To: 5.1.2e [5.1.2e @rivm.nl]; 5.1.2e [5.1.2e @rivm.nl]; 5.1.2e 5.1.2e [5.1.2e @rivm.nl]; 5.1.2e [5.1.2e @rivm.nl]
Cc: 5.1.2e [5.1.2e @rivm.nl]; 5.1.2e [5.1.2e @rivm.nl]
From: 5.1.2e
Sent: Wed 1/20/2021 7:28:36 AM
Subject: FW: RIVM approach to power of sequencing
Received: Wed 1/20/2021 7:28:36 AM

Ter info: we zijn dus op de goede weg en wel fijn dat het in overeenstemming is met de adviezen van ECDC (maak het leven makkelijker, niet continue uit te leggen waarom we minder doen, ik zag die bui nl al hangen).
Gr 5.1.2e

From: 5.1.2e <5.1.2e @ecdc.europa.eu>
Sent: woensdag 20 januari 2021 08:12
To: 5.1.2e <5.1.2e @rivm.nl>
Cc: 5.1.2e <5.1.2e @rivm.nl>
Subject: RE: RIVM approach to power of sequencing

Dear 5.1.2e

I have looked at this now and I think that both your assumptions and conclusions are both correct and well-motivated. Thank you for sharing.

In our upcoming RRA we give a blanked recommendation for countries to sequence 500 samples per week as a bare minimum, but your more elaborate approach makes more sense.

Best wishes,
5.1.2e

From: 5.1.2e <5.1.2e @rivm.nl>
Sent: 18 January 2021 17:41
To: 5.1.2e <5.1.2e @ecdc.europa.eu>
Cc: 5.1.2e <5.1.2e @rivm.nl>
Subject: RIVM approach to power of sequencing

Dear 5.1.2e

Thank you for sharing your ideas with us. We have looked at it at RIVM and we would like to provide our feedback and inform you about the conclusions we have drawn with respect to the power we need.

We have based our discussions only on the most upper table as 1) all positives determined in a country are not the number of real positives (it is always an underestimation, so it makes the validity of distributional assumptions underlying these tables uncertain) and 2) this table represents the most cautious scenario.

Our goals for sequencing are defined as follows:

1) random sequencing based surveillance. Currently: 17-21 Labs send in at a weekly basis 24 randomly selected samples from SARS-CoV-2 positive patients for sequencing.
2) SARS-CoV-2 positive individuals with a recent history of travel from UK, South-Africa, Brazil (dynamic list of countries) that come up in follow-up of cases by Municipal Health Services
3) sampling of approx. 10% of cases in suspicious outbreaks (outbreaks with an unusual signature, e.g. unusual speed of spread in a nursing home)
4) sequencing in response to alerts from epidemiological surveillance -> if a variant of concern is found we continue under pint a) below

5) SARS-CoV-2 positive individuals that come up in contact tracing of SARS-CoV-2-specific variant positive individuals by municipal health services
6) special SARS-CoV-2 cases (e.g. unusual disease, re-infection cases/vaccine break thru's, linked to animals)

With respect **to random sequencing** the following goals are defined:

A. Global alert for certain variants: through weekly monitoring we will be able to determine whether this particular variant is present in the Netherlands (retrospective and prospective) and to model its effects
B. Monitoring appearance of variants that need more detailed investigation because they show mutations in functional domains (with putative effect on transmission efficiency, symptoms, immune evasion etc.).

With regard to A). to feed our modeling and forecasting we believe that a threshold of 1% (with an absolute precision of 0.5%) is sufficient. We believe that that will give us sufficient time to prepare for such new variant becoming dominant and affecting transmission in the population, given the rate of replacement as currently seen with VOC-202012/01. In your table that comes to 1521 RANDOM sequences per week to be determined. Our conclusions will even be more precise as we take the data from previous weeks also into account.
With regard to B) tasking the 1521 sequences per week we would find such variant when it is present for at least 0.2% in random sampling.

As our labs are overflown with work we have decided at this point not to confer to regional sampling with e.g, 292 samples per region per week.

In addition to the 1500 random sequences we still sequence for the goals 2-6 and we apply a wide range of epidemiological tool to monitor the situation.

We are looking forward to your view on this. We hope that the ECDC advise will be a rational one based on considerations as described above.

Best wishes 5.1.2e

From: 5.1.2e < 5.1.2e @ecdc.europa.eu>
Sent: dinsdag 12 januari 2021 09:08
To: 5.1.2e < 5.1.2e @rivm.nl>
Subject: RE: FYI prior to publication – ECDC Threat Assessment Brief entitled "Rapid increase of a SARS-CoV-2 variant with multiple spike protein mutations observed in the United Kingdom"

Dear 5.1.2e

After thinking more about your question I did an attempt o make a set of tables for this purpose (attached). We will most likely update our sequencing guidance doc with this information.

Let me know if you have any comments on this.

Best wishes,
5.1.2e

From: 5.1.2e < 5.1.2e @rivm.nl>
Sent: 08 January 2021 12:02
To: 5.1.2e < 5.1.2e @ecdc.europa.eu>
Subject: RE: FYI prior to publication – ECDC Threat Assessment Brief entitled "Rapid increase of a SARS-CoV-2 variant with multiple spike protein mutations observed in the United Kingdom"

Hi 5.1.2e

Thanks for you answer (I already read it on mondag but still needed to reply). It seems to me there is no rationale or caculations behind what is the needed sequencing level. We are going to try to do that ourselves. What are the questions and what does that mean for sequencing strategy.
Thanks 5.1.2e

From: 5.1.2e < 5.1.2e @ecdc.europa.eu>
Sent: maandag 4 januari 2021 10:40
To: 5.1.2e < 5.1.2e @rivm.nl>
Subject: RE: FYI prior to publication – ECDC Threat Assessment Brief entitled "Rapid increase of a SARS-CoV-2 variant with multiple spike protein mutations observed in the United Kingdom"

Dear 5.1.2e

Sorry for not replying earlier, I took a few days off from all work-related issues over the new year.

I agree that it is not possible to base any conclusions on the percentage of sequences samples alone, the sampling strategy is also crucial.

The statement in the RRA (that only Denmark would be able to detect an emerging or introduced VOC at low levels with <30 days delay) is largely based on these factors and assumptions:

- The GISAID data reflects what is actually produced.
- The UK has a representative sequencing programme with approximately 5% of cases sequenced, it was successful in detecting this VOC at an early stage and follow its increase.
- ECDCs influenza sentinel guidance suggests sequencing 10% of cases to be able to catch the diversity of variants at a high enough resolution.
- The jump from Denmark to the other countries is about a factor of 10, it is likely that any reasonable cut-off for a representative sequencing programme would be in this interval.

In the RRA we also suggest that if representative sequencing at a level similar to the UK or Denmark (or Iceland, though they have not been submitting to GISAID) is not possible, a smarter sampling strategy needs to be employed to catch VOCs, and we outline some suggestions.

I think these issues needs to be discussed further, I do not see the RRA as a guidance document for sequencing programmes, and I agree with you that with more time we could have put more thought into this. I hope we will be able to discuss further in the ECOVID lab network in the near future.

Best wishes and happy new year,
5.1.2e

From: 5.1.2e < 5.1.2e @rivm.nl>
Sent: 30 December 2020 00:12
To: 5.1.2e < 5.1.2e @ecdc.europa.eu>
Subject: RE: FYI prior to publication – ECDC Threat Assessment Brief entitled "Rapid increase of a SARS-CoV-2 variant with multiple spike protein mutations observed in the United Kingdom"

Hi 5.1.2e

Thanks for the latest RRA.
Could you explain to me why ecdc states in the latest RRA that denmark (with 13% sequencing of pos cases) has enough coverage. What is this conclusion based on? Why is 13% enough and not 7% or 5% or 1%? It makes no sense to me and I see no evidence to base this conclusion on.
It is not the % that matters for VOC monitoring but how samples are selected. For all you know countries largely sequence outbreak while you need random sampling with good geographic coverage from both clincal cate setting and population screening set up (testing lanes).
I really would like to understand what the rationale is for statements on what % of pos cases needs to be sequenced to answer what specific questions.
Thanks 5.1.2e

Van: 5.1.2e < 5.1.2e @ecdc.europa.eu>
Datum: 19 december 2020 om 11:49:26 CET
Aan: 5.1.2e < 5.1.2e @rivm.nl>
CC: 5.1.2e @ecdc.europa.eu>, 5.1.2e @ecdc.europa.eu>, 5.1.2e < 5.1.2e @rivm.nl>, 5.1.2e < 5.1.2e @rivm.nl> 5.1.2e @rivm.nl>, 5.1.2e 5.1.2e < 5.1.2e @rivm.nl>
Onderwerp: RE: FYI prior to publication – ECDC Threat Assessment Brief entitled "Rapid increase of a SARS-CoV-2 variant with multiple spike protein mutations observed in the United Kingdom"

Thank you 5.1.2e for the rapid response.

Best wishes,
5.1.2e

Den 19 dec. 2020 11:45 skrev 5.1.2e < 5.1.2e @rivm.nl>:

HI,

We will put the info in EWRS as well. One case in our weekly national surveillance of the genetic make-up of SARS2 circulating in the Netherlands, sampled on 5 December. We had a delay with submission in GISAID, next year we will upload on a more real-time basis. Yes you can share this.

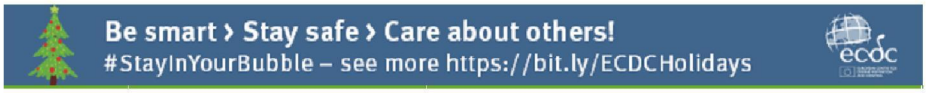
Best 5.1.2e

From: 5.1.2e < 5.1.2e @ecdc.europa.eu>
Sent: zaterdag 19 december 2020 11:34
To: 5.1.2e < 5.1.2e @rivm.nl>
Cc: 5.1.2e @ecdc.europa.eu>; 5.1.2e @ecdc.europa.eu>; 5.1.2e < 5.1.2e @rivm.nl>; 5.1.2e < 5.1.2e @rivm.nl> 5.1.2e @rivm.nl>
Subject: RE: FYI prior to publication – ECDC Threat Assessment Brief entitled "Rapid increase of a SARS-CoV-2 variant with multiple spike protein mutations observed in the United Kingdom"

Dear 5.1.2e

Thank you for the information, how many cases and when were they detected? Can this be shared in the ECDC Threat Assessment to be published on Monday?

Best wishes,
5.1.2e



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Surveillance, PHF
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5.1.2e @ecdc.europa.eu

European Centre for Disease Prevention and Control (ECDC)
Gustav III:s boulevard 40, 169 73 Solna, Sweden
Phone +46 5.1.2e
www.ecdc.europa.eu

Follow ECDC on:

Den 19 dec. 2020 11:31 skrev 5.1.2e < 5.1.2e @rivm.nl>:

EXTERNAL EMAIL - Do not click on any links, open attachments or reply, unless you recognise the sender's email address (5.1.2e **@rivm.nl**') and believe the content is safe.

Hi,

We found the exact same strain in the Netherlands in the Amsterdam area on 5 December 2020. We have not been able to upload it to GISAID yet.

Best wishes 5.1.2e

From: 5.1.2e @ecdc.europa.eu>
Sent: vrijdag 18 december 2020 16:24
To: 5.1.2e @moh.gov.cy; 5.1.2e @mphs.moh.gov.cy; 5.1.2e @hpsc.ie; 5.1.2e @phe.gov.uk; 5.1.2e @santepubliquefrance.fr; 5.1.2e @nvsc.lt; 5.1.2e @nvspl.lt; 5.1.2e @hzjz.hr; 5.1.2e @hzjz.hr; 5.1.2e @landspitali.is; 5.1.2e @santepubliquefrance.fr; 5.1.2e @eody.gov.gr; 5.1.2e @spkc.gov.lv; 5.1.2e @szu.cz; 5.1.2e @folkhalsomyndigheten.se; 5.1.2e @hse.ie; 5.1.2e @meduniwien.ac.at; 5.1.2e @cytanet.com.cy; 5.1.2e @rki.de; 5.1.2e < 5.1.2e @rivm.nl>; 5.1.2e @iss.it; 5.1.2e @ssi.dk; 5.1.2e @opbg.net; 5.1.2e @ages.at; 5.1.2e @folkhalsomyndigheten.se; 5.1.2e @hse.ie; 5.1.2e @dgs.min-saude.pt; 5.1.2e @thl.fi; 5.1.2e @thl.fi; 5.1.2e @eody.gov.gr; 5.1.2e @rki.de; 5.1.2e @fhi.no; 5.1.2e @fhi.no; 5.1.2e @nijz.si; 5.1.2e @nijz.si; 5.1.2e < 5.1.2e @rivm.nl>; 5.1.2e @terviseamet.ee; 5.1.2e @pzh.gov.pl; 5.1.2e @landlaeknir.is; 5.1.2e @nnk.gov.hu; 5.1.2e @nnk.gov.hu; 5.1.2e @szu.cz; 5.1.2e @gov.mt; 5.1.2e @gov.mt; 5.1.2e @insp.gov.ro; 5.1.2e @insp.gov.ro; 5.1.2e @isciii.es; 5.1.2e @isciii.es; 5.1.2e @spkc.gov.lv; 5.1.2e @uvzsr.sk; 5.1.2e @uvzsr.sk; 5.1.2e @ssi.dk; 5.1.2e @sciensano.be; 5.1.2e @ncipd.org; 5.1.2e @santepubliquefrance.fr; 5.1.2e @ms.etat.lu; 5.1.2e @folkhalsomyndigheten.se; 5.1.2e @santepubliquefrance.fr; 5.1.2e @nnk.gov.hu; 5.1.2e @nnk.gov.hu; 5.1.2e @folkhalsomyndigheten.se; 5.1.2e @mscbs.es; 5.1.2e @hzjz.hr; 5.1.2e @thl.fi; 5.1.2e @nvsc.lt; 5.1.2e @hzjz.hr; 5.1.2e @rki.de; 5.1.2e @spkc.gov.lv; 5.1.2e @thl.fi; 5.1.2e @sanita.it; 5.1.2e @terviseamet.ee; 5.1.2e @landlaeknir.is; 5.1.2e @eody.gov.gr; 5.1.2e @mzcr.cz; 5.1.2e @essc.sam.lt; 5.1.2e @hse.ie; 5.1.2e @ssi.dk; 5.1.2e @nijz.si; 5.1.2e @phe.gov.uk; 5.1.2e @santepubliquefrance.fr; 5.1.2e @insp.gov.ro; 5.1.2e @rki.de; 5.1.2e @phe.gov.uk; 5.1.2e @sciensano.be; 5.1.2e @mphs.moh.gov.cy; 5.1.2e @sciensano.be; 5.1.2e @eody.gov.gr; 5.1.2e @fhi.no; 5.1.2e @fhi.no; 5.1.2e @mh.government.bg; 5.1.2e @nijz.si; 5.1.2e < 5.1.2e @rivm.nl>; 5.1.2e @terviseamet.ee; 5.1.2e @gis.gov.pl; 5.1.2e @pzh.gov.pl; 5.1.2e @mzcr.cz; 5.1.2e @gov.mt; 5.1.2e @gov.mt; 5.1.2e @insp.gov.ro; 5.1.2e @mscbs.es; 5.1.2e @spkc.gov.lv; 5.1.2e @uvzsr.sk; 5.1.2e @nvsc.lt; 5.1.2e @ssi.dk; 5.1.2e @landlaeknir.is; 5.1.2e < 5.1.2e @rivm.nl>; 5.1.2e @sanita.it; 5.1.2e @sozialministerium.at; 5.1.2e @hse.ie; 5.1.2e @sam.lt; 5.1.2e @folkhalsomyndigheten.se; 5.1.2e @nnk.gov.hu; 5.1.2e @folkhalsomyndigheten.se;


5.1.2e @health.fgov.be; 5.1.2e @mscbs.es; 5.1.2e @eody.gov.gr; 5.1.2e @sst.dk; 5.1.2e @thl.fi;
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5.1.2e < 5.1.2e @rivm.nl>; 5.1.2e < 5.1.2e @rivm.nl>; 5.1.2e @terviseamet.ee;
5.1.2e @terviseamet.ee; 5.1.2e @pzh.gov.pl; 5.1.2e @thl.fi; 5.1.2e @ages.at; 5.1.2e @ages.at;
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5.1.2e @folkhalsomyndigheten.se; 5.1.2e @aslimnica.lv; 5.1.2e
< 5.1.2e @ema.europa.eu>
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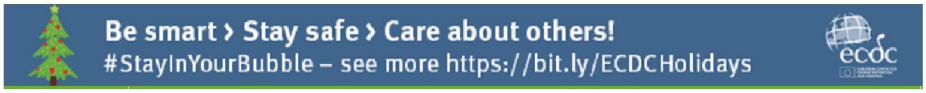
< 5.1.2e @ecdc.europa.eu>; Editors < 5.1.2e @ecdc.europa.eu>; 5.1.2e @who.int
Subject: FYI prior to publication – ECDC Threat Assessment Brief entitled "Rapid increase of a SARS-CoV-2 variant with multiple spike protein mutations observed in the United Kingdom"

Dear Colleagues,

Please find attached the Threat Assessment Brief titled "Rapid increase of a SARS-CoV-2 variant with multiple spike protein mutations observed in the United Kingdom."

ECDC plans to publish an edited version of this Threat Assessment Brief on its website on Monday 21 December.

Warmest regards,
Anastasia and Teymur
ECDC Response Duty Officers



European Centre for Disease Prevention and Control (ECDC)
Gustav III:s boulevard 40, 169 73 Solna, Sweden
Phone 5.1.2e
www.ecdc.europa.eu

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