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Estimates of the incidence, growth advantage and increased infectiousness of the Delta variant in Belgium vs. the United Kingdom

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KEYPOINTS:

- The Delta variant has a clear advantage in transmissibility and is therefore expected to become dominant in Belgium as well, potentially already in early July 2021.
- In addition to being more contagious, data from the UK suggest that people infected with the Delta variant have a ca. 2 fold increased risk of hospitalization and show that 1 dose of vaccination only offers partial protection against symptomatic disease and hospitalization.
- In comparison with the UK, the Belgian vaccination campaign kicked-off more slowly, but benefits from a shorter delay to the second vaccine shot than in the UK and deployment of a greater share of mRNA vaccines, which seem to offer better protection. At the same time, the share of the adult population that is fully vaccinated is still rather low and a significant share of the population at risk is still only partially vaccinated.
- A multinomial model fit to baseline surveillance sequencing and genotyping (VOC PCR) data from Belgium estimates that the Delta variant has an 8.6% growth rate advantage per day [6.8-10.4%] 95% CLs over the Alpha variant, which would translate to a 50% [38-63%] 95% CLs increased infectiousness (due to a combination of a transmission advantage and immune escape).
- The observed growth rate advantage is only slightly lower than the one observed in England (11.8% per day [11.4-12.1%] 95% CLs based on a multinomial fit to Sanger Institute baseline surveillance data), where nation-wide 96.9% of all new diagnoses today [96.6-97.2%] 95% CLs are the Delta variant. In Belgium, an estimated 16% [11-21%] 95% CLs of all confirmed infections today concern the Delta variant.
- At the current growth rate, the Delta variant would become dominant (>50% share) in Belgium around the 5th of July (95% CLs: between the 29th of June and the 14th of July).
- Long-term predictions are difficult to make since the effect of relaxation of restrictions, contact behavior, international mobility, variant replacement, vaccine effectiveness and the speed of the remainder of the vaccination program (including projected vaccine deliveries) etc. all need to be taken into account. A close monitoring of the situation and careful evaluation before proceeding with further relaxations will be paramount.

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1. Vaccination strategy and coverage:

- Target groups for prioritization of vaccination in the UK and Belgium are very similar.
- However, the UK vaccination strategy aimed mostly to speed up the delivery of the first dose to be able to offer at least partial early protection to as many people as possible. Hence, until the 14th of May, the UK adopted a long interval of 12 weeks between the 1st and 2nd dose, both for Vaxzevria (AstraZeneca-Oxford) and Comirnaty (Pfizer).
- If we want to determine when the UK was in "a similar position as Belgium" regarding vaccination coverage, it is therefore important to determine whether we look at coverage of the 1st dose or rather coverage of the 2nd dose. Because the current data indicate that protection of vaccination against the Delta variant is significantly reduced in partially vaccinated individuals [1], we suggest to focus on the coverage offull vaccination.

	Coverage 1 st dose	Coverage fully vax	% mRNA vaccines	14d Inc /100k	7d new hosp /100k	R _{t (cases)}
Belgium current	49%	27%	75%	133	434	0.7
UK current	61%	44%	39%	127	136	1.4
Date UK similar to current BE	18 th April	8 th May	/	21 st Feb	21 st Mar	~26 th Jan

Table 1: Comparison of key metrics for the UK and Belgium (source UK: ourworldindata.com)

The progress of the vaccination campaign in Belgium versus the UK is presented in the figures below, which show the percentage of the population that are fully vaccinated (a) and partially vaccinated (b). This is against the entire population (not the 18+ population).









Vaccine effectiveness:

Data from the UK suggests that protection against the Delta variant is not only determined by the number of doses, but also by the type of vaccine [1],[2]. For example, protection against symptomatic disease after full vaccination is estimated at 59.8% for the Vaxzevria vaccine (AstraZeneca-Oxford) compared to 87.9% for Comirnaty (Pfizer). Protection against hospitalization following infection with the Delta variant is high after full vaccination with both doses of either vaccine (92% Vaxzevria vs. 96% Comirnaty), but significantly reduced after just a single dose of Vaxzevria (71% protection against hospitalization) compared to 1 dose of Comirnaty (94%)², see Table 2. The UK vaccination campaign has relied more heavily on the Vaxzevria vaccine (61% of all administered doses [3]) than the Belgian one (25% Vaxzevria). Although no data is available for the Moderna vaccine, it seems reasonable to assume that it would offer similar protection as the Comirnaty (Pfizer) vaccine.

		Vaccine effectiveness symptomatic disease	Hospitalization
Comirnaty (Pfizer)	1 dose	36% [23 - 46%]	94% [46 - 99%]
	2 doses	88% [85 – 90%]	96% [86 - 99%
Vaxzevria (Az-Ox)	1 dose	30% [24 – 35%]	71% [51 – 83%]
	2 doses	67% [61 – 72%]	92% [75 - 97%]

Table 2: UK Estimates of vaccine effectiveness against the Delta variant

Source: Public Health England, pre-print Public library - PHE national - Knowledge Hub (khub.net)

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On the 8th of May 2021, the date with a similar coverage of fully vaccinated individuals in England as currently in Belgium, the estimated share of the Delta variant among confirmed cases was higher (29%) than that estimated at this moment (16%) in Belgium, but this difference is only slight and given the observed growth rate advantage of the Delta variant in both countries would represent a lag of only ca. 1 week. Absolute incidence and test-positivity rate were both much lower in the UK though than the currently observed values in Belgium, but there was a clear increasing trend.

	14d incidence /100k	Test-positivity rate	R _{t (cases)}	% Delta variant [95% CLs]
Current situation in Belgium	133	2.9%	0.6	16% [11-21%] ª
Situation 8 May 2021 in England	44	0.2%	1.0	29% [28-30%] ^b

a Estimated incidence on the 15th of June 2021 based on a multinomial fit to baseline surveillance whole genome sequencing data from the federal test platform (weeks 49-53 2020 + weeks 1-23 2021, *n*=24814) and baseline surveillance genotyping from the National Reference Lab (VOC PCRs) (weeks 23-24 2021, *n*=141) (model: lineage in function of a 2 degree of freedom natural cubic spline in function of collection date, fit using the multinom function in R's nnet package, code at

https://github.com/tomwenseleers/newcovid_belgium/blob/main/analysis%20VOCs%20baseline%20s urveil lance%20BE LGIUM_15%20ju n e%202021.R)

^b Estimated incidence on the 8th of May 2021 based on a multinomial fit to the Wellcome Sanger Institute baseline surveillance whole genome sequencing data for England (<u>https://covid-surveillance-data.cog.sanger.ac.uk/download/lineages by Itla and week.tsv</u>, weeks 36-53 2020 & weeks 1-23 2021, *n*=241356, model: lineage in function of ONS region and a 2 degree of freedom natural cubic spline in function of collection date, fit using the multinom function in R's nnet package, code at

https://github.com/tomwenseleers/newcovid_belgium/blob/main/analysis_VOCs_UK_sanger.R).





2. Measures to contain the epidemic

2.1 General measures in society

The table below summarizes the major relaxations in relation to the date with the current vaccination coverage level in Belgium. It shows that overall Belgium is relaxing at a faster pace than England. in response to the Delta variant, the UK has now delayed further relaxations by one month?

A detailed overview of the measures can be found in the Appendix.

# of weeks before current vaccination coverage	England	Belgium
Nine weeks earlier	Reopening schools	
Eight weeks earlier		Reopening schools
Seven weeks earlier		Relaxation social contacts outside
Six weeks earlier	Relaxation social contacts outside	
Five weeks earlier		Reopening amusement parks and café terraces; more people in outdoor events
Four weeks earlier	Reopening of several businesses and outdoor activities; more people attending services	
Three weeks earlier		
Two weeks earlier		
One week earlier		Reopening of several businesses and indoor activities; relaxation social contacts inside; many more people attending services
One week after	Reopening of several businesses and indoor activities; relaxation social contacts inside; many more people attending services	

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The "**stringency index**" is an indicator proposed by the University of Oxford to quantify the measures that are applied in different countries to contain the epidemic. It takes into account several aspects, like school closures, stay-at-home orders, impact on businesses, etc. Comparing the stringency indices between Belgium and the UK gives the same messages as the table above, that Belgium is relaxing measures at a faster pace than the UK. *Source: ourworldindata.org*



2.2 Testing and tracing

The UK has a comprehensive testing scheme in place with widespread use of rapid antigen-tests in e.g. schools and workplaces. On the other hand, rules on quarantine for high-risk contacts are less strict in the UK. In Belgium, each high-risk contact needs to quarantine for 10 days after the last high-risk contact (which means that, in households, this can be up to 20 days after symptom onset of the index case) and is tested at least once, regardless of symptoms. Public Health England advises to quarantine the entire household for 10 days after symptom onset of the index case and only test high-risk contacts in case of symptoms.¹

2.3 International travel

Like Belgium, the UK has a system with colour coding. Every traveller to the UK is obliged to have a negative test result before arrival in the UK and to have at least one PCR test upon arrival. Travellers arriving from amber zones need to quarantine for 10 days and are required to take 2 PCR tests, regardless of vaccination status. Amber zones include many zones outside the EU. For red zones, hotel quarantine is mandatory.

With regards to the Delta variant, which was first detected in India and southern Asia, the UK holds a different position than Belgium. For historical reasons, the UK has a high share of people of Indian, Pakistani or Bengal descent and thus more intense traffic to and from these regions.

¹ <u>ttps://www.nhs.uk/conditions/coronavirus-covid-19/self-isolation-and-treatment/how-long-to-self-isolate/</u>

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3. Incidence and hospitalizations in Belgium versus UK

The following figure displays the 14 day incidence (number of new cases per 100,000 over a 14 day period), for Belgium and the UK. *Source: ourworldindata.org*



The following figure depicts the weekly hospital admissions in both countries per million inhabitants. *Source: ourworldindata.org*



Public Health England reports a hazard ratio for hospitalization after infection with Delta, relative to Alpha, of 2.26 [95% CI 1.32-3.89] based on an English data, and 1.85 [95% CI 1.39-2.47] based on Scottish data [4]. A hazard ratio of 1 would imply no difference.

The British modeling consortium SPI-M-O in its Consensus Statement on COVID-19 of 12 May 2021, reports that modeling of the London School of Hygiene and Tropical Medicine and Warwick, based on an increased transmissibility of 40% leads to the following conclusions: if Step 3 of the British Roadmap

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were taken, then peaks like in Spring 2020 and January 2021 are possible; if Steps 3 and 4 are taken, then the peak could be double that of January 2021.

The BBC, using data from the UK Department of Health/National Health Service (NHS) illustrated, by way of the following figure, that, in spite of vaccination, hospitalizations still occur, albeit at a reduced rate.

The link between infections and hospitalisations weakened



Source: Dept of Health/NHS

Data on the daily new confirmed SARS-CoV2 cases in England by age show that cases started rising first among teenagers (age category 6-17), but then further diffused to other age categories. Data also show that cases are now rising at a similar rate across most age categories, but that the age cohorts with the highest vaccination coverage start from a much lower baseline. The rise in hospitalizations, however, is fortunately less steep than the rise in cases and is as yet still most pronounced in the 18-54 category.





4. Growth advantage and increased infectiousness of the Delta Variant: Genomic surveillance

Baseline surveillance data from Belgium and the UK allow us to assess how fast the Delta variant is displacing the Alpha variant, which in turn can be compared with the speed with which Alpha displaced the other variants before. This rate of displacement measures the difference in growth rate between pairs of lineages, and if we take the exponent of the product of this growth rate advantage and the generation time and subtract one, we obtain the % increase in infectiousness of a given variant relative to the background in which it spreads [7]. The generation time is the mean time between one person getting infected and passing on the virus to someone else, and appears unaltered for the Delta variant [5]. In our calculation, we will use an estimated value for the generation time of 4.7 days [6], which is also the value that Sciensano uses in the dashboard and reports to calculate the effective reproduction number Re. This calculated increase in infectiousness can arise due to a combination of an intrinsic transmission advantage and immune escape and potentially also a change in duration of infectiousness, which remains to be quantified. It is important that for such analyses baseline surveillance data is used, i.e. an approximately random sample of confirmed infections, and that travelers and surge testing data are excluded. For this reason, estimates such as those given by the covSPECTRUM or covariants websites are not reliable, as they use lineage frequencies of all sequenced genomes deposited into the GISAID database, which is subject to a multitude of sampling biases and for the Delta variant comprises a large share of traveler-related cases for Belgium (cf. Sciensano weekly reports, section 3.4.1). Below we will use the baseline surveillance genomic surveillance data from the federal test platform (for weeks 49-53 2020 + weeks 1-23 2021, n=24814) and baseline surveillance genotyping from the National Reference Lab (VOC PCRs) (weeks 23-24 2021, n=141) for Belgium and the baseline surveillance genomic surveillance of the Wellcome Sanger Institute for the data from England (https://covid-surveillance-data.cog.sanger.ac.uk/download/lineages by Itla and week.tsv, weeks 36-53 2020 & weeks 1-23 2021, n=241356), and fit multinomial models incorporating a two degree of freedom natural cubic spline in function of day and also ONS region for the English data to estimate growth rate advantages and corresponding increased infectiousness (for method see [7]). These fits were performed using the *multinom* function in R's *nnet* package and growth rate differences were calculated using the *emtrends* function in the *emmeans* package.

4.1 Growth rate advantages and increased infectiousness of the Delta and Alpha variants in Belgium

The fitted multinomial model (shown on a logit Y scale) demonstrates that the current speed by which the Delta variant is displacing the Alpha variant is roughly equivalent to the speed by which the Alpha variant displaced the earlier lineages (category "other") in January/February. We estimate that today, Delta has a growth rate advantage over Alpha of 8.6% per day [6.8-10.4%] 95% CLs, which with a generation time of 4.7 days would translate to a 50% [38-63%] 95% increased infectiousness [8]. We estimate that 16% [11-21%] 95% CLs of all confirmed infections today concern the Delta variant. By comparison, the growth rate advantage of Alpha over the earlier lineages evaluated on 21^t January 2021, when Alpha was estimated to make up 16% of all infections (\approx the estimated share of Delta in Belgium today), was 7.7% per day [7.4-8.1%] 95% CLs, which would have translated to an increased infectiousness of 44% [41-47%] 95% CLs. Hence, the growth rate advantage of Delta versus Alpha is comparable to the advantage that Alpha had over the lineages before. At the current growth rate, the Delta variant would become dominant (>50% share) in Belgium around the 5th of July (95% CLs: between 29 June and 14 July 2021), with near-complete dominance (ca. 90% of all diagnosed

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infections) likely near the end of July. We should note that the time of infection is estimated to be circa 1 week earlier than the time of diagnosis, and if we would count the time of infection this would still be one week earlier.



Phylogenetic analyses of the National Reference Laboratory (led by Emmanuel André), reported in the weekly situation update of 8 June 2021 show that the circulation of Delta in Belgium is due to various independent introductions [9]. In their report of 2 June 2021, devoted to travel, a similar phenomenon had occurred for Alpha, in contrast to Gamma (Brazilian variant P.1), which stemmed from a very small number of introductions.

The following graph shows the growth of Alpha over the period December – April 2021, over which time it went from 1% to 90%. This graph is based on a logistic curve with a ceiling, to allow for other circulating variants, such as Gamma in particular.



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As a sensitivity analysis, we also fitted a logistic growth model to the share of confirmed infections that are by Delta variant. This is less sophisticated than the aforementioned analysis, and merely contrasts Delta with all other circulating variants. According to this fit, dominance (>50% circulation) would be estimated to occur only about one week later. This underscores the robustness of the results reported above.



4.2 Growth rate advantages and increased infectiousness of the Delta variant in England

If we employ the same methodology to the English Wellcome Sanger Institute data, we estimate that at the most recent time point in the dataset (5 June 2021), Delta there has an average growth rate advantage over Alpha of 11.8% [11.4-12.1%] 95% CLs per day, which with a generation time of 4.7 days would translate to an increased infectiousness of 74% [71-77%] [10]. Across England, we estimate that today, 96.9% of all confirmed diagnoses [96.6-97.2%] 95% CLs are now by the Delta variant.







References:

[1] Bernal et al. Effectiveness of COVID-19 vaccines against the B.1.617.2 variant | medRxiv

[2] Public library - PHE national - Knowledge Hub (khub.net)

[3] <u>https://www.gov.uk/government/publications/coronavirus-covid-19-vaccine-adverse-reactions/coronavirus-vaccine-summary-of-yellow-card-reporting</u>

[4] PHE technical report 15.

https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file /993879/Variants_of_Concern_VOC_Technical_Briefing_15.pdf

[5] Pung et al. Serial intervals observed in SARS-CoV-2 B.1.617.2 variant cases. https://www.medrxiv.org/content/10.1101/2021.06.04.21258205v1

[6] Nishiura et al. Serial interval of novel coronavirus (COVID-19) infections. https://www.sciencedirect.com/science/article/pii/S1201971220301193

[7] Davies et al. Estimated transmissibility and impact of SARS-CoV-2 lineage B.1.1.7 in England. https://science.sciencemag.org/content/372/6538/eabg3055.abstract

[8]

https://github.com/tomwenseleers/newcovid_belgium/blob/main/analysis%20VOCs%20baseline%2 Osurveillance%20BELGIUM_15%20june%202021.R

[9] NRC. <u>https://www.uzleuven.be/nl/laboratoriumgeneeskunde/genomic-surveillance-sars-cov-2-belgium</u>

[10] https://github.com/tomwenseleers/newcovid_belgium/blob/main/analysis_VOCs_UK_sanger.R

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Appendix: Chronology of relaxation of measures in England and Belgium (note Scotland and Wales have their own plans)

The **UK** initiated a 'roadmap out of lockdown' in England[YL1] from March 8, 2021 onwards, comprising four steps.

Step 1a – 8th March (+/- 9 weeks before May 8)

• Schools reopened, with secondary schools requiring masks in lessons and twice-weekly tests for students and teachers.

Step 1b – 29th March (+/- 6 weeks before May 8)

- People allowed to meet in groups of up to 6 people outside
- Outdoor sports facilities allowed to reopen, and formally organized outdoor sports allowed
- Travel allowed outside local areas, but no international travel allowed yet

Step 2 – 12th April (+/- 4 weeks before May 8)

- Reopening of several businesses and activities: Non-essential retail, personal care premises (nonmedical contact professions), zoos, theme parks, drive-in cinemas, campsites and holiday lets, outdoor pubs and restaurants, indoor gyms...
- Funerals with up to 30 mourners, weddings, receptions and commemorative events up to 15

Step 3 – 17th May (+/- 1 week after May 8)

- Most rules affecting outdoor social contact removed (up to 30 people), two households or six people allowed to meet indoors
- Most businesses in all but the highest risk sectors reopened: Indoor hospitality services (pubs and restaurants), hotels, hostels and B&Bs, indoor entertainment venues (cinemas, children's play areas)
- Larger performances and sporting events in indoor venues up to 1,000 people, and in outdoor venues up to 4,000 people and up to 10,000 people in the largest outdoor seated venues, where crowds can be spread out.
- Up to 30 people can attend weddings, receptions and wakes, as well as funerals.

<u>Step 4</u> included the removal of all legal limits on social contact and was planned to start June 21, but has been put on hold.

The major relaxations in *Belgium* during the past months were:

April 19 (+/- 8 weeks ago)

• Schools reopened, travel ban lifted

April 26 (+/- 7 weeks ago)

- People allowed to meet in groups of up to 10 people outside
- Reopening non-medical contact professions, shopping without appointment

May 8 (+/- 5 weeks ago)

• Amusement parks and café terraces reopened, curfew replaced by a ban on gathering





• Outdoor events allowed with a maximum of 50 participants

June 9 (+/- 1 week ago)

- People allowed to meet in groups of 4 people inside
- Reopening of several businesses and activities: Pubs and restaurants reopened indoors, cultural and sporting events (up to 200 people inside and 400 people outside), fairs and markets, nonprofessional sports (up to 50 people indoors and 100 people outdoors), youth and social activities (up to 50 persons, without overnight stay), parties and receptions inside (up to 50 persons), cinemas and all kinds of recreation centres, fitness centres, saunas and the like
- Religious services, weddings and funerals up to 100 persons inside and 200 persons outside
- Door-to-door selling permitted, as are the activities of sex workers
- Events and demonstrations of up to 100 people