

ASSESSMENT OF THE EPIDEMIOLOGICAL SITUATION

20/12/2020

This assessment was done by the experts of the RAG epidemiology, with input from the GEMS-members.

1. Elements that induce the update

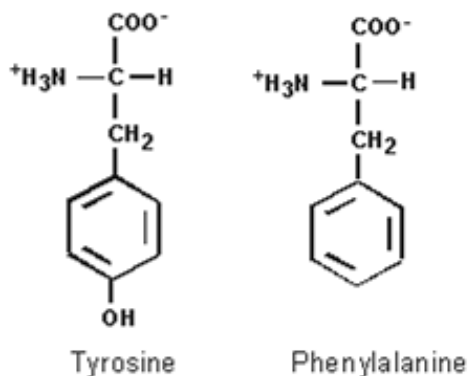
1.1. MUTATION OF THE SARS-COV-2 VIRUS DETECTED IN GREAT BRITAIN

1.1.1. Overview of data

The COVID-19 Genomics Consortium UK report on a rapidly growing lineage (B.1.1.7) in the UK associated with an unexpectedly large number of genetic changes including in the receptor-binding domain and associated with the furin cleavage site [Rambaut et al. 2020]. It emerged in England in September either in London or in the nearby county of Kent and appears to be spreading more rapidly than earlier variants up to 70% early analysis suggests. By mid-November, 28% of cases in London were attributable to the new variant. In the week starting Dec. 9, it was responsible for 62% of cases in the capital. The variant seems strongly associated with regions where an increasing rate of COVID-19 is seen. Although this observation indicates a possible correlation, there is no prove of causation at this moment [Jacqui, 2020].

The variant appears to be more contagious (higher growth rate) and lethality seems similar. The growth might be the “by chance” growth for reasons like regional quirks in restrictions but it looks like it is displacing other lineages too which raises a number of concerns though all of which is unknown.

The binding of the viral receptor-binding domain (RBD) of the SARS-CoV-2 to the human ACE2 receptor is currently relatively suboptimal. We know that a N501F mutation increases the affinity of the viral RBD for the human ACE2. It is likely that the N501Y mutation also will have an improved binding capacity to ACE (because Phenylalanine (F) and Tyrosine (Y) have a very similar aromatic structure). This would obviously not be good news.



Belgium:

In the database of 2000 virus strains that have been sequenced in the National Reference Center (KU Leuven), 4 strains with the N501Y mutation were found. All 4 N501Y-samples date back to 30 November 2020. Three of the N501Y-patients are children part of a cluster, linked to The Netherlands. One is an adult. Investigation conducted so far did not identify a link with the UK, for none of the cases.

International

In the Netherlands, one N501Y-containing strain was found (beginning of December), but they sequenced the complete genomes of fewer strains.

Neville Sanjana of the New York Genome Center says there is no evidence to suggest the variant has spread to the U.S.

1.1.2. Risk assessment

Possible points of entry in Belgium

On Sunday 20/12, the Belgian borders have been closed for 24 hours for travelers from the UK. If flights from the UK and the Eurostar are cancelled, there are 2 remaining points of entry.

1) The most important uncontrolled port of entry to and from the UK is the freight traffic (with a lot more travelers than by train/air) that enters Belgium over land, via France. Within the context of Brexit, there is also a risk of accumulation of trucks and contact between drivers at large park sites at the borders.

2) The port of Antwerp, and by extension the Channel ports of Zeebrugge and Oostende. In that sense, it is relevant to realize that:

- Ordinarily, there are 21 ferries via Calais, 12 via Dunkerque, and every 15 to 30 minutes a 'Le Shuttle' freight and car train.
- Vessels do come in into our large ports, but there is extensive and repeated control on crew. Non EU-residents do not have a tourist visa and cannot enter Belgian territory. Exceptionally, they disembark to be hospitalized. However EU residents don't need a visa.
- There is nearly no contact between crew and landside dockers. The only contact the crew has is with the pilotage crews (loodswezen); they are strictly controlled – control should be increased.
- Containers that disembark typically remain untouched for a fortnight.

Overall risk

There are a lot of uncertainties hampering the evaluation of the risk of the UK variant strain for Belgium. It is unknown yet whether it could be quite different in terms of its transmission (e.g., age ranges) or clinical progression of disease. It is also unknown whether this will have an impact on antigenic escape, on the quality of diagnosis and on the vaccine efficacy (VE).

However, it is important to note that this identification of a mutant strain in the UK is the result of a very strong genomic surveillance (between 5 and 10% of all COVID-19 cases are regularly sequenced in the UK). Similar events possibly occur elsewhere but go unnoticed. In addition, the expected social mix of people from different countries during the coming holidays is increasing the risk of spread of fitter viral clades throughout Europe.

Overall, there is a certainty that if one of the above unknown elements would be confirmed (either increased transmission or impact on the diagnostic accuracy or vaccine efficacy), the

impact of this will likely be large. Therefore the precautionary principle should be applied, and possible measures taken already to avoid introduction of the virus/limit spread while collecting more evidence on the above mentioned questions during the next days and weeks.

References:

Andrew Rambaut, Nick Loman, Oliver Pybus, Wendy Barclay, Jeff Barrett, Alesandro Carabelli, Tom Connor, Tom Peacock, David L Robertson, Erik Volz, on behalf of COVID-19 Genomics Consortium UK (CoG-UK). 2020 Preliminary genomic characterisation of an emergent SARS-CoV-2 lineage in the UK defined by a novel set of spike mutations Report <https://virological.org/t/preliminary-genomic-characterisation-of-an-emergent-sars-cov-2-lineage-in-the-uk-defined-by-a-novel-set-of-spike-mutations/563>

Wise Jacqui. Covid-19: New coronavirus variant is identified in UK BMJ 2020; 371 :m4857

Emma Hodcroft and Richard Neher Phylogenetic analysis of SARS-CoV-2 clusters in their international context - cluster S.N501 https://nextstrain.org/groups/neherlab/ncov/S.N501?c=gt-S_501.69&p=grid&r=country

1.2. CHANGE IN EPIDEMIOLOGICAL SITUATION

1.2.1. Increase in new hospitalisations

Since 18 December, the number of new hospitalizations over a 7-day period has increased by 4% to reach a mean of 186 new hospitalizations per day from 13 to 19 December. This compared with a mean of 180/day for the previous period.

The number of persons discharged from the hospital remains higher than the new hospitalizations meaning that the total number of persons hospitalized and in ICU is still decreasing. However these numbers remains high with overall still 2527 beds occupied by COVID-patients and 525 ICU-beds occupied (Phase b of surge capacity plan).

An increase in hospitalization of the 80+ and some outbreaks in nursing homes are observed. This increase in the number of new hospitalizations takes place in a context of an increase in the number of new diagnoses and of outbreaks in nursing homes.

1.2.2. Factors affecting epidemiological evolution in coming weeks

The others factors which could have an impact on the epidemiological situation in the coming days are :

- School holidays: less contacts expected.
- Nursing home
- Student in study period : less contacts expected.
- Shops opening: neutral or possibly slightly increased if rules are respected. But crowding in cities related to shopping is observed.
- Travel: large increase expected.
- Cross-border travel from neighboring countries: increase expected, since different measures (shops closed in the Netherlands and Germany). See more detailed analysis in annex, with a focus on the province of Antwerp. Further work on other provinces will be done the coming week.
- Christmas and New year times: neutral if rules are respected. But serious concern that this will not be the case.
- Possible decrease in testing in holidays and overall fatigue to be tested (patients) and to perform tests (by physicians): false decrease in number of cases.
- Respiratory viruses Season: general increased risk in January-February-March, which is the usual time of year with intense circulation of respiratory viruses because conditions are suited for those viruses during this period. Since SARS-CoV-2 is a respiratory virus, its circulation is expected to be influenced in the same way.

- Vaccination of at risk persons: 150.000 persons in nursing homes, possibly protected from begin February (vaccination starts end of December/beginning of January + 2 doses) but no impact yet on virus circulation.

1.2.3. Risk characterization

The trends in the number of cases is currently slightly increasing what was expected due to :

- Restart testing of high risk contacts;
- Schools activity, shops opening, ... illustrated by an increased mobility;
- Increased number of contacts between people, as illustrated by preliminary results of a study on contacts. Especially work contacts have increased after the autumn holiday and prior to this week – in terms of transmission potential they increased medianwise with 12% and 23% respectively (analysis based on Comix study UHasselt-UAntwerp ; EC H2020 EpiPose Consortium).

The trends in the number of hospitalizations is slightly increasing with provincial variations. In a context where the absorption capacity of the hospitals is still very low, this is particularly of concern.

We are currently at the beginning of the period that is usually the most intense period for the circulation of respiratory viruses in Belgium and therefore the probability to reach the thresholds defined in the Management strategy is currently almost nihil within the next 6 weeks. Depending on the behavior of the population and number of contacts during Christmas and New Year gatherings, the reaching of thresholds could even be further delayed, see also: <https://covid-en-wetenschap.github.io/restore.html>.

It is still too early to assess whether the epidemiological situation will evolve to a further increase or a stabilization to a new baseline level because the impact of the above mentioned factors is difficult to quantify while some restrictive control measures are already in place. The epidemiological follow up will allow alerting in time in case of increasing trends. Complementary measures will have then to be taken rapidly because the current pressure on the health care system remains high and it will possibly not be able to absorb a third wave.

2. Propositions

2.1. SURVEILLANCE OF MUTANT STRAIN

This novel lineage requires urgent laboratory characterization and enhanced genomic surveillance worldwide, and in Belgium more specifically (see also recommendations GEMS). A plan and protocol for genomic surveillance in Belgium should be developed.

ECDC recommendations

<https://www.ecdc.europa.eu/en/publications-data/threat-assessment-brief-rapid-increase-sars-cov-2-variant-united-kingdom>

National public health authorities should:

- Continue to monitor for abrupt changes in rates of transmission or disease severity as part of the process of identifying and assessing the impact of variants.
- Notify new SARS-CoV-2 variants of potential concern through the EWRS.

- Follow-up reports of suspected cases of COVID-19 reinfection and initiate sequence analysis of virus isolates from these cases.
- Follow-up reports of cases with treatment failures using convalescent plasma or monoclonal antibodies as recently described [9] and initiate sequence analysis of virus isolates from these cases.
- Ensure that close monitoring of COVID-19 vaccinated individuals regarding vaccination failure and breakthrough infections is in place and initiate sequence analysis of virus isolates from these cases and then conduct antigenic characterisation to confirm or exclude vaccine escape mutants.
- Develop standardised mechanisms, in partnership with global stakeholders, including triggers to investigate and assess newly emerging variants of SARS-CoV-2 in terms of animal reservoir, antigenic characteristics, transmissibility, severity, cross-protection and also with regard to adapting vaccine strain recommendations. If needed, establish systems for reassessing vaccine composition and strategy.

2.2. INCREASING TREND OF INFECTIONS AND HOSPITALISATIONS

The highest risk for further increase of new infections the coming weeks will come from 1) the international and transnational travelers and 2) (subsequent) gatherings of families and friends. Therefor measures should focus to these groups (see recommendations GEMS).

The RAG-experts will further describe the criteria they will use to alert on need for additional measures and will continue performing weekly evaluations of the epidemiological situations and provide an urgent advice if the evolution is of concern.

De following persons participated to this advice :

RAG Epidemiologie

Emmanuel André, Katrien Bonneux, Steven Callens, Bénédicte Delaere, Frédéric Fripiat, Alexandra Gilissen, Herman Goossens, Naima Hammami, Niel Hens, Tinne Lernout, Romain Mahieu, Geert Molenberghs, Paul Pardon, Sophie Quoilin, Stefan Teughels, Roel Van Giel, Steven Van Gucht, Marc Van Ranst.

GEMS

Mathias Dewatripont, Lode Godderis, Christel Meuris, Michel Thieren, Liesbeth Van Der Bauwhede, Dimitri Van der Linden, Yves Van Laethem, Erika Vlieghe, Dirk Wildemeersch.

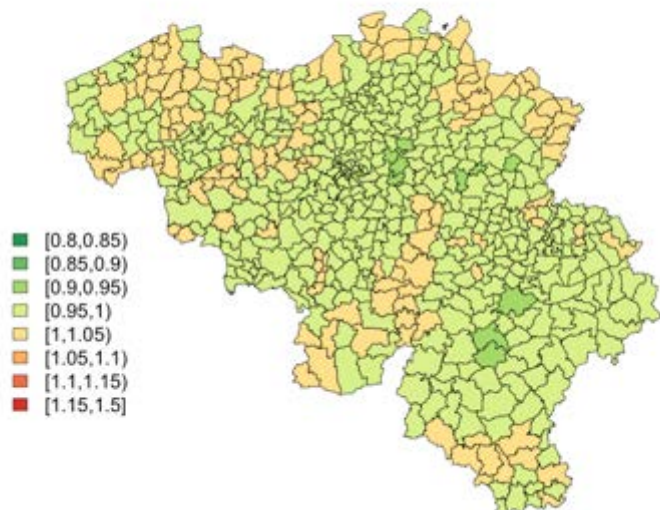
Observers

Barend Cochez, Koen Magnus, Sam Proesmans, Bart Raeymaekers, Carole Schirvel.

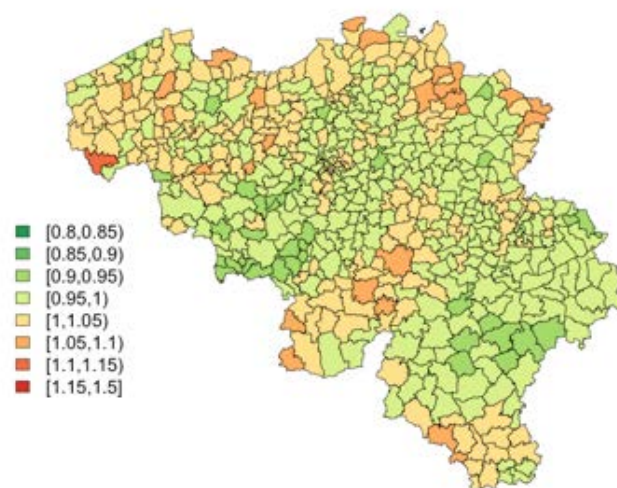
Annex: Evaluation of the risk on cross-border transmission, with a focus on the province of Antwerpen

Growth rates of positivity and incidences at town level

GR Positiv Ratio 2020-12-16



GR Incidence 2020-12-16



It is clear that positivity and incidences are growing rapidly in border regions: (a) clearly with the Netherlands, over the entire northern border, and then the north-east; (b) in the south of Luxembourg, (c) on the southwestern border with France.

This is unsurprising, given the incidences:

Province	Incidence (8/12 → 15/12 → 20/12)	Neighboring province/region	Incidence (8/12 → 15/12)
Oost-Vlaanderen	303 → 346 → 313	Zeeland (NL)	268 → 354
West-Vlaanderen	319 → 398 → 353		
Antwerpen	248 → 266 → 298	Noord-Brabant (NL)	474 → 605
Limburg	228 → 234 → 254	Limburg (NL)	422 → 655
Luxembourg	400 → 392 → 369	Luxembourg (LUX)	1182 → 1197
Namur	291 → 268 → 305	Dept. des Ardennes (FR)	419 → 527

The foreign incidences are coming from the Working Group on color codes (Tuesday, December 8 and Tuesday, 15, 2020). (The ECDC national figures are currently unreliable due to an apparent error; therefore not used.)

The Belgian incidences come from three Sciensano daily reports, on December 8, 15, and in addition from December 20.

Note that in the Dutch provinces of Noord-Brabant (NL) and Limburg (NL), the incidences have been increasing rapidly and are well above the Belgian level. In Zeeland, the increase is also rapid, so as to now match that of the Belgian provinces Oost-Vlaanderen en West-Vlaanderen.

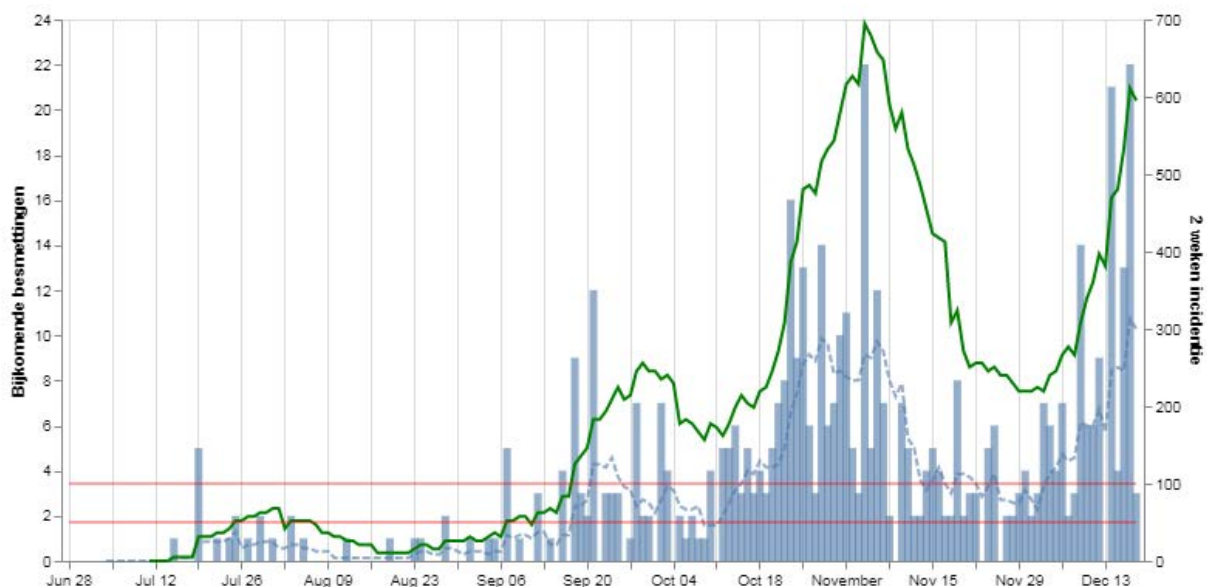
The largest discrepancy, and hence threat, comes from the provinces in yellow.

Towns in Arrondissement Antwerpen and Arrondissement Sint-Niklaas

Focusing on the northern part of Arrondissement Antwerpen (right bank of Schelde) and Arrondissement Sint-Niklaas (left bank of Schelde), we see the following:

- There is an extremely rapid incline in: Essen, Wuustwezel (both border towns); Essen is surrounded by the Netherlands from three sides.
- There is an increase in:
 - o Right bank: Kalmthout (border), Brasschaat.
 - o Left bank: Sint-Gillis-Waas, Temse, Kruibeke, Zwijndrecht, Hamme.
- There is a gentle incline in: Beveren (left bank).
- We observe a steady state in:
 - o Right bank: Stabroek, Schilde, Brecht, Schilde.
- There is a gentle decline in:
 - o Right bank: Schoten, Kapellen .
 - o Left bank: Sint-Niklaas, Waasmunster.

Increase in Essen



Evidence from the field (Province Antwerpen)

- Very high positivity rates are observed in both nursing homes and schools.
- Typical situations where (large) clusters are forming:
 - o Secondary school

- Primary school
- Industry (e.g., Novartis and Pfizer in Puurs!)
- Extra-scholarly activities: youth movement, music academy,...

By way of comparison, the **Brussels Capital Region** has been examined. All of the 19 towns show a plateau (flat curve), except Woluwe-Saint-Pierre, Watermael-Boitsfort, and Evere, where a decrease is observed, and notably Ixelles, which shows a gentle increase.

Of note, the towns in the immediate vicinity of Brussels National Airport show a tendency to remain at steady state, not to incline.