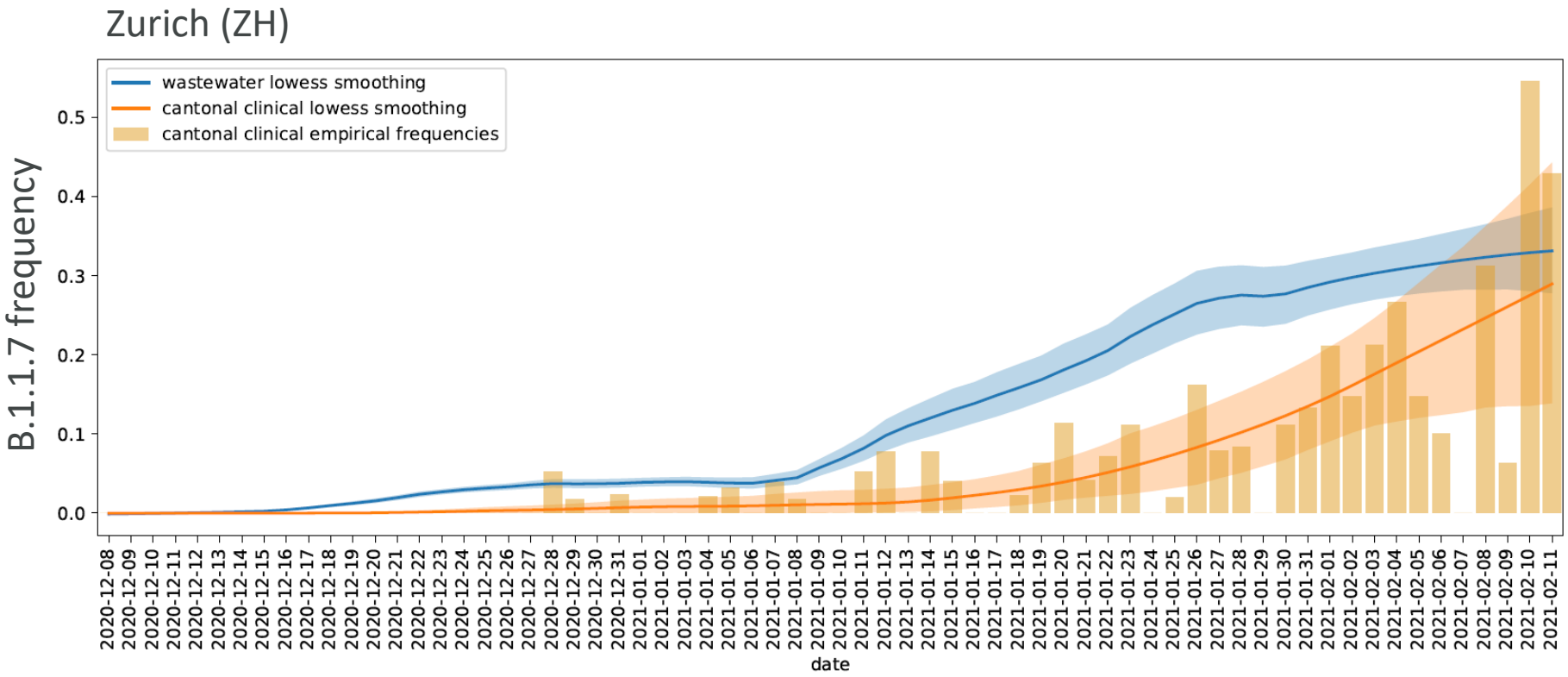
Sample	Amplicon 92 27809-28144 C27972T, G28048T, A28111G (B.1.1.7)	Amplicon 93 28105-28441 A28111G GAT28280CTA (B.1.1.7)	Amplicon 76 22822-23188 G23012A, A23063T (B.1.351)	Amplicon 77 23145-23499 A23403G (B.1)
2020-12-21 Ski resort	514 / 3689 13.93%	0 / 20672	0 / 165	36208 / 36209 100.00%
2020-12-21 Lausanne	0 / 10	93 / 3393 2.74%	0 / 0	10 / 10 100.00%
2020-12-14 Lausanne	0 / 4858	816 / 35838 2.28%	0 / 177	20280 / 20284 99.98%
2020-12-11 Lausanne	154 / 13504 1.14%	0 / 82020	0 / 802	93625 / 93659 99.96%
2020-12-09 Lausanne	5 / 457 1.09%	0 / 40213	0 / 76	12846 / 12847 99.99%
Patient sample 410256 (B.1.351 positive)	0 / 2601	0 / 3526	8 / 8 100.00%	6570 / 6574 99.94%
Patient sample 410279 (B.1.351 positive)	0 / 20487	0 / 16822	156 / 156 100.00%	32633 / 32699 99.80%
Patient sample 420389 (B.1.1.7 positive)	389 / 389 100.00%	1498 / 1501 99.80%	0 / 3	3184 / 3184 100.00%
Patient sample 420394 (B.1.1.7 positive)	207 / 207 100.00%	739 / 742 99.60%	0 / 7	2067 / 2068 99.95%

Jahn et al. 2021, https://doi.org/10.1101/2021.01.08.21249379

WASTEWATER VS. CLINICAL SAMPLES

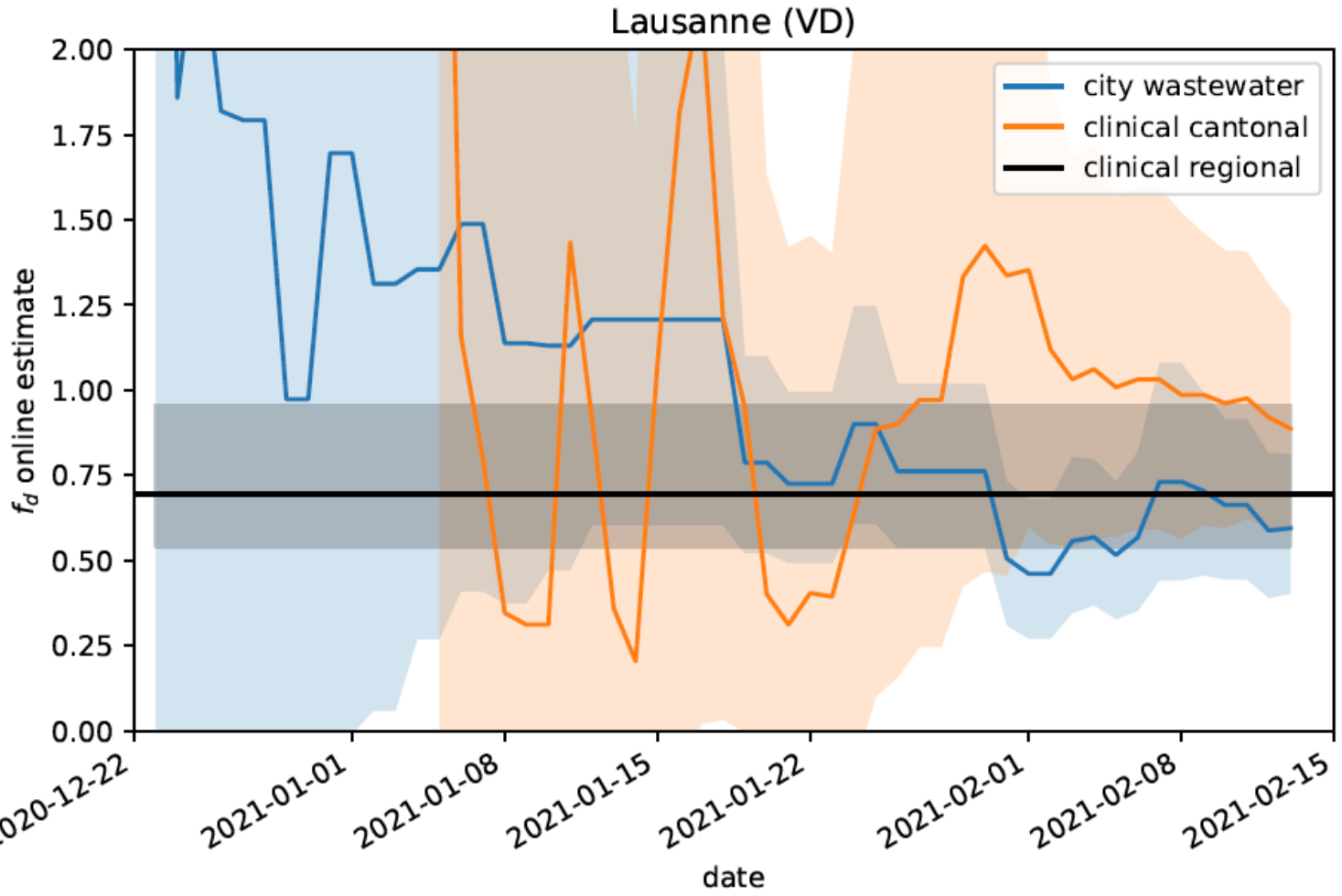


WASTEWATER VS. CLINICAL SAMPLES



TRANSMISSION FITNESS ONLINE ESTIMATE

$$R_{\text{B.1.1.7}} = (1 + f_d)\, R_{\text{wild type}}$$



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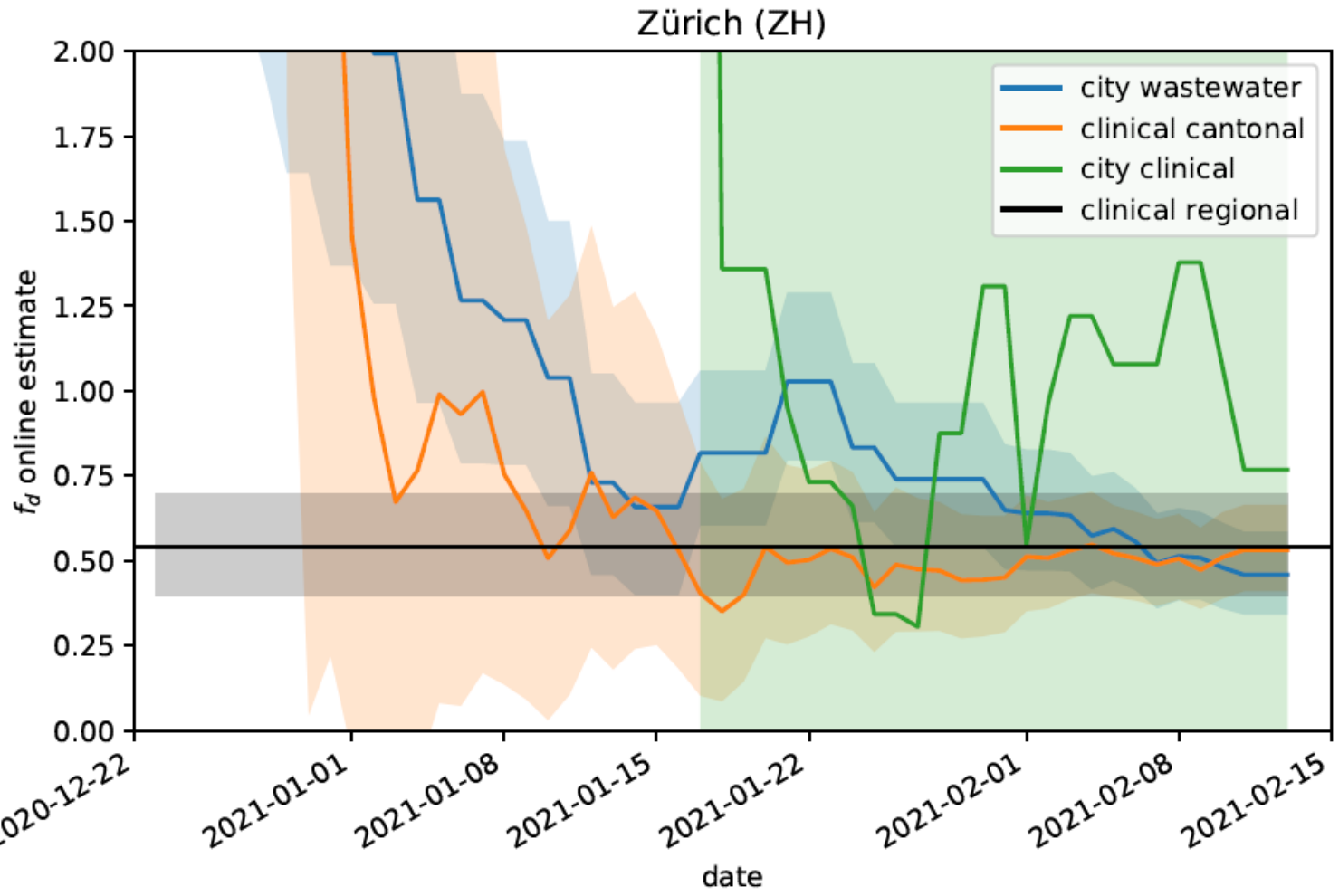
$$R_{\text{B.1.1.7}} = (1 + f_d)\, R_{\text{wild type}}$$



THANKS TO…

the international water association

EPFL

Federica Cariti
Xavier Fernandez-Cassi
Alex Tuñas Corzón

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D BSSE

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Chaoran Chen
David Dreifuss
Lara Furhmann
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Katharina Jahn
Tanja Stadler
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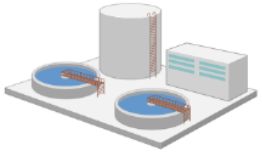
eawag aquatic research

Carola Bänziger
Lea Caduff
Pravin Ganesandamoorthy
Tim Julian
Anina Kull
Christoph Ort
Elyse Stachler



EPFL

eawag aquatic research

FNSNF
Fonds national suisse
Schweizerischer Nationalfonds
Fondo nazionale svizzero
Swiss National Science Foundation

Schweizerische Eidgenossenschaft
Confédération suisse
Confederazione Svizzera
Confederaziun svizra

Federal Office for the Environment (FEON)

Schweizerische Eidgenossenschaft
Confédération suisse
Confederazione Svizzera
Confederaziun svizra

Federal Office of Public Health (FOPH)

SIB Swiss Institute of Bioinformatics

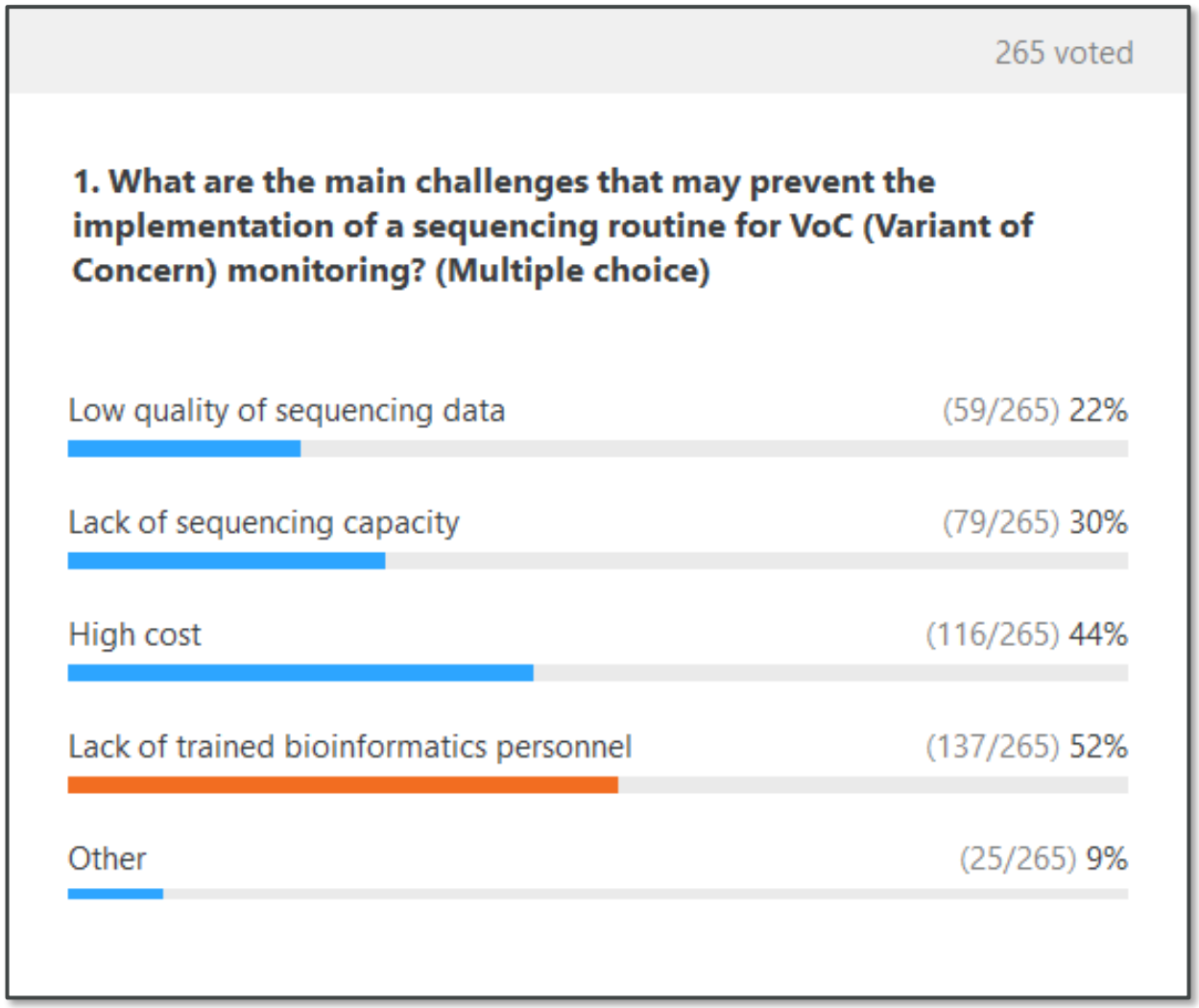
POLL 2: MONITORING CHALLENGES

Multiple choice

1. What are the main challenges that may prevent the implementation of a sequencing routine for VoC (Variant of Concern) monitoring?

- Low quality of sequencing data
- Lack of sequencing capacity
- High cost
- Lack of trained bioinformatics personnel
- Other

POLL 2: MONITORING CHALLENGES



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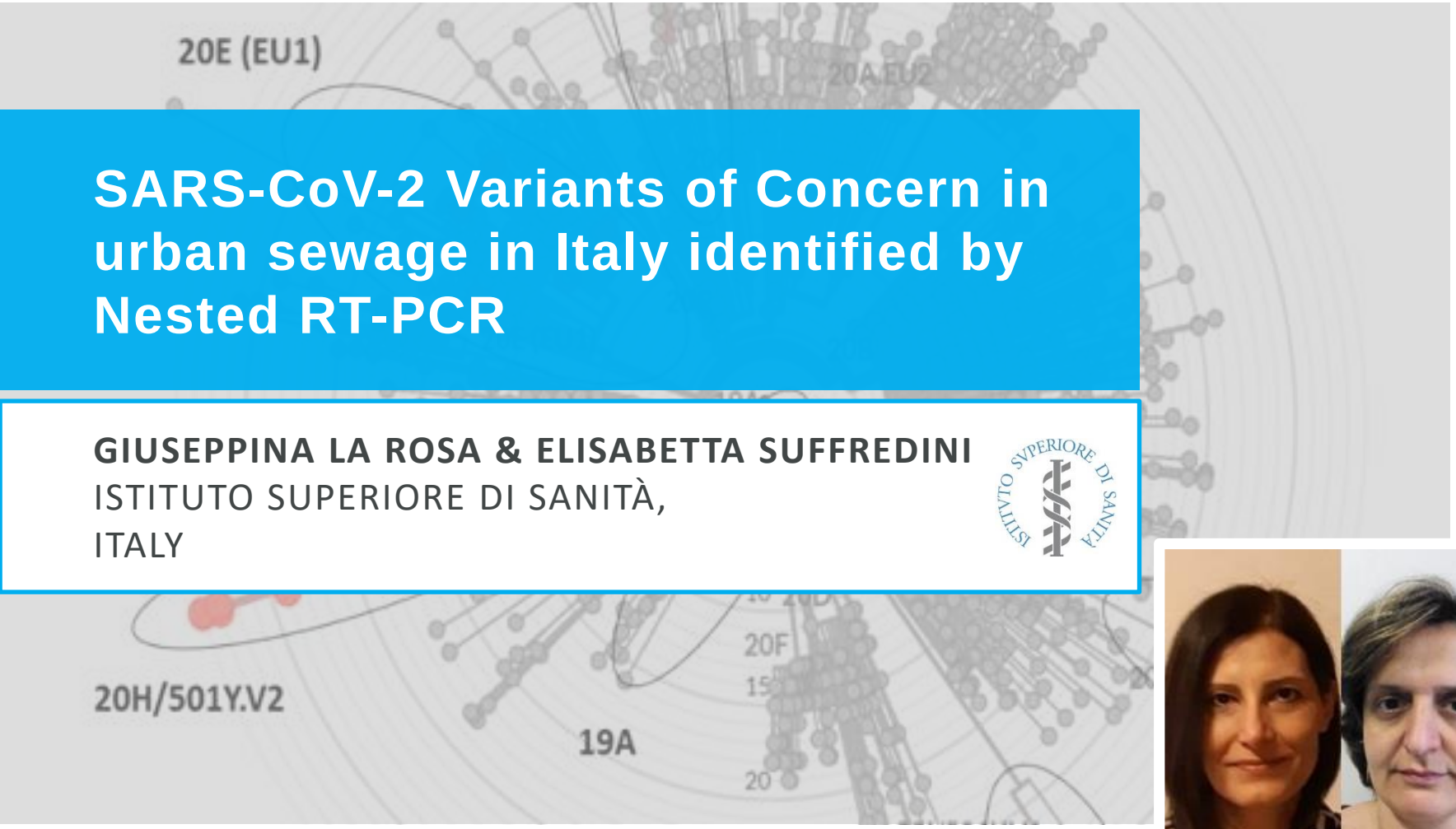


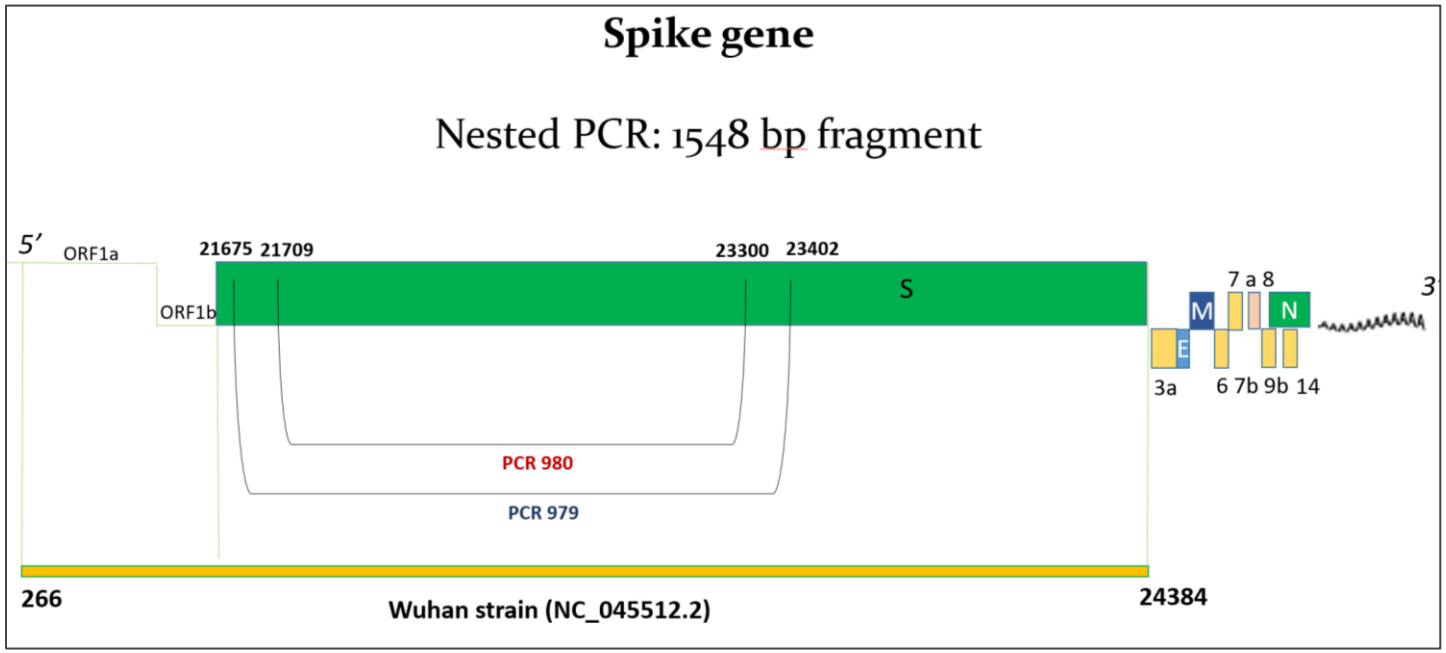
SARS-CoV-2 Variants of Concern in urban sewage in Italy identified by Nested RT-PCR

GIUSEPPINA LA ROSA & ELISABETTA SUFFREDINI
ISTITUTO SUPERIORE DI SANITÀ,
ITALY

inspiring change

AIM

- Develop a rapid screening method for variants of concern in clinical and environmental samples: nested RT-PCR + Sanger sequencing



The amplified fragment codes for 515 amino acids of the spike protein (positions 58-573)

MUTATIONS DETECTABLE BY THE NEWLY DESIGNED PCR ASSAY

the international water association

VOCs

Variant	First detected	LONG PCR ID 980 (a)																	
B.1.1.7 (501Y.V1)	UK		H69 del	V70 del			Y144 del											N501Y	A570D
B.1.351 (501.V2)	South Africa				D80A					D215G		L242H	A243/4 /5del	R246I	K417N			E484K	N501Y	
P.1 (501Y.V3)	Brazil					D138Y			R190S						K417T			E484K	N501Y	
B.1.177 (20E.EU1)	Spain										A222V									
B.1.429 (20C/S:452R)	US-California							W152C									L452R			
B.1.1.298 (Mink Cluster V)	Denmark		H69 del	V70 del														Y453F		
B.1.525	Nigeria	A67V	H69 del	V70 del			Y144 del											E484K		
B.1.36	India															N440K				
R.1	Japan							W152L										E484K		

a) Amino acid position 58 to 573 of the spike protein (primers excluded)

IN-SILICO STUDY: GISAID

the international water association

Are specific **combinations of mutations** sufficiently informative to screen for specific SARS-CoV-2 variants?

Lineage GR B.1.1.7 (UK)

Mutations detectable in the long fragment:

HV69-70del, Y144del, N501Y and A570D

i. Among the complete genomes belonging to **this** lineage **any combination of two mutations** was present at a frequency ranging from 97.6% to 99.4%.

ii. **All** of the complete genomes displaying **at least two of the aforementioned mutations** belonged to the B.1.1.7 lineage.

Last run: 14.01.2021 h 23.30-23.40
tot GISAID CoV-2 complete genome seq 371470
tot GR B.1.1.7 complete genome seq 17798

Complete genomes classified as GR B.1.1.7 that display the following combinations of mutations

H69del	Y144del	N501Y	A570D	n°	n°/GR B.1.1.7
1	1	1	1	17353	97,50%
1	1	1	0	17355	97,51%
0	1	1	1	17372	97,61%
1	0	1	1	17510	98,38%
1	1	0	1	17371	97,60%
1	1	0	0	17374	97,62%
0	0	1	1	17691	99,40%
1	0	0	1	17529	98,49%
0	1	1	0	17374	97,62%
1	0	1	0	17517	98,42%
0	1	0	1	17390	97,71%
1	0	0	0	17537	98,53%
0	1	0	0	17393	97,72%
0	0	1	0	17703	99,47%
0	0	0	1	17829	100,17%
0	0	0	0	17798	100,00%

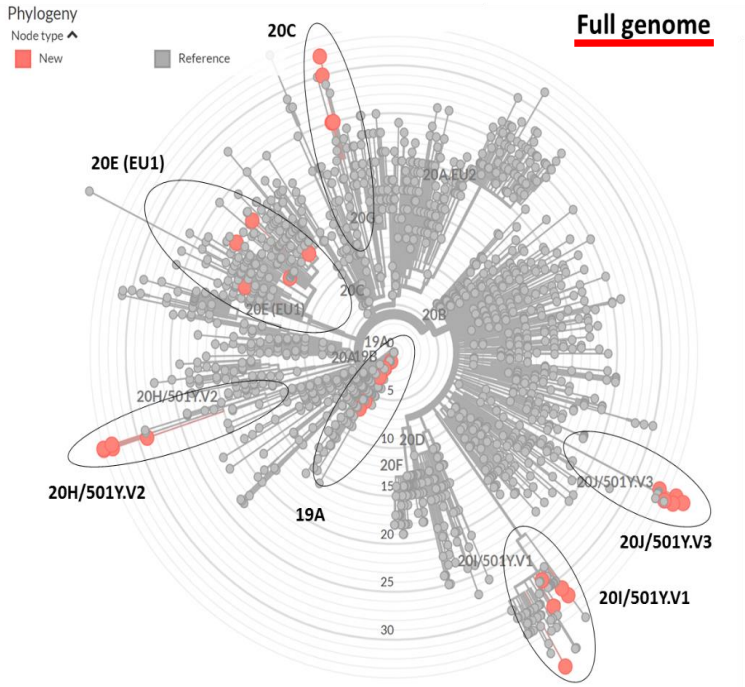
Complete genomes with the following combinations of mutations that are classified as GR B.1.1.7

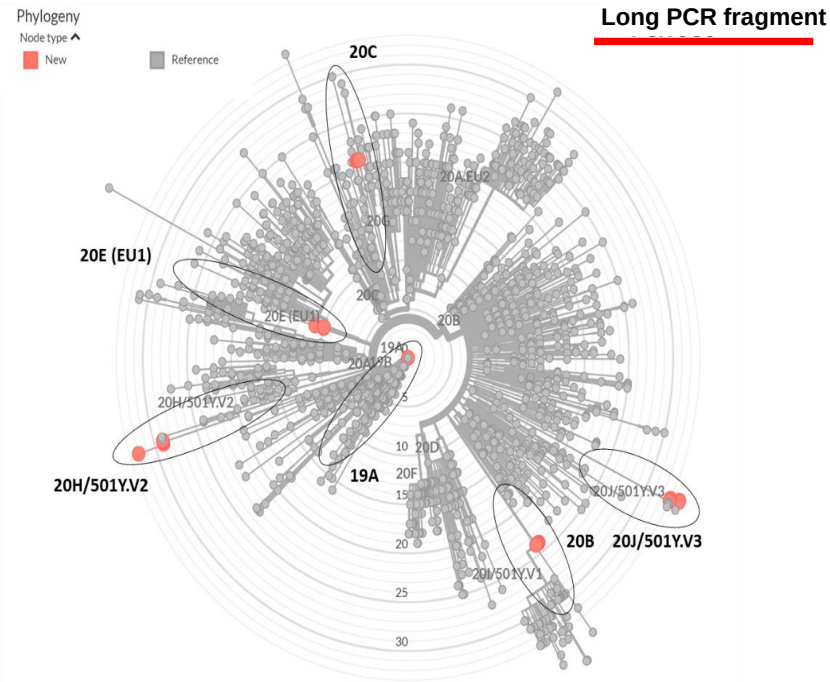
H69del	Y144del	N501Y	A570D	n°	GR B.1.1.7	GR B.1.1.7/n°
1	1	1	1	17355	17355	100,00%
1	1	1	0	17357	17357	100,00%
0	1	1	1	17374	17374	100,00%
1	0	1	1	17512	17512	100,00%
1	1	0	1	17373	17373	100,00%
1	1	0	0	17376	17376	100,00%
0	0	1	1	17693	17693	100,00%
1	0	0	1	17531	17531	100,00%
0	1	1	0	17376	17376	100,00%
1	0	1	0	17519	17519	100,00%
0	1	0	1	17392	17392	100,00%
1	0	0	0	24166	17537	72,57%
0	1	0	0	17908	17395	97,14%
0	0	1	0	18751	17705	94,42%
0	0	0	1	17833	17831	99,99%
0	0	0	0	17798	17798	100,00%

IN-SILICO STUDY: NEXTCLADE

5 GISAID strains for each of the the following clades/variants:

Wuhan (19A), UK (501Y.V1), **South Africa** (501Y.V2), **Brazil** (501Y.V3), **Spain** (20E.EU1), **California** (CAL.20C) for a total of 30 sequences.





All of the variants were correctly assigned on the sole basis of the genome region amplified by the long PCR.

PRIMER VALIDATION ON CLINICAL SAMPLES

- **7 SARS-CoV-2 RNA samples** originating from nasopharyngeal swabs, collected in Apulia and Basilicata (August-December 2020)
  - isolated on Vero E6 cells
  - **characterized by WGS** as 20A, 20B, 20E.EU1 (Spanish variant), and 20I/501Y.V1 (UK variant),

- **24 RNA samples** originating from nasopharyngeal swabs collected in Apulia and Basilicata (November-January 2021) that tested positive for SARS-CoV-2 by real-time RT-PCR
  - **not characterized**

PRIMER VALIDATION ON CLINICAL SAMPLES

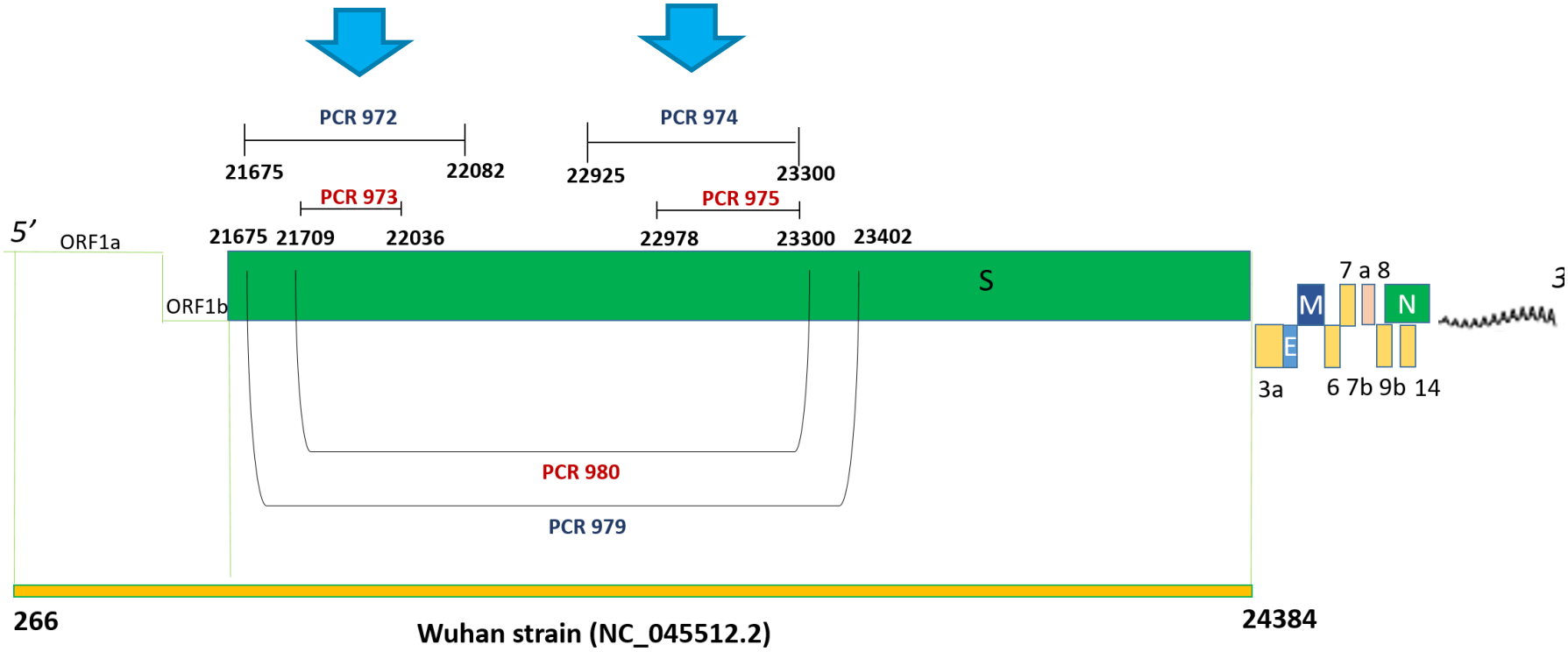
Sample	Identification based on WGS	Mutation map	GISAID blast
swab_1	-	A222V	GV_B.1.177
swab_2	-	S477N	GH_B.1.160
swab_3	-	S477N	GH_B.1.160
swab_4	-	A222V	GV_ B.1.177
swab_5	-	A222V	GV_ B.1.177
swab_6	-	A222V	GV_ B.1.177
swab_7	-	A222V	GV_ B.1.177
swab_8	-	A222V	GV_ B.1.177
swab_9	-	A222V	GV_ B.1.177
swab_10	-	A222V	GV_ B.1.177
swab_11	-	A222V	GV_ B.1.177
swab_12	-	A222V	GV_ B.1.177
swab_13	-	S477N	GH_B.1.160
swab_14	-	-	Not assignable
swab_15	-	-	Not assignable
swab_16	-	S477N	GH_B.1.160
swab_17	-	A222V	GV_ B.1.177
swab_18	-	A222V, A262S, P272L	GV_ B.1.177
swab_19	-	S98F	G_B.1.221
swab_20	-	A222V	GV_ B.1.177
swab_21	-	n.d.	n.d.
swab_22	-	n.d.	n.d.
swab_23	-	S477N	GH_B.1.160
swab_24	-	A222V, A411S	GV_B.1.177
swab_25	20A	-	Not assignable
swab_26	20A	D215H	Not assignable
swab_27	20B	-	Not assignable
swab_28	20B	-	Not assignable
swab_29	GV_ B.1.177	A222V	GV_ B.1.177
swab_30	GV_ B.1.177	A222V	GV_ B.1.177
swab_31	GR B.1.1.7	H69del, V70del, Y144del, N501Y, A570D	GR B.1.1.7

The Spanish variant was found in 14/24 uncharacterized swabs (mutation A222V alone or combined with A262S and P272L in one sample or with A411S in another sample)

The long assay allowed the correct identification of the UK and the Spanish variants present in the panel of previously characterized samples.

DESIGN OF SHORT ASSAYS TO BE USED IN SEWAGE SAMPLES

Two additional short nested RT-PCRs
targeting portions of the region spanned by the long assay



DESIGN OF SHORT ASSAYS TO BE USED IN SEWAGE SAMPLES

Mutations indicative of the main SARS-CoV-2 VOCs detectable by the newly designed short nested PCR assays.

Variant	Amino acid position in the S gene																	
20I/501Y.V1 (GR, B.1.1.7), UK		H69 del	V70 del			Y144 del											N501Y	A570D
20H/501Y.V2 (GH, B.1.351), SA				D80 A				D215G	L242H	A243 del	L244 del	H245 del	R246I	K417N		E484K	N501Y	
20J/501Y.V3 (GR, P1), Brazil					D138Y		R190S							K417T		E484K	N501Y	
Mink clust. V (GR,B.1.1.298), Denmark		H69 del	V70 del												Y453F			
(G, B.1.525), Nigeria	A67 V	H69 del	V70 del			Y144 del										E484K		
	SHORT PCR 973 (aa 58-150)															SHORT PCR 975 (aa 480-573)		
	LONG PCR 980 (aa. 58-573 of the spike protein)																	

TESTING THE LONG AND SHORT ASSAYS ON SEWAGE SAMPLES

the international water association

Environmental samples tested with the three assays:

1. **20 SARS-CoV-2 positive sewage samples**
   Rome (Sept-Dec 2020)
2. **8 sewage samples**
   Guardiagrele, Abruzzo (21-25 January 2021) – where a cluster of clinical cases of the UK variant had been reported
3. **6 sewage samples**
   Perugia, Umbria (5 - 8 February 2021) – where clinical cases of the UK variant and of the Brazilian variant had been identified

Aim: to verify whether the S mutations associated with these variants were detectable in the local sewage using the newly designed assays.

TESTING THE LONG AND SHORT ASSAYS ON SEWAGE SAMPLES

1. **20 SARS-CoV-2 positive sewage samples**
   Rome (Sept-Dec 2020)

   → None of the samples collected in Rome displayed mutations indicative of VOCs

2. **8 sewage samples**
   Guardiagrele, Abruzzo (21-25 January 2021) – where a cluster of clinical cases of the UK variant had been reported

   → Mutations characteristic of the Spanish variant were detected, but not the UK variant

3. **6 sewage samples**
   Perugia, Umbria (5 - 8 February 2021) – where clinical cases of the UK variant and of the Brazilian variant had been identified

   → Mutations characteristic of the UK, and Brazilian variants were detected

TESTING THE LONG AND SHORT ASSAYS IN SEWAGE SAMPLES

Sample ID	Sampling location	Long-PCR ID 980		Short-PCR ID 973		Short-PCR ID 975	
		Result	Mutations	Result	Mutations	Result	Mutations
3863	Abruzzo	+	A222V	+	none	+	none
3865		+	A222V	+	none	-	
3944	Umbria	-	-	+	D138Y	+	E484K, N501Y
3945		-	-	+	D138Y	+	E484K, N501Y
3947		+	**D138Y, R190S, K417T, E484K, N501Y**	+	D138Y	+	E484K, N501Y
3949		-	-	+	E96G	+	N501Y, A570D

Spanish mutation, detected by long PCR

Brazilian mutations, detected by long + both short PCRs

UK mutations, detected by only one of the short PCRs

Sequence did not show the expected mutations (HV69-70del and Y144del) of the UK variant

Sample collected on 6 February 2021 from a WTP serving the outskirts of Perugia, including the local hospital, which had reportedly been experiencing a nosocomial cluster of the Brazilian variant

CONCLUSIONS

We were able to detect key mutations of the Spanish, Brazilian and UK variants in urban wastewaters in Italy.

Advantages:

- ✓ Rapidly identifies VOCs in the catchment of any WTP to identify areas where clinical surveillance and/or targeted preventive intervention is required.
- ✓ Can be performed routinely at a low cost, easy to interpret.
- ✓ In clinical settings, can be used as a rapid screening test to select clinically relevant specimens for WGS.

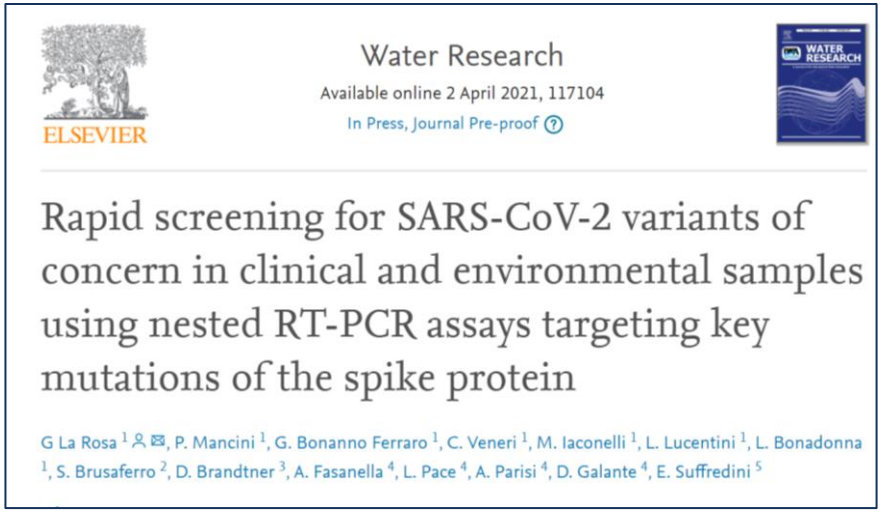
Disadvantages:

- ✓ In environmental samples, Sanger sequencing may underestimate some, possibly less prevalent, strains.
- ✓ In environmental samples, use of 2 short assays may result in each of the tests amplifying a different target.

WORK IN PROGRESS

1. Optimize the long PCR for environmental samples

2. Combine the protocol with NGS or Long-read sequencing (e.g. Oxford Nanopore sequencing) for a more in-depth analysis of sequences.



ELSEVIER

Water Research

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Rapid screening for SARS-CoV-2 variants of concern in clinical and environmental samples using nested RT-PCR assays targeting key mutations of the spike protein

G La Rosa [1], P. Mancini [1], G. Bonanno Ferraro [1], C. Veneri [1], M. Iaconelli [1], L. Lucentini [1], L. Bonadonna [1], S. Brusaferro [2], D. Brandtner [3], A. Fasanella [4], L. Pace [4], A. Parisi [4], D. Galante [4], E. Suffredini [5]

the international water association

General Q&A Discussion

GERTJAN MEDEMA, TAMAR KOHN, NIKO BEERENWINKEL, GIUSEPPINA LA ROSA, ELISABETTA SUFFREDINI

(MODERATED BY JOAN ROSE)

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