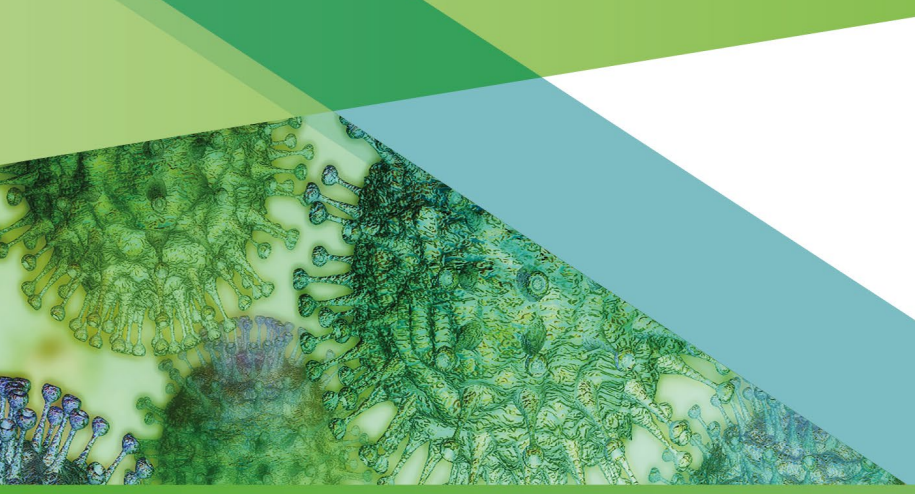

TECHNICAL REPORT

Public health impact of SARS-CoV-2 variants of concern: scoping review protocol

18 May 2021

Background

Several SARS-CoV-2 variants have been identified. Some of these variants have mutations that (alone or in combination) may provide the virus with a selective advantage, such as increased transmissibility or the ability to evade the host immune response, or cause possible changes in pathogenicity, thus increasing disease severity.

On 25 February 2021, the World Health Organization (WHO) proposed the following working definitions to differentiate SARS-CoV-2 variants of the greatest public health relevance:

- **Variant of interest (VOI)** is phenotypically changed compared to a reference isolate or has a genome with mutations that lead to amino acid changes associated with established or suspected phenotypic implications; AND has been identified to cause community transmission/multiple COVID-19 cases/clusters, or has been detected in multiple countries; OR is otherwise assessed to be a VOI by WHO in consultation with the WHO SARS-CoV-2 Virus Evolution Working Group [1].
- **Variant of concern (VOC)** is a VOI that, through a comparative assessment, has been demonstrated to be associated with:
  - Increase in transmissibility or detrimental change in COVID-19 epidemiology; AND/OR
  - Increase in virulence or change in clinical disease presentation; AND/OR
  - Decrease in effectiveness of public health and social measures or available diagnostics, vaccines, therapeutics; AND/OR
  - is assessed to be a VOC by WHO in consultation with the WHO SARS-CoV-2 Virus Evolution Working Group [1].

As of 7 May 2021, the following SARS-CoV-2 VOCs have been identified:

- Variant B.1.1.7, first reported by the United Kingdom on 14 December 2020 [2], is defined by multiple spike protein changes (deletion 69-70, deletion 144, amino acid change N501Y, A570D, D614G, P681H, T716I, S982A, D1118H) [3], as well as by mutations in other genomic regions [4]. This VOC belongs to Nextstrain clade 20B [5,6], GISAID clade GR [7,8] and PANGO lineage B.1.1.7 [9,10].
- Variant B.1.1.7 with an additional mutation (E484K) is also designated as a variant of concern.
- Variant B.1.351, first reported in South Africa on 18 December 2020 [2], is defined by multiple spike protein changes (amino acid change D80A, D215G, D614G, E484K, K417N, N501Y, and A701V) [11]. This VOC belongs to Nextstrain clade 20C [5,6], GISAID clade GH [7,8], and PANGO lineage B.1.351 [9,10].

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- Variant P.1, first reported by Japan in returning travellers from Brazil, and later in Brazil, has 11 amino acid changes in the spike protein compared to its ancestral lineage B.1.1.28, three of which are located in the receptor-binding domain. Spike protein changes for the variant are L18F, T20N, P26S, D138Y, R190S, K417T, E484K, N501Y, H655Y and T1027I [12]. This VOC belongs to Nextstrain clade 20B [5,6], GISAID clade GR [7,8] and PANGO lineage P.1. [9,10].

The potential public health implications of these VOCs need to be understood and assessed, since their increased circulation may affect overall prevention and control strategies employed by ECDC and European Union/ European Economic Area (EU/EEA) countries.

As a result, ECDC will conduct a scoping review on SARS-CoV-2 VOCs, with the purpose of identifying relevant emerging data that could inform ECDC's scientific guidance and risk assessments.

Target audience

ECDC experts and public health authorities in EU/EEA Member States.

Objective and review questions

The objective of this scoping review is to map and summarise the emerging evidence on SARS-CoV-2 VOCs and provide an overview of their potential impact on public health measures. The questions to be addressed in this scoping review are presented in Table 1.

Table 1. Review questions

Type of question	Review question
Main question	What is the potential impact of SARS-CoV-2 VOCs on public health?
Sub-questions	What has been reported on the potential or confirmed negative impact of VOCs (as compared to previously circulating or co-circulating strains) regarding: • SARS-CoV-2 diagnostics? • Transmissibility? • Disease severity? • Immune responses following natural infection and following vaccination? • Vaccine efficacy and effectiveness?

This protocol has been developed following the guidance of the Johanna Briggs Institute [13,14]. The final report will be guided by the standards of the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR)[15].

On 19 March 2021, the following databases were searched with the purpose of identifying systematic reviews or scoping reviews on this topic:

- Open Science Framework [16];
- COVID-19 Living Overview of Evidence (COVID-19 L•OVE) [17];
- COVID-19 Evidence Network to support Decision-making (COVID-END) [18];
- PROSPERO: International prospective register of systematic reviews [19];
- WHO COVID-19 Global literature on corona virus disease [20];
- Joanna Briggs Institute: Systematic Review Register [21].

Only one source indicated the existence of a living evidence synthesis with a similar scope to the scoping review proposed in this protocol [22]. Specific details on the mentioned living evidence synthesis have been requested from the McMaster Health Forum (COVID-END secretariat). At present, it is not possible to assess how our proposed scoping review differs from the already existing work. Research briefs with a summary of results on health system and public health impacts on this living evidence synthesis were published on 3 May 2021, containing results through 7 April 2021 [23,24]. These included a review of guidelines and articles that focused on public health or health systems but did not focus directly on the same outcomes of interest in the ECDC review. ECDC determined that these reviews would be complementary.

Inclusion criteria

Participants

This scoping review will focus on publications of studies relevant to human health, regardless of age, sex, geographic origin, or occupation, of the study participants, including characterisation of human clinical specimens.

Concepts

The concepts to be explored are:

- Detection of SARS-CoV-2 VOCs (e.g. negative impact on available diagnostics, development of new diagnostic assays or protocols);
- Transmissibility of SARS-CoV-2 VOCs in comparison to previously circulating or co-circulating strains;
- Disease severity and mortality of COVID-19 caused by SARS-CoV-2 VOCs in comparison to previously circulating or co-circulating strains;
- Immune escape of SARS-CoV-2 VOCs post-natural infection (e.g. reduced neutralisation capacity of convalescent serum, antigenic cross-reactivity between VOCs);
- Immune escape of SARS-CoV-2 VOCs post-vaccination (e.g. reduced neutralisation capacity of post-vaccination serum); and
- Impact on vaccine effectiveness.

Context

Publications from any geographic setting will be considered if they provide relevant information for the European public health measures.

Type of sources

Primary studies regardless of study design, both peer-reviewed and grey literature (e.g. preprints, institutional and governmental reports) will be included.

Editorials, commentaries, and media reports will be excluded.

Publications written in English will be included. If possible, publications in other languages will be included, depending on the availability of translation services during screening and data extraction.

To be eligible, publications must provide evidence on any of the following aspects in relation to SARS-CoV-2 VOCs:

- Detection of SARS-CoV-2 VOCs, including changes in the performance characteristics of available diagnostics;
- Estimates of SARS-CoV-2 VOCs transmissibility, severity, or mortality;
- Viral load/viral concentration of SARS-CoV-2 VOCs in human clinical specimens;
- Symptoms associated with SARS-CoV-2 VOCs;
- Cellular and humoral immunity against SARS-CoV-2 VOCs;
- Neutralisation assay results, using either convalescent serum/serum from vaccinated human populations (regardless of age, sex, or geographic origin) against SARS-CoV-2 VOCs;
- Effect on vaccine effectiveness.

Type of outcomes

Table 2 summarises the type of outcomes that will be considered in this scoping review.

Outcomes not considered initially may be included if relevant to the main review question.

Search strategy

Literature searches will be conducted in the following databases from 1 December 2020 onwards: PubMed, Embase.com, Scopus; Preprint platforms: bioRxiv, medRxiv, virological.org; In-house PHE COVID-19 EndNote library; COVID-19 specific databases: WHO COVID-19 Global literature on corona virus disease [20], COVID-19 L•OVE [17].

The search strategy combines the concept of VOCs with SARS-CoV-2, represented by controlled vocabulary where available (i.e. MeSH and Emtree terms) and natural vocabulary in multiple field search combinations. EndNote (Clarivate Analytics, Philadelphia, U.S.) [25] will be used for deduplication of identified records.

A preliminary search was done on 4 March 2021; details of the search strategy used are available in Annex 1.

External peer review of the final search strategy will be conducted during the pilot testing period.

In addition, targeted websites from public health authorities in EU/EEA and non-EU/EEA countries and international organisations will be searched for relevant reports (Annex 3).

Table 2. Outcomes of interest

Concept	Example of outcomes of interest
Detection	• Effect of VOC mutations on RT-PCR diagnostics (e.g. primer/probe mismatch) • Effect of VOC mutations on antigen test performance • Change in performance characteristics (e.g. sensitivity and specificity)
Transmissibility	• Incidence of the VOC compared to previously circulating or co-circulating strains • Transmissibility calculations • R0 • Secondary attack rates • Viral load • Viral shedding duration
Severity	• Symptoms • Severity in clinical symptoms • Hospitalisation, duration of hospitalisation • ICU admission, duration of ICU admission • Need for mechanical ventilation • Time to recovery after admission/after start of symptoms • Mortality rate (e.g. case fatality rate or infection fatality rate) in comparison to previously circulating or co-circulating strains • Case distribution by age, sex, and underlying conditions
Immune escape post-natural infection	• Neutralisation of VOCs with convalescent serum • Reinfection post-natural infection • Cross protection against the different VOCs
Immune escape post-vaccination	• Neutralisation of VOCs with post-vaccination serum
Vaccine efficacy and effectiveness	• Breakthrough infection with VOC • Effect on vaccine efficacy and effectiveness: – direct effects: mild, moderate, severe disease – indirect effects (transmission): secondary attack rates, symptomatic and asymptomatic infection, viral load, duration of viral shedding

Selection process

In the first step, titles and abstracts of the identified publications will be screened by two independent reviewers. Similarly, in the second step, the full text of pre-selected publications will be independently screened by two reviewers. Any discrepancies will be resolved by consensus between the two reviewers. If consensus cannot be reached, a third reviewer will be consulted until final agreement is reached.

Covidence systematic review software (Veritas Health Innovation, Melbourne, Australia)[26] will be used for title/abstract screening and for full text screening. EndNote (Clarivate Analytics, Philadelphia, U.S.) [25] will be used for managing the collection of selected articles.

Checklists for the title/abstract and full text screening will be developed to promote a consistent approach is applied by all reviewers. Annex 3 describes the draft checklists. The review team will discuss any challenges encountered during the screening process on a weekly basis. If necessary, the screening procedures will be adapted.

Data extraction

Data extraction forms will be developed in Microsoft Excel (Microsoft, Redmond, WA, U.S.)[27], containing a priori categories described in Annex 4.

The data extraction forms will be pilot tested using at least two publications for each of the concepts of interest.

One reviewer will independently extract data from selected publications and a second reviewer will screen 20% of the data extracted.

Analysis of the evidence

Data will be summarised to describe basic characteristics of the evidence found, e.g. number of publications, study designs, and outcomes, in relation to the concepts being explored in this scoping review. The review team will apply an iterative process to assess a priori categories and post hoc considerations.

A critical appraisal of included publications (i.e. assessment of methodological considerations or risk of bias) will not be performed as this is a scoping review.

Presentation of the results

Results will be summarised in tables and diagrams that align with the objective and review questions of the scoping review. Narrative summaries will further describe the main findings. The final scoping review will be reported in compliance with the PRISMA-ScR [15].

Timeline

Start date: 12 April 2021

Anticipated completion date: June 2021

Stage	Started	Completed
Preliminary searches	Yes	Yes
Piloting of the study selection process	Yes	Yes
Formal screening of search results against eligibility criteria	Yes	No
Data extraction	No	No
Data analysis	No	No

Review team (in alphabetical order)

Internal experts: Charlotte Deogan, Kate Olsson, Ajibola Omokanye, Pasi Penttinen, Anastasia Pharris, Senia Rosales-Klintz.

ECDC Library: Ana-Belen Escriva, Helena Simanova.

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Annex 1. Search strategy and results from a pilot search conducted 4 March 2021

PubMed

No.	Query	Results
#1	("VUI 202012/01"[TW] OR "VOC 202012/01"[TW] OR "VOC-202012/01"[TW] OR "B.1.1.7"[TW] OR "501.V2"[TW] OR "501Y.V2"[TW] OR "B.1.351"[TW] OR "N501Y"[TW] OR "E484K"[TW] OR "P.1 lineage*"[TW] OR "P.1 variant*"[TW] OR "P.1 strain*"[TW] OR "variant* under investigation"[TW] OR "variant* of interest"[TW] OR "variant* of concern"[TW] OR "20H/501Y.V2"[TW] OR "20H 501Y.V2"[TW] OR "20H501Y.V2"[TW] OR "20H-501Y.V2" OR "20I/501Y.V1"[TW] OR "20I 501Y.V1"[TW] OR "20I501Y.V1"[TW] OR "20I-501Y.V1"[TW] OR "20J/501Y.V3"[TW] OR "20J 501Y.V3"[TW] OR "20J501Y.V3"[TW] OR "20J-501Y.V3"[TW] OR "VUI 202101/01"[TW] OR "VOC 202102/02"[TW] OR "B.1.525"[TW] OR "Virus variant 202012 01"[TW] OR "virus variant 202012-01"[TW] OR "variant of concern 202012-01"[TW] OR "VOC 202012-01"[TW] OR "VUI-202012 01"[TW] OR "VUI-202012-01"[TW])	105
#2	("SARS-CoV-2"[Mesh] OR "SARS-CoV-2"[TW] OR "SARS-CoV2"[TW] OR SARS2[TW] OR "SARS-CoV-19"[TW] OR "SARS-CoV-2019"[TW] OR "2019-nCoV*"[TW] OR "2019 nCoV*"[TW] OR "SARS Coronavirus 2"[TW] OR "2019 novel coronavirus*"[TW] OR "severe acute respiratory syndrome coronavirus 2"[TW] OR "SARS-CoV-2 variant*"[TW])	68 066
#3	#1 AND #2	87

Embase.com

No.	Query	Results
#1	'vui-202012/01':ab,ti,kw OR 'b.1.1.7':ab,ti,kw OR '501.v2':ab,ti,kw OR '501y.v2':ab,ti,kw OR 'b.1.351':ab,ti,kw OR (('p.1' NEAR/3 (variant* OR strain* OR lineage*)):ab,ti,kw) OR ((variant* NEAR/3 (investigation* OR interest* OR concern*)):ab,ti,kw) OR '20h/501y.v2':ab,ti,kw OR '20h 501y.v2':ab,ti,kw OR '20h501y.v2':ab,ti,kw OR '20h-501y.v2':ab,ti,kw OR '20i/501y.v1':ab,ti,kw OR '20i 501y.v1':ab,ti,kw OR '20i501y.v1':ab,ti,kw OR '20i-501y.v1':ab,ti,kw OR '20j/501y.v3':ab,ti,kw OR '20j 501y.v3':ab,ti,kw OR '20j501y.v3':ab,ti,kw OR '20j-501y.v3':ab,ti,kw OR 'vui 202101/01':ab,ti,kw OR 'voc 202102/02':ab,ti,kw OR 'b.1.525':ab,ti,kw OR ((('virus variant' OR 'variant of concern' OR 'voc' OR 'vui') NEAR/2 ('202012 01' OR '202012-01' OR '202012/01')):ab,ti,kw) OR 'vui-202012 01':ab,ti,kw OR 'vui-202012-01':ab,ti,kw	2 592
#2	((coronavirus OR ncov) NEAR/3 (19 OR 2019 OR novel OR wuhan)):ab,ti,kw	29 933
#3	'severe acute respiratory syndrome coronavirus 2'/exp OR 'sars-cov-2':ab,ti,kw OR 'sars-cov2':ab,ti,kw OR 'sars2':ab,ti,kw OR 'sars 2':ab,ti,kw OR 'ncov-2019':ab,ti,kw OR 'sars-cov-19':ab,ti,kw OR 'wuhan seafood market pneumonia virus':ab,ti,kw	42 269
#4	#2 OR #3	57 235
#5	#1 AND #4	29

Scopus

No.	Query	Results
#1	(TITLE-ABS ((coronavirus OR ncov) W/3 (19 OR 2019 OR novel OR wuhan)) OR TITLE-ABS ("sars-cov-2" OR "sars-cov2" OR sars2 OR "sars 2" OR "severe acute respiratory syndrome coronavirus 2" OR "sars-cov-19" OR "wuhan seafood market pneumonia virus")) AND (TITLE-ABS ("vui-202012/01" OR "b.1.1.7" OR "501.v2" OR "501y.v2" OR "b.1.351" OR ("p.1" W/3 (variant* OR strain* OR lineage*)) OR (variant* W/3 (investigation* OR interest* OR concern*)) OR "20h/501y.v2" OR "20h 501y.v2" OR "20h501y.v2" OR "20h-501y.v2" OR "20i/501y.v1" OR "20i 501y.v1" OR "20i501y.v1" OR "20i-501y.v1" OR "20j/501y.v3" OR "20j 501y.v3" OR "20j501y.v3" OR "20j-501y.v3" OR "vui 202101/01" OR "voc 202102/02" OR "b.1.525" OR (("virus variant" OR "variant of concern" OR voc OR vui) W/2 ("202012 01" OR "202012-01" OR "202012/01")) OR "vui-202012 01" OR "vui-202012-01"))	23

In-house COVID-19 references library

Time limit: 04/02/2021-

No.	Query	Results
#1	Any field contains (VUI 202012/01 VOC 202012/01 VOC-202012/01 VUI 202101/01 VOC 202101/01 VOC 202102/02 VUI 202102/02 VOC-202101/01 VOC-202102/02)/or	14
#2	Any field contains (VUI 202012-01 VOC 202012-01 VOC-202012-01 VUI 202101-01 VOC 202101-01 VOC 202102-02 VUI 202102-02 VOC-202101-01 VOC-202102-02)/or	0
#3	Any field contains (VUI 202012 01 VOC 202012 01 VOC-202012 01 VUI 202101 01 VOC 202101 01 VOC-202102 02 VUI 202102 02 VOC-202101 01 VOC-202102 02)/or	0
#4	Any field contains (B.1.1.7 501.V2 501Y.V2 B.1.351 N501Y E484K B.1.525)/or	110
#5	Any field contains (P.1 lineage P.1 variant P.1 strain)/or Title contains P.1 OR Abstract contains P.1	17
#6	Any field contains (variant under investigation variants under investigation variant of interest variants of interest variants of concern variant of concern)/or	34
#7	Any field contains (20H/501Y.V2 20H 501Y.V2 20H501Y.V2 20H-501Y.V2 20I/501Y.V1 20I 501Y.V1 20I501Y.V1 20I-501Y.V1)/or	5
#8	Any field contains (20J/501Y.V3 20J 501Y.V3 20J501Y.V3 20J-501Y.V3)/or	4
	Total	133

Preprint platforms

Time limit: 04/02/2021-

Platform name, URL and search terms	References retrieved
1foldr Hub Coronavirus Research Repository (https://coronavirus.1science.com): ("VUI 202012/01" OR "VOC 202012/01" OR "VUI 202102/02" OR "VOC 202102/02" OR "VOC 202101/01" OR "VUI 202101/01" OR B.1.1.7 OR 501.V2 OR 501Y.V2 OR B.1.351 OR N501Y OR E484K OR 20I/501Y.V1 OR 20H/501Y.V2 OR 20J/501Y.V3)	39
BioRxiv (www.biorxiv.org): full text or abstract or title ""VOC 202012/01" "VOC 202102/02" "VOC 202101/01" B.1.1.7 501.V2 501Y.V2 B.1.351 N501Y E484K P.1 20I/501Y.V1 20H/501Y.V2 20J/501Y.V3" (match whole any) and posted between "04 Feb, 2021 and 31 Dec, 2021" Include articles in bioRxiv and medRxiv	100
Virological.org (https://virological.org): "VUI 202012/01" - 0 hits "VOC 202012/01" - 4 hits "VUI 202102/02" - 0 hits "VOC 202102/02" - 0 hits "VOC 202101/01" - 0 hits "VUI 202101/01" - 0 hits B.1.1.7 - 6 hits 501.V2 - 1 hit 501Y.V2 - 1 hit B.1.351 - 4 hit N501Y - 5 hits E484K - 5 hits 20I/501Y.V1 - 2 hits 20H/501Y.V2 - 2 hits 20J/501Y.V3 - 1 hit **P.1 hits - 5 hits**	7

Annex 2. Targeted websites

National authorities from EU/EEA countries

Website	Links
AGES - Austrian Agency for Health and Food Safety Ltd: SARS-CoV-2-Varianten in Österreich	https://www.ages.at/themen/krankheitserreger/coronavirus/sars-cov-2-varianten-in-oesterreich
Sciensano- Belgian Institute for health: Coronavirus COVID-19	https://covid-19.sciensano.be/fr https://epistat.wiv-isp.be/covid/covid-19.html
UZ Leuven University Hospital: Genomic surveillance of SARS-CoV-2 in Belgium	https://www.uzleuven.be/nl/laboratoriumgeneeskunde/genomic-surveillance-sars-cov-2-belgium
Bulgaria: COVID-19 Unified information portal	https://coronavirus.bg/
Croatian Institute of Public Health	https://www.hzjz.hr/
Institute of Health Information and Statistics of the Czech Republic: COVID - 19: Overview of the current situation in the Czech Republic	https://onemocneni-aktualne.mzcr.cz/covid-19
Republic of Cyprus, Ministry of Health: New coronavirus disease (COVID-19)	https://www.pio.gov.cy/coronavirus/eng
Danish Ministry of Health, Statens Serum Institut: COVID-19	https://covid19.ssi.dk
Republic of Estonia, Ministry of Social Affairs: Coronavirus disease COVID-19	https://www.terviseamet.ee/et/uuskoroonaviirus
Finnish Institute for Health and Welfare: Coronavirus COVID-19 – Latest updates	https://thl.fi/en/web/infectious-diseases-and-vaccinations/what-s-new/coronavirus-covid-19-latest-updates
Sante publique France: Coronavirus (COVID-19)	https://www.santepubliquefrance.fr/dossiers/coronavirus-covid-19
Robert Koch Institut (Germany's public health institute)	https://www.rki.de/EN/Home/homepage_node.html;jsessionid=8900383BCD44D9D6705C7CBB6B48E812.internet091
Greece National Organization of Public Health (EODY): New coronavirus Covid-19 – Instructions	https://eody.gov.gr/neos-koronaios-covid-19
Hungarian Government: Information page on the coronavirus	https://koronavirus.gov.hu
Iceland, Directorate of Health and The Department of Civil Protection and Emergency Management	https://www.covid.is/english

Website	Links
Ireland, Health Protection Surveillance Centre	https://www.hpsc.ie
Italy, Istituto Superiore di Sanita	https://www.iss.it
Latvia, Center for Disease Prevention and Control (SPKC)	https://www.spkc.gov.lv/lv/aktualitates-par-covid-19
Liechtenstein, Ministry of Society and Culture: Coronavirus	https://www.regierung.li/coronavirus
Government of the Republic of Lithuania: Korona Stop	https://koronastop.lrv.lt/en
The Luxembourg Government: Coronavirus	https://covid19.public.lu/en.html
Government of Malta	https://deputyprimeminister.gov.mt/en/health-promotion/covid-19/Pages/landing-page.aspx
The Netherlands, National Institute for Public Health and the Environment (RIVM): COVID-19	https://www.rivm.nl/coronavirus-covid-19
Norway, National Institute of Public Health (FHI): Coronavirus	https://www.fhi.no/sv/smittsomme-sykdommer/corona
Republic of Poland: Coronavirus	https://www.gov.pl/web/coronavirus
Portugal, Directorate-General for Health	https://covid19.min-saude.pt
Ministry of Investment, Regional Development and Informatization of the Slovak Republic: Coronavirus and Slovakia	https://korona.gov.sk
Republic of Slovenia: Coronavirus disease COVID-19	https://www.gov.si/en/topics/coronavirus-disease-covid-19
Gobierno de España COVID-19 en España	https://cnecovid.isciii.es
Public Health Agency of Sweden: COVID-19	https://www.folkhalsomyndigheten.se/smittskydd-beredskap/utbrott/aktuella-utbrott/covid-19

National authorities from non-EU/EEA countries

Website	Links
United States, Centers for Disease Control and Prevention	https://www.cdc.gov/coronavirus/2019-nCoV/index.html
Government of the United Kingdom: Coronavirus (COVID-19)	https://www.gov.uk/coronavirus
Switzerland, Federal Office of Public Health: Coronavirus- Situation in Switzerland	https://www.bag.admin.ch/bag/en/home/krankheiten/ausbrueche-epidemien-pandemien/aktuelle-ausbrueche-epidemien/novel-cov/situation-schweiz-und-international.html
Government of Canada: Coronavirus disease (COVID-19)	https://www.canada.ca/en/public-health/services/diseases/coronavirus-disease-covid-19.html
Australian Government, Department of Health: Coronavirus (COVID-19) current situation and case numbers	https://www.health.gov.au/news/health-alerts/novel-coronavirus-2019-ncov-health-alert/coronavirus-covid-19-current-situation-and-case-numbers
South Africa, National Institute for Communicable Diseases	https://www.nicd.ac.za

International organisations

Website	Links
World Health Organisation, Coronavirus disease (COVID-19)	https://www.who.int/emergencies/diseases/novel-coronavirus-2019
Foundation for Innovative New Diagnostics (FIND)	https://www.finddx.org/covid-19
Coalition for Epidemic Preparedness Innovations (CEPI)	https://cepi.net
European Medicines Agency (EMA)	https://www.ema.europa.eu/en/human-regulatory/overview/public-health-threats/coronavirus-disease-covid-19
COVID-19 Evidence Network to support Decision-making (COVID-END)	https://www.mcmasterforum.org/networks/covid-end
National Collaborating Centre for Methods and Tools	https://www.nccmt.ca/covid-19/covid-19-evidence-reviews

Annex 3. Checklists

Title/abstract screening	
Criteria for inclusion (all must be present)	Yes/No
The publication relates to any of SARS-CoV-2 VOCs	
The publication is a primary study (including rapid or systematic literature reviews)	
The publication is in English or in another language where translation might be available	

Full text screening	
Criteria for inclusion (all must be present)	Yes/No
The publication reports on at least one of the concepts of interest: • **Detection of VOCs** • **Transmissibility of VOCs in comparison to previously circulating or co-circulating strains** • **Disease severity of COVID-19 caused by VOCs in comparison to previously circulating or co-circulating strains.** • **Immune response post-natural infection** • **Immune response post-vaccination** • **Impact of VOCs on vaccine efficacy and effectiveness**	
The publication is a primary study (including rapid or systematic literature reviews)	
The publication is in English or in another language where translation might be available	
Most current version of the document	
Criteria for exclusion (any of them justifies exclusion)	
The publication is an editorials or commentaries	
The publication is a media report	
The publication was a draft or summary version or has been replaced with another document	

Annex 4. Data extraction

Concept	Fields for data extraction
General (Study information)	• Reference ID number • Author • Year/ month publication • Publication status (peer-reviewed or pre-print) • Country • Study design • Study period (if applicable) • Number of study participants • Variant(s) of concern • Objective • Link to publication
Detection	• Purpose of the study: – Assessment of the VOC impact on diagnostics ▪ Effect of VOC mutations on RT-PCR diagnostics (primer/probe mismatch) ▪ Effect of VOC mutations on antigen test performance – New diagnostic protocol or assay for detection of VOCs • Method • Outcome measure(s) • Key findings • Conclusions (as reported by authors) Comments
Transmissibility	• Method • Outcome measure(s) – Incidence data over time – Transmissibility calculations – R0 – Secondary attack rates – Viral load – Viral shedding duration • Key findings • Conclusions (as reported by authors) • Comments
Severity	• Method • Outcome measure(s) – Symptoms – Severity in clinical symptoms – Hospitalisation, duration of hospitalisation – ICU admission, duration of ICU admission – Need for mechanical ventilation – Time to recovery after admission/after start of symptoms – Mortality rate (e.g. case fatality rate or infection fatality rate) in comparison to previously circulating or co-circulating strains – Case distribution by age, sex, and underlying conditions • Key findings • Conclusions (as reported by authors) • Comments
Immune response post-natural infection	• Method – Neutralisation assays – Other • Outcome measure(s) – Neutralisation of VOCs with convalescent serum – IC50/ID50/PRNT 50 – Neutralisation titres – Cross protection against the different VOCs – Neutralisation titres – VOC reinfection post-natural infection • Key findings • Conclusions (as reported by authors) Comments

Concept	Fields for data extraction
Immune response post-vaccination	• Method – Neutralisation assays – Other • Outcome measure(s) – Neutralisation of VOCs with convalescent serum ▪ IC50/ID50/PRNT 50 ▪ Neutralisation titres – Cross protection against the different VOCs ▪ Neutralisation titres • Key findings • Conclusions (as reported by authors) • Comments
Impact on vaccine effectiveness	• Method • Outcome measure(s) – Breakthrough infection with VOCs – Direct effects: mild, moderate, severe disease – Indirect effects (transmission): secondary attack rates, symptomatic and asymptomatic infection, viral load, duration of viral shedding • Key findings • Conclusions (as reported by authors) • Comments