



Safety Platform for Emergency vACcines

## SO2-D2.1.2 Priority List of COVID-19 Adverse events of special interest: Quarterly update December 2020

*Additions: 1) subacute thyroiditis, 2) pancreatitis and  
3) rhabdomyolysis*

Work Package: WP2 Standards and tools

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## DOCUMENT INFORMATION

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Description of the deliverable	This deliverable provides the methods and results of the second quarterly update to the Priority List of potential Adverse events of special interest relevant to COVID-19 vaccine trials (SO1 deliverable 2.3 V2.0, May 25, 2020)
Key words	Toolbox, adverse events of special interest, guidance documents

## DOCUMENT HISTORY

NAME OF DOCUMENT	DATE	VERSION	CONTRIBUTOR(S)	DESCRIPTION
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SO2-D2.1.2 Priority List of COVID-19 Adverse events of special interest: Quarterly update 2 _ v1.1	15/12/2020	V1.1	Barbara Law	Revision in response to reviews by Cornelia L Dekker and Marc Gurwith
SO2-D2.1.2 Priority List of COVID-19 Adverse events of special interest: Quarterly update 2 _ v1.2	23/12/2020	V1.2	Barbara Law	Revision in response to reviews by Miriam Sturkenboom and Robert Chen

## EXECUTIVE SUMMARY

As part of its work to harmonize safety assessment of CEPI-funded vaccines, the Safety Platform for Emergency vAccines (SPEAC) Project has generated a list of adverse events of special interest (AESI) for safety monitoring based on one or more of the following criteria:

- 1) known association with immunization or a specific vaccine platform;
- 2) theoretical association based on animal models;
- 3) occurrence during wild-type disease as a result of viral replication and/or immunopathogenesis.

COVID-19 is unique as an emerging pandemic pathogen with an ever-expanding variety of clinical manifestations which might occur as presenting complaints and/or emerge during and following the course of acute disease. The first SPEAC COVID-19 AESI list was created in March 2020 based on the experience in China; it was updated in May 2020 as the global experience with the SARS-CoV-2 viral infection expanded. The May 2020 list was adopted by the WHO Global Advisory Committee on Vaccine Safety (GACVS) at their May 27-28, 2020 meeting. Subsequently, SPEAC implemented a systematic review process to ensure an ongoing understanding of the full spectrum of COVID-19 disease and modification of the AESI list accordingly. The first evidence-based update was completed in September 2020 with no AESIs added to the May 2020 list.

This document provides detailed methods and results of the December 2020 COVID-19 quarterly update. Separate annexes are included consolidating all reviews since March 2020, summarizing publication type and frequency of events, by body system. A companion excel spreadsheet has been prepared which contains the full citations with download links included in the March, May, September and December 2020 updates separated into tabs by body system. Four secondary objectives are also addressed: 1) a reassessment of the need for Brighton case definitions to be created for all the AESIs on the May 2020 list, 2) consideration of new AESIs for addition to the list, 3) consolidation of the systematic reviews presented in May, September and December 2020 and 4) consideration of the need for a change in focus of the next update due in March 2021.

Based on the findings presented in the December 2020 update SPEAC recommends the following:

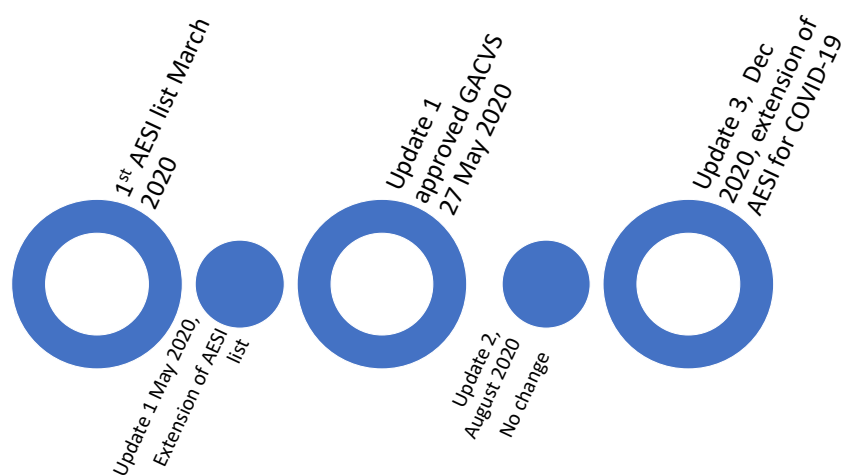
1. Three new events are added to the COVID-19 AESI list: rhabdomyolysis, subacute thyroiditis and acute pancreatitis.
2. For the prior listed AESI acute kidney injury recommend use of the international criteria defined by the Kidney Disease Improving Global Outcomes (KDIGO) expert consensus group in 2012 rather than develop a new Brighton case definition.
3. For the prior listed AESI acute liver injury, adopt what has been used in many COVID-19 publications reporting elevations above the upper normal limit of >3-fold for AST/ALT and >2-fold for total bilirubin, GGT and ALP rather than develop a Brighton case definition.
4. Pending publication of the Brighton case definition on cardiovascular injury which will focus on myocarditis and pericarditis, and in-depth review of existing meta-analyses and systematic reviews, defer a decision regarding development of additional Brighton case definitions for the other entities included in cardiovascular injury (arrhythmia, acute coronary syndrome, heart failure, cardiogenic shock, stress cardiomyopathy and microangiopathy).
5. For the next COVID-19 update, due in March 2021, limit the focus to COVID-19 disease outcomes in pregnancy and childhood along with long term complications.

## 1. Background

CEPI has contracted with the Brighton Collaboration, through the Task Force for Global Health, to harmonize the safety assessment of CEPI-funded vaccines via its Safety Platform for Emergency vACCines (SPEAC) Project.

A key aspect of this harmonization has been creation of lists of priority potential adverse events of special interest (AESI) that are relevant to vaccines targeting CEPI target diseases.

The first AESI list for COVID-19 was approved March 5, 2020 based on the first published experiences from China. Subsequently PubMed searches were done on a daily basis and new articles screened for newly emerging COVID-19 clinical patterns and complications. A full description of the methodology and results including citations for the first two COVID-19 AESI lists is available on the Brighton website ([tps://brightoncollaboration.us/wp-content/uploads/2020/06/SPEAC\\_D2.3\\_V2.0\\_COVID-19\\_20200525\\_public.pdf](https://brightoncollaboration.us/wp-content/uploads/2020/06/SPEAC_D2.3_V2.0_COVID-19_20200525_public.pdf)). Figure 1 shows the timelines of different updates.



**FIGURE 1. SEQUENCE OF UPDATES ON THE COVID-19 AESI LIST**

A first extended/updated COVID-19 AESI list was presented to the WHO global Advisory Committee on Vaccine safety (GACVS) at a virtual meeting held May 27-28, 2020. The GACVS agreed to adopt that AESI list.<sup>1</sup> At the time it was clearly understood that new AESI could be added to the COVID-19 list as needed based on new knowledge learnt during the global pandemic. Accordingly, SPEAC put in place a plan for a continued systematic search of the published literature related to COVID-19 disease complications. The next update covered citations published from May 16 through August 8, 2020. (SO2\_D2.1.1\_V1.1\_COVID-19\_AESI update Aug 20, available in the Developers Toolbox and the Brighton website). No changes to the AESI list were recommended based on the update in September 2020 but several potential entities were flagged as possibilities pending further evidence, including subacute thyroiditis, pancreatitis, rhabdomyolysis and autoimmune hemolytic anemia. These were one focus of the subsequent quarterly update which is presented in this deliverable.

One reason for updating the AESI list is to be prepared to monitor these events pre and post-introduction and to assess whether case definitions are needed.

From May through August 2020, BC working groups were set up to develop Brighton case definitions for various COVID-19 AESI. These included Vaccine Associated Enhanced Disease (VAED), Acute Respiratory Distress Syndrome (ARDS), Multisystem Inflammatory Disease in Children (MISC), acute cardiovascular injury (including myocarditis, pericarditis, arrhythmia, heart failure, cardiogenic shock, stress cardiomyopathy, coronary artery disease and microangiopathy) and coagulation disorders (including thrombosis, thromboembolism and bleeding disorder/DIC). The acute cardiovascular injury working group decided in September to limit the focus of the case definition to myocarditis and pericarditis. Similarly, the coagulation disorder working group decided, also in September, to limit the focus of that case definition to thrombosis and thromboembolism. Thus, a second focus of the second quarterly update was to monitor the emerging evidence on the other manifestations of acute cardiovascular injury as well as COVID-19 related hemorrhagic disorders to discern whether or not additional case definitions were needed.

A call for working groups on acute kidney injury and liver injury was posted on the Brighton Collaboration site in August 2020 but neither had been formed as of the end of the screening period for the second quarterly review (November 13<sup>th</sup>). Thus, a third needed focus of the second quarterly review was to re-examine the evidence for acute kidney and liver injury in order to revisit the need for a new Brighton case definition.

## 2. Objectives of this deliverable

### Primary

1. Present the results of the December 2020 quarterly update for the COVID-19 AESI priority list.

### Secondary

Revisit prioritization of AESI for development of new Brighton case definitions related to acute cardiovascular injury other than myocarditis/pericarditis, bleeding disorders, acute kidney injury and acute liver injury.

2. Propose additions to the AESI list if supported by the evidence related to complications of COVID-19 infection.
3. Consolidate the literature reviewed as part of the COVID-19 landscape analysis from January 1 through the end of the period for the December 2020 quarterly update. Determine whether any changes to the COVID-19 literature update processes are indicated going forward for the next quarterly update.

## 3. Methods

### 3.1 December 2020 quarterly update of literature regarding COVID-19 disease complications

To develop the May 2020 list of potential COVID-19 AESI, a very broad search strategy was used capturing all COVID-19 publications from PubMed as well as pre-prints from bioRxiv and medRxiv. All citation titles were screened by one reviewer (Barb Law) from Feb 17, 2020 and those that addressed the clinical course and complications of COVID-19 were included in a further screen of abstract and/or full text. Duplicates were removed as were non-English articles. Letters to the editor were included as many of these contained relevant case report

and case series data that informed the early development of the AESI list. Given the overwhelming volume of publications, the screening was not done in a systematic fashion following PRISMA guidelines. All articles included in the AESI list finalized May 25, 2020 were captured in the appendices of the D2.3 V2.0 deliverable document (available at Brighton website link in Background above).

Searches were discontinued May 16, 2020 in order to develop the final AESI list based on screened in citations and prepare a presentation to the WHO Global Advisory Committee on Vaccine Safety.

From May 16 through the end of May, over 5000 new citations were published. Ongoing review of such a large volume of literature using similar methods as those used to generate the first list was deemed impossible. Accordingly, the screened in articles for the May AESI list were reviewed and key words identified to inform a new search strategy. Also, the nature of the excluded articles which did not inform the AESI list (e.g. therapeutic/prevention strategies, infection control, transmission and other basic virology articles, changes in patterns of healthcare during the pandemic) was used to develop a list of exclusionary terms.

For the quarterly update in September 2020 a revised search strategy was developed. The second and final search strategy developed for the September 2020 quarterly update was used also for this December quarterly update (Annex 1). The only change in the final September 2020 search strategy was to exclude, based on PMID number, all articles included in the searches conducted prior to August 8<sup>th</sup>, 2020.

Searches for this December 2020 quarterly update were conducted Sept 9<sup>th</sup>, Oct 9<sup>th</sup> and Nov 13<sup>th</sup>. The first search captured articles published from Aug 8 which was the end date for the 1<sup>st</sup> quarterly update searches. The results from each search were loaded into an excel spreadsheet. A single expert (Barb Law) screened all citations. Several could be screened out based on title alone. Any that could not clearly be screened in or out were then retrieved for abstract and/or full text review.

The brief category name and descriptive rationale for exclusion included:

- 'Duplicate': duplicate of previously captured citation.
- 'Therapy/Testing/Prevention': as implied, articles with the main focus on COVID-19 therapy, testing or prevention of disease.
- 'Healthcare': focus on healthcare during the COVID-19 pandemic.
- 'Unrelated': article unrelated to COVID-19 infection in humans, such as animal model studies or other Coronavirus or related pathogens.
- 'Limited focus': clinical course information included but on a very small scale such as the first case report in a country.
- 'Noncontributory': articles that addressed entities already included on the AESI list with no new information such as an additional case report or limited series of cases.
- 'Non-English': articles in any language other than English.
- 'Comment/Response/Erratum': commentaries including editorials, letters to the editor, author responses to letters to the editor and errata. Of note, full text screening was required for most commentaries because several letters to the editor include case reports, case series and some studies relevant to the AESI list.

For all articles screened out, a distinction was made for whether it was done based on title alone or after abstract and/or full text review.



All screened in articles were categorized according to: 1. Primary topic (mainly by body system); 2. Subgroup 1 (mainly specific diagnosis or population subgroup); and 3. Subgroup 2 (type of article) using the following terms:

### 1. Primary topic:

- A. **Categories from previous AESI list:** Cardiac, Neurologic, Dermatologic, Hematologic, Gastrointestinal, Liver, Kidney, Multisystem inflammatory syndromes, Musculoskeletal, Ocular and Respiratory.
- B. **Additional categories relevant to AESI list:** Autoimmune, Co-infection, Endocrine, Enhanced disease, Pregnancy, Psychiatric, Mixed clinical (for reports, mainly reviews and meta-analyses, of extra-pulmonary manifestations of COVID19) and Other. A new category for chronic complications was added as part of this review given the emergence of the 'long haul' syndrome.
- C. **Articles to keep for potential relevance to AESI Tools but not to the AESI list per se:** Background rate, Risk factor, and Pathology were also categorized and kept but not all reviewed in depth for the AESI list. Within the pathology subgroup, any relating to autopsy findings were to be reviewed in full.

### 2. Subgroup 1:

Two groups of terms were used based on whether or not an AESI was already included in the list for COVID19 finalized in May 2020.

#### A. Relevant to already identified AESI:

- **Cardiovascular:** acute coronary syndrome, aneurysm, arrhythmia, endothelial dysfunction, heart failure, MI, myocarditis (including pericarditis), STEMI (For ST elevation myocardial infarction), sudden death, Takotsubo syndrome (stress cardiomyopathy);
- **Neurologic:** acute disseminated encephalomyelitis (ADEM), CNS bleed, encephalitis, encephalopathy, Guillain Barré Syndrome (GBS), myelitis, seizure, Smell/Taste (for anosmia, ageusia, hyposmia, hypogeusia and dysgeusia); Cranial Nerve – other;
- **Hematologic:** coagulopathy, idiopathic thrombocytopenic purpura, ischemia, pulmonary embolus, stroke, thrombocytopenia, thromboembolism, thrombosis;
- **Dermatologic:** angioedema, chilblain, erythema multiforme, urticaria, vasculitis, other rash;
- **Liver:** injury;
- **Kidney:** injury;
- **Multisystem inflammatory syndromes:** multisystem inflammatory syndrome in children (MISC);
- **Respiratory:** ARDS

#### B. Entities not on the May AESI list:

several were known to have been reported but not in sufficient numbers to merit inclusion on the AESI list; others were added as search results were screened from May 16 to Aug 15. These included:

- **Clinical diagnoses:** abscess, adrenal injury, alopecia, arthritis, autoimmune hemolytic anemia, cholecystitis, chronic complication, conjunctivitis, diarrhea, enteritis/colitis, hemophagocytic lymph histiocytosis, hepatitis, hyperferritinemic syndrome, hyperglycemia, hyponatremia, Kawasaki syndrome, mania, myositis, pancreatitis, parotitis, peripheral neuropathy, pneumomediastinum, pneumothorax, psychosis, retinopathy, rhabdomyolysis, sudden death, thyroiditis, uveo-retinitis;
- **Pregnancy/post-partum related:** breast milk, ectopic pregnancy, foetal, HELLP syndrome, mortality, neonatal, outcomes, placenta, preeclampsia/eclampsia, transmission;

- **Non-specific entities that could lead to identification of new AESI:** autopsy, general, mixed clinical, other, outcomes, severity, virus in tissue
  - **Host-specific other than pregnancy-related:** Adult, Geriatric, HIV, Pediatric
3. **Subgroup 2:** Case Reports (including case series), Commentary (mostly excluded but some kept because of reference to important publications to ensure captured in review), Guideline, Meta-analysis, Pathogenesis, Registry, Review, Study.

### 3.2 Review of evidence related to COVID-19 AESI adopted in May 2020

In the September 2020 quarterly update for AESI already on the May 2020 COVID-19 list and targeted for new case definitions, the number of new articles published for each entity by subgroup and article type were counted but the full article was not reviewed. A spreadsheet for each system group was created to capture all newly published citations in order to support the case definition working groups.

Initially a similar process was intended for the December 2020 quarterly update. However, as noted in the Background section above, the cardiovascular injury and coagulation disorder working groups decided to limit their case definition scope to myocarditis/pericarditis and thrombosis/thromboembolism respectively. These decisions raised a question of whether or not the other entities related to cardiovascular injury as well as hemorrhagic manifestations of coagulation disorders merit a separate Brighton case definition. As a first step to address this a quantitative and qualitative summary of all articles included in the COVID-19 landscape analyses from January 1 through November 13<sup>th</sup> was prepared to capture total number of citations for each manifestation of cardiac injury and coagulation disorders as well as to look at the distribution by article type (meta-analysis, systematic review, pathogenesis/hypothesis, study and case report/case series).

A slightly different approach was used for acute liver injury (ALI) and acute kidney injury (AKI) since the working groups had not yet been formed. A decision was made to review these AESI in greater depth as part of the second quarterly review to learn of any new evidence or greater understanding of the pathogenesis of these entities that might change the priority for having a new Brighton case definition. A secondary objective was to understand what, if any, definitions of ALI and AKI were being used in the COVID-19 literature. Reviews and meta-analyses of each were given priority for full text review.

### 3.3 Evidence Review for Consideration of Additions of New AESIs to the COVID-19 list

The full articles for all included citations with a focus on rhabdomyolysis, pancreatitis, acute thyroiditis and autoimmune hemolytic anemia was read in order to capture age, gender, timing of onset relative to general symptoms and course of COVID-19 as well as underlying comorbidities. For other entities accompanying COVID-19 illness, not yet on the AESI list, the number of case reports for each was determined and summarized in a tabular format, similar to what was done in the September 2020 quarterly update.

### 3.4 Consolidation of all Systematic search results for COVID-19 complications

The May 2020 COVID-19 landscape analysis covered January 1<sup>st</sup> through May 16. To enable summarizing the emerging evidence by body system a tabular summary was used to note publication type (Review, Meta-analysis, Pathogenesis/hypothesis, Study, Case Report), first author, country of origin and topic area. A full citation list was provided, below each tabular summary. Appendices were presented by system including Cardiovascular, Neurologic, Hematologic, Dermatologic, Gastrointestinal, Kidney, Multisystem inflammatory disease, Musculoskeletal, Ocular and Respiratory.

The September 2020 quarterly update, covered May 16 through August 8<sup>th</sup>. All citations from each search period were loaded into an excel spreadsheet to facilitate screening. All included publications were then distributed to separate tabs for each of the body systems included in the May search. Cited references in the September 2020 quarterly update deliverable itself were limited to those discussed in the results section related to the four entities flagged as possible new AESI for future consideration (rhabdomyolysis, pancreatitis, subacute thyroiditis and autoimmune hemolytic anemia). At the time the September 2020 quarterly update was presented a request was made to consolidate all the COVID-19 systematic search results. This is being done as part of the December 2020 quarterly update.

The screening process for the December 2020 quarterly update is described in 3.1 above. All included citations were added to those from the September quarterly update. In order to have the January to May 16 citations included in the spreadsheets the PMIDs from screened in citations for that period were used to gather the citations and they were added to the spreadsheet. Differentiation of articles acquired in the separate search periods can be identified using the 'search date' column: January to May search (16<sup>th</sup> May 2020); September 2020 quarterly update (06/12/2020, 07/08/2020, 07/21/2020, 07/31/2020, 08/07/2020); and December 2020 quarterly update (09/09/2020, 10/09/2020, 11/13/2020).

In addition, the appendices included in the May 2020 COVID-19 review were updated to add a tabular summary for all the September 2020 quarterly and December 2020 quarterly added citations. For AESI already on the May 2020 list, numbers of new publications were captured rather than itemizing them individually. For new entities, individual itemization was used. A separate Annex was created for acute liver injury instead of including it within the Gastrointestinal Annex. New appendices were added for endocrine and long-term complications of COVID-19.

### 3.5 Consideration of Need for Changes to the Systematic Review Process for the next Quarterly Update

The enormous volume of publications relevant to COVID-19 disease course and complications merits an ongoing consideration of whether or not the exhaustive process currently in place for the quarterly updates is justified. This is underscored by the initiation of the first COVID-19 vaccine programs in several countries which will require an increased focus on vaccine safety issues. Thus, as part of the December 2020 quarterly update records were kept of the time required for each aspect (screening, detailed review of articles to summarize evidence and creating the update deliverable).

## 4. Results

### 4.1 Summary of Excluded Publications

From Aug 7 through Nov 13, 3 separate searches were run; yielding 3901 citations, of which 2141 (54.9%) were screened in and the other 1760 (45.1%) screened out. Among the articles screened out the decision was based on title alone for 68.3% (1202) and on review of abstract and/or full text article for 31.7% (558). Table 1 summarizes the reason articles were screened out for all search dates, separated by whether it was based on title alone or review of abstract/full text. The table also shows variation in distribution of reason excluded for all separate search dates without distinguishing whether exclusion was by title alone or abstract / full text.

A notable change from the September 2020 Quarterly Update was a decrease in duplicates (36.4% of articles screened out in Q1 versus 0.6% in Q2) as a result of adding already screened PMIDs to the exclusion terms for the search strategy.

The search period was 3 months for both September 2020 and December 2020, but the total numbers of articles retrieved by the same search strategy decreased from 4679 in September to 3901 in December and the major reason for the drop was exclusion of duplicates ahead of time by including the PMIDs in the 'not' part of the search strategy.

**TABLE 1. REASONS FOR EXCLUDING ARTICLES OVERALL AND BY INDIVIDUAL SEARCH DATE FOR DECEMBER 2020 QUARTERLY UPDATE**

Reason for Exclusion	All Search Dates: Total (%) Excluded by:		Distribution of Reason for Exclusion by Search Date % all excluded (title & abstract/full text)		
	Title alone	Abstract / Full Text	Sept 9	Oct 9	Nov 13
Duplicate	9 (0.5%)	1 (0.1%)	0.6%	1.2%	0
Therapy/Testing/Prevention	231 (13.1%)	65 (3.7%)	19.6%	15.9%	14.3%
Healthcare	306 (17.4%)	52 (3.0%)	15.4%	30.4%	17.4%
Unrelated	194 (11.0%)	22 (1.3%)	13.2%	11.3%	12.0%
Limited focus	0	4 (0.2%)	0.6%	0	0
Non-contributory	268 (15.2%)	264 (15.0%)	26.9%	25.2%	38.7%
Non-English	1 (0.1%)	23 (1.3%)	2.3%	0.6%	0.9%
Comment/Response/Erratum	193 (11.0%)	127 (7.2%)	21.5%	15.3%	16.7%
Total excluded/all retrieved (% excluded)	1202/3901 (30.8%)	558/3901 (14.3%)	689/1415 (48.7%)	503/1201 (41.9%)	568/1285 (44.2%)

#### 4.2 Summary of Included Publications for the December 2020 Quarterly Update

Table 2 provides a summary by body system of the articles remaining after screening. These are ordered by Primary Topic as described in Methods.

AESIs already on COVID-19 list: The vast majority of the recently published articles involved AESIs already identified on the COVID-19 list. These are itemized in the 3<sup>rd</sup> column of Table 2 and the proportions of all new publications were:

- Cardiac: 118 (87.4%) of 135 new publications.
- Neurologic: 216 (63.3%) of 341 new publications.
- Hematologic: 372 (98.9 %) of 376 new publications.
- Dermatologic: 46 (43.0%) of 107 new publications. An additional 41 (29.4%) related to entities that were well described but not considered a priority for the AESI list including urticaria, maculopapular, vesicular and livedoid rashes.
- Gastrointestinal: 7 (26.9%) of 26 new publications
- Liver: 36 (90 %) of 40 new publications
- Kidney: 37 (84.1%) of the 44 new publications addressed acute kidney injury.
- Multisystem inflammatory syndrome: 91 (64.1%) of 142 articles focused on children.

For each of the above, the new publications in the 'General Articles' column focused on the breadth of clinical complications already added to the COVID-19 AESI list. All new publications have been added to the COVID-19 spreadsheet created for the September 2020 literature update (COVID Update Jan\_Nov13\_2020\_Final). The

spreadsheet contains separate tabs for each of the Primary Topics (1 A, B and C identified above). Given smaller numbers a 'Miscellaneous Other' tab combines citation for auto-immune disease, co-infection, enhanced disease and psychiatric illnesses. In addition, the spreadsheet was updated to include all citations that were part of the search done for January 1 through May 16, 2020. The spreadsheet along with this deliverable document is posted on the Brighton Collaboration COVID-19 website page (add link).

**TABLE 2. DECEMBER 2020 QUARTERLY UPDATE: QUANTITY AND SCOPE OF ARTICLES RELEVANT TO COVID-19 INFECTION BY BODY SYSTEM AND PRESENCE OR ABSENCE ON CURRENT COVID-19 LIST**

BODY SYSTEM	Total Articles	AESI (number articles) already on COVID-19 List	Entities (number articles) Not yet on the AESI list	General Articles
Cardiac (Annex 2)	135	Myocarditis (42), acute cardiac injury (19), STEMI (5), arrhythmia(31), heart failure(3), endothelial dysfunction(1), acute coronary syndrome(1), Takotsubo stress cardiomyopathy(13), MI(3),	cardiac tamponade (3), dilated cardiomyopathy (1), non-bacterial thrombotic endocarditis(1), postural tachycardia syndrome(1), large vessel vasculitis(1)	Meta-analysis (1) Reviews (3) Guideline (1) Pathogenesis (2) Studies (2) Commentary (1)
Neurologic (Annex 3)	341	Anosmia/Ageusia (79), GBS (33), encephalitis (24) encephalopathy (32), brain hemorrhage (14), seizure (15), ADEM (3), myelitis (12), aseptic meningitis (4)	Myoclonus-ataxia (4), myoclonus(5), vasculitis(3), sensorineural hearing loss(2), ophthalmoplegia(5), facial palsy(8), hypoglossal nerve palsy(1), vestibular neuritis(1),cranial polyneuropathy(1), oropharyngeal dysphagia(1), dysesthesia with exanthem(1), persistent hiccups(1), hyponatremia with urinary retention(1), COVID19-associated insomnia(1), dizziness(1), tremors & gait disturbance(1)	Reviews (35) Meta-analyses (3) Pathogenesis (30) Studies (19) Guideline(1)
Hematologic (Annex 4)	376	Thrombosis (97), Stroke(94), Coagulopathy(42), Pulmonary embolus(51), thrombocytopenia(17), Ischemia(10), other thromboembolism(57), endothelial dysfunction(4)	Autoimmune hemolytic anemia (1), cold agglutinin syndrome (1), methemoglobinemia (1),	Reviews (1)
Dermatologic (Annex 5)	107	Chilblain (34), cutaneous vasculitis (7), erythema multiforme (4), alopecia (1)	Maculopapular rash (11), Urticaria (5), levedo reticularis (3), hyperkeratosis(1), oral vesiculobullous lesions(1), angioedema(1), Gianotti-Crosti rash(1), follicular eruption(1), seborrheic	Reviews (10) Meta-analysis (1) Studies (14) Pathogenesis (2)

BODY SYSTEM	Total Articles	AESI (number articles) already on COVID-19 List	Entities (number articles) Not yet on the AESI list	General Articles
			dermatitis(1), lower extremity bullae(1), pustular eruption(1), Grover-like eruption(1), unilateral later thoracic exanthem(1), painful cystic lesion(1), nail bed red hal-moon sign(1), prolonged skin manifestations for 4 weeks in a child(1), erythema nodosum(1), pityriasis rosea Gilbert type(1)	
Gastrointestinal (Annex 6)	26	ischemia/thrombosis (7)	Enterocolitis (4), oral manifestations (2), acute acalculous cholecystitis (2), paralytic ileus (1), tongue ulcers (1), spontaneous splenic rupture(1), spontaneous hemoperitoneum(1), angular cheilitis(1), intussusception(1), pediatric manifestations(1)	Studies (3 – all on general GI manifestations in hospitalized patients), Pathogenesis (1)
Liver (Annex 7)	40	Acute liver injury (36)	Fulminant hepatic failure (2), acute hepatitis (1)	Meta-analysis (1)
Kidney (Annex 8)	44	Acute kidney injury (37)	Collapsing glomerulopathy (2), renal infarction (1), hypernatremia (1), ANCA -associated vasculitis with glomerulo-nephritis (1), IgA vasculitis with nephritis (1),	Study (1)
Multisystem Inflammatory Syndrome (Annex 9)	142	MIS-Children (91)	MIS-Adult (15), Kawasaki disease (9), Hemophagocytic lymphohistiocytosis(5), Hyperferritinemic syndrome(2), eosinophilic pulmonary vasculitis(1), inflammatory syndrome presenting as refractory status epilepticus(1)	Review (2), Meta-analysis (1) Pathogenesis (14) Study (2) Commentary (1)
Musculoskeletal (Annex 10)	16		Rhabdomyolysis (12), arthritis(4), myositis(3), ICU acquired muscle weakness(1)	Reviews (2)
Respiratory (Annex 11)	66		Pneumothorax(24), hemopneumotorax (1), pneumomediastinum(15), Pneumothorax & pneumomediastinum(7) pediatric croup (1), hemoptysis (1), bullous lung disease(1), hilar lymphadenopathy(1), silent hypoxia(1), happy hypoxia(1), platypnea-orthodeoxia(1), acute chest syndrome in children with sickle cell disease(1)	Reviews (1), Pathogenesis (10)
Ocular (Annex 12)	18		Uveo-retinitis (3), conjunctivitis(1), Bilateral visual loss due to stroke(1), episcleritis(1), bilateral macular bleed(1), ocular myasthenia gravis(1)	Reviews (5), Meta-analyses(2) Studies (3)

BODY SYSTEM	Total Articles	AESI (number articles) already on COVID-19 List	Entities (number articles) Not yet on the AESI list	General Articles
Endocrine (Annex 13)	43		Pancreatitis (19), Thyroiditis(8), adrenal injury(3), hyperglycemia(4), parotitis(3), orchitis(1), prostatic infarction(1), male sexual dysfunction as a late complication(1), myxedema coma(1),	Reviews (1) Studies (1)
Long-term complications including 'long haul' syndrome (Annex 14)	19		Post-COVID, non-post encephalitis Parkinsonism (1), early lung fibrosis(1), orthostatic cerebral hypoperfusion syndrome with small fiber neuropathy(1),	Reviews (6) Pathogenesis (7) Study (3)
<b>Miscellaneous other</b>				
Co-infection	53	HIV (15), hepatitis(4); other viral: influenza(4), EBV(2), CMV(2), HZ(2), Dengue(2), Enterovirus(1), Adenovirus(1), hMPV(1); bacterial: TB(5), bacterial sepsis(2), bacterial endocarditis(1), meningococcal meningitis(1), Mycoplasma pneumonia(1); fungal: Aspergillus sp(2), Candidiasis(1), Candida glabrata(1), Cryptococcus(1); parasitic: Filariasis(1), Strongyloides(1), Chagas disease(1); Mixed: Malaria/Dengue(1)		
Enhanced disease	8	Case report (4 recurrence/reinfection - no evidence for enhanced disease), Pathogenesis(2), review(2);		
Psychiatric	5	5 case reports or case series: Psychoses-case series (1), suicide attempt as presenting COVID symptom(1), sudden and persistent dysphonia(1), altered mental status and weakness(1), case reports of first psychiatric presentations during COVID19(1).		
Autoimmune	5	4 Case reports (2 new onset SLE, 1 ANCA vasculitis, 1 autoantibody (SSA/Ro) detected post COVID); 1 pathogenesis		
Mixed Clinical	55	<b>28 Neonatal/Pediatric cases:</b> 14 case reports, 4 studies, 8 reviews, 1 meta-analyses. <b>11 - Pregnancy focus:</b> 2 case reports, 7 studies, 1 review, 1 meta-analysis <b>2 - Adult clinical overviews:</b> 1 case report, 1 review of COVID in geriatric patients <b>14 - Outcomes/severity:</b> 4 descriptive studies of hospital cases (1 each USA, Spain, China, Western India); 2 meta-analyses (1 critical complications of COVID, 1 review of multi-organ dysfunction); 5 reviews – focus on extra-pulmonary manifestations; 2 studies (1 on COVID disease burden; 1 on prevalence and impact of hyponatremia in COVID cases); 1 case report of fatal outcome of a patient with common variable immunodeficiency.		
Pregnancy	152	<b>Publication type:</b> Reviews (25), Meta-analyses(6), Pathogenesis (6), Guidelines (1) Registry Studies (44), Case Reports (41), Commentary(2), Not classified(26)  <b>Publication Focus:</b> Maternal mortality (6), pregnancy/neonatal outcomes (74), vertical transmission (25), placenta (15), preeclampsia/eclampsia (4), breast milk (4), miscarriage(3), miscellaneous case reports of COVID complication in pregnancy (11: 2 myocarditis, 1 takotsubo, 2 coagulopathy, 1 encephalopathy, 1 acute liver injury, 1 pituitary apoplexy, 1 seizure, 1 thrombocytopenia, 1 report from Columbia – no specific complication).		
<b>Articles screened in for potential relevance to AESI Tools but not to the AESI list per se</b>				
Pathology	34	Autopsy studies (20)	Mortality (14)	
Risk Factors	450	Mortality (396), Severity (46), Mixed outcomes (8)		



BODY SYSTEM	Total Articles	AESI (number articles) already on COVID-19 List	Entities (number articles) Not yet on the AESI list	General Articles
Background rate	6	Premature births during lockdown in Denmark (1), cardiac arrest(2), STEMI(1), stroke(1), cardiovascular death rates in COVID19 low prevalence area(1)		

### 4.3 Evidence Related to Entities on the May 2020 COVID-19 and Prioritization for a Formal Brighton Case Definition

**4.3.1 Cardiovascular injury** (Annex 2 and the Cardiac tab in the excel spreadsheet 'COVID Update Jan\_Nov13\_2020\_Final').

Table 3 provides a summary of the total number of publications focused on COVID-19 associated cardiovascular injury that have been screened in as part of the landscape analyses covering January 1<sup>st</sup> – November 13<sup>th</sup>, 2020. It also provides a distribution by type of article. Myocarditis has the greatest number of publications, the majority of which are case reports along with 4 reviews and 1 meta-analysis. The next largest number was for cardiac injury which is itself a broad category and could include many of the other cardiac manifestations shown in the table. Most of the articles on cardiac injury focus on pathogenesis (22) and there have been many reviews (10) and meta-analyses (6). Arrhythmias are the next most frequent, most of which are case reports (24) but there also have been 7 reviews and one meta-analysis. Acute coronary syndrome and Takotsubo syndrome (i.e., stress cardiomyopathy) are next in frequency followed by acute heart failure/cardiogenic shock. A total of 46 broad focus articles have been published including 21 reviews and 5 meta-analyses. Full text review of this extensive literature was beyond the scope of this second quarterly update.

**TABLE 3. CARDIOVASCULAR INJURY PUBLICATIONS SINCE THE START OF THE COVID-19 PANDEMIC**

Publication type Focus / Topic (total)	Review	Meta-analysis	Pathogenesis	Guideline / Registry	Study	Case Report Or Series	Comment
<b>Myocarditis (99)</b>	4	1	2	1	6	77	8
<b>Cardiac Injury (81)</b>	10	6	22	2	18	9	14
<b>Arrhythmias (57)</b>	7	1	5	--	15	24	5
<b>Acute coronary syndromes (49)</b>	--	--	--	2	12	31	4
<b>Takotsubo cardiomyopathy (24)</b>	1	--	--	--	1	22	--
<b>Cardiac failure/shock (19)</b>	1	--	2	1	--	9	6
<b>General / Multiple entities (46)</b>	21	5	8	2	9	--	1
<b>Miscellaneous (8)</b>	--	--	--	--	--	8	--



#### 4.3.2 Haemorrhagic Disorder, including Disseminated Intravascular Coagulation (Annex 4 and the Hematologic tab in the excel spreadsheet 'COVID Update Jan\_Nov13\_2020\_Final').

From January 1 through November 13<sup>th</sup>, 2020 there have been 696 publications focused on hematologic manifestations of COVID-19. Of these 537 (77.2%) have been focused on thrombosis, thromboembolism, stroke and pulmonary embolus. There have been 99 articles focused on coagulopathy and many of these included thrombosis as well as hemorrhagic manifestations of COVID-19.

#### 4.3.3 Acute Liver Injury (see Annex 7 and the Liver Injury tab in the excel spreadsheet 'COVID Update Jan\_Nov13\_2020\_Final')

Since placing acute liver injury (ALI) on the May COVID-19 AESI list, an additional 12 reviews, 16 meta-analyses and 22 studies have been published summarizing the nature and extent of ALI and examining pathogenesis. Overall abnormal liver function tests are common among hospitalized COVID-19 patients. Any elevation of liver enzymes has been reported in 20-30% of inpatients. Mild abnormalities of liver function tests are usually transient and thought to be a nonspecific reaction to general inflammation. The meta-analysis by Ahmed included articles published to June 18 of 2020 whereas most others did not extend past March or April. Moreover, the Ahmed analysis only included studies with a pre-defined criterion for acute liver injury which was an elevation in transaminases  $\geq 3$  times the upper limit of normal. A total of 27 studies with 8817 patients were included and the prevalence of liver injury was 15.7% (9.5-23%). One of the articles included in the Ahmed meta-analysis was not recovered as part of the first or second quarterly update (Cai Q, J Hepatology 2020; 73:566-574; <https://doi.org/10.1016/j.jhep.2020.04.006>). A unique aspect of the Cai study is that they defined two patterns of abnormal liver function tests based on whether the picture was primarily hepatocellular (ALT and/or AST  $>3$  times upper normal limit), cholestatic (ALP or GGT  $>2$  times upper limit of normal) or mixed with elements of both. They then defined acute liver injury as: ALT and/or AST  $>3$  times upper limit of normal OR ALP, GGT and/or Total bilirubin  $>2$  times upper limit of normal. ALI was further classified as hepatocyte (Type 1) if the AST/ALT activity exceeded that of ALP/GGT; and as cholangiotype (Type 2) if AST/ALT activity was less than that of ALP/GGT. Their study included 417 patients with confirmed COVID-19 admitted to a single referral hospital in Shenzhen China. 76.3% had abnormal LFTs and 21.5% met the criterion for ALI during hospitalization. There was a significant link between those with type 1 ALI and severe COVID-19 (Odds Ratio 2.73; 95% Confidence Interval 1.19 - 6.3) especially if it was a mixed pattern (Odds Ratio 4.44; 95% Confidence Interval 1.93-10.23). In contrast Type 2 ALI was not significantly associated with COVID-19 severity. This was also the study that showed that ALI was associated with combination lopinavir/ritonavir therapy. There is no distinct COVID-19 liver pathology based on limited autopsy studies. Several mechanisms have been proposed for COVID-19 associated ALI including drug-toxicity (documented with the combination of Lopinavir-ritonavir), myositis which could also elevate liver enzymes, aggravation of liver injury among those with pre-existing viral hepatitis, viral binding to cholangiocytes leading to liver damage and direct damage to the liver. There is no consensus among the many published reviews and meta-analyses as to cause.

#### 4.3.4 Acute Kidney Injury (see Annex 8 and the Kidney Injury tab of the excel spreadsheet 'COVID Update Jan\_Nov13\_2020\_Final')

Acute kidney injury (AKI) is clearly associated with COVID-19 disease affecting over 20% of hospitalized COVID-19 patients and over 50% of those admitted to ICU (Nadim – multi-country expert consensus report of 25<sup>th</sup> Acute Disease Quality Initiative Workgroup). A large meta-analysis including 40 studies and 24,527 patients (Shao) showed that development of AKI is clearly associated with mortality: 63% if present versus 13% if not, with Odds Ratio for fatality if AKI present of 14.63 (95% Confidence Interval 9.94-2.51). Overall proteinuria has been documented in 44% of cases, hematuria in 27% and elevated serum creatinine in 14%. In infected individuals with no prior kidney disease, AKI onset is usually 7 to 10 days after admission, whereas it is much earlier, within a few

days of admission, among those with chronic kidney disease prior to infection. Early in the pandemic, evidence suggested that the kidney was a target of SARS-CoV-2 virus based on presence of ACE-2 receptors in the proximal tubules, reports of detection of the virus in urine by PCR and ultrastructure postmortem and biopsy studies claiming to visualize viral particles in the peritubular space and in endothelial cells of glomerular capillary loops. Since May 16 when the SPEAC COVID-19 AESI list, as adopted by the WHO-GACVS, was finalized, a growing body of new evidence, including 10 reviews, 11 meta-analyses and 36 studies, supports pre-renal mechanisms as the cause of AKI. Specifically, the dominant impact is ischemic acute tubular injury due to one or more of: hypoxia, cardiac injury and thrombosis. Four studies claiming to see virus-like particles in the kidney based on autopsy (Su, Farkash, Werion) or biopsy (Kissling) have been disputed by findings in 11 new studies (Diao, Larsen, Peleg, Rossi, Wu, Golmaj, Sharma, Kudose, Roufsse, Santoriello, Akilesh). Two studies demonstrated that SARS-CoV-2 has a tropism for the kidney (Puelles, Braun) but as pointed out by Parmar in an extensive review of the evidence to date, tropism does not equate with pathogenicity. More specifically, while kidney tubular cells have ACE-2 receptors, they lack the transmembrane protease, serine 2 (TMPRSS2), which is needed to facilitate viral entry into the cell.

There have been a few case reports of kidney-specific pathology in COVID-19 including: several reports of collapsing glomerulopathy which is seen in high-risk individuals with a specific variant of the APOL1 gene that is most prevalent in those of African ancestry (Sharma); 2 cases of ANCA-associated vasculitis with glomerulonephritis (Uppal) and 1 case of IgA vasculitis with nephritis – Henoch Schönlein Purpura (Suso).

#### 4.4 Entities Not Yet included on the COVID-19 AESI List

For the September 2020 quarterly update, 4 entities were flagged as possible candidates for addition to the COVID-19 AESI list. Each of these has been updated in this report. Since all citations are in the companion excel spreadsheet, the references are not added as citations for this document. However, they are presented in the appendices as noted below, which identify all relevant citations by review period (16May2020, Q1 review, Q2 review). The full citations can then be found in the excel spreadsheet 'COVID Update Jan\_Nov13\_2020\_Final'.

##### 4.4.1 Autoimmune hemolytic anemia (AIHA) (Hematologic system – see Annex 4 and the Hematologic tab of the excel spreadsheet 'COVID Update Jan\_Nov13\_2020\_Final')

- Prior to Aug 8<sup>th</sup>: Seven cases of AIHA were reported prior to May 2020 and an additional 5 from May to Aug 8<sup>th</sup>. Most had underlying conditions that could be associated with the development of AIHA including cancer. One case involved a previously healthy 13-year-old girl (Vega Hernandez P).
- Aug 8 – Nov 13, 2020: There was only a single case report and no other publications related to AIHA.

##### 4.4.2 Rhabdomyolysis Musculoskeletal system – see Annex 10 and the Musculoskeletal tab of the excel spreadsheet 'COVID Update Jan\_Nov13\_2020\_Final')

- Prior to Aug 8<sup>th</sup>: There were 2 cases reported prior to May 16<sup>th</sup> and an additional 11 cases from May 16<sup>th</sup> to Aug 8<sup>th</sup>. All were male, aged 16-88 years and most had comorbidities (type 2 diabetes, obesity, hypertension). In 10, rhabdomyolysis was the presenting complaint and 3 developed it during the course of hospitalization for COVID-19. Creatinine kinase elevation ranged from mild (1859 U/L) to massive (276,664 U/L). Six had associated acute kidney injury with 4 needing hemodialysis but all recovered.
- Aug 8<sup>th</sup> – Nov 13, 2020: An additional 19 case reports of rhabdomyolysis were published, bringing the total to 32 since the pandemic started. All together there have been 29 involving males and 3 females. Age has ranged from 15 to 88 years with a median of 48.5 years. Ten had no co-morbidities whereas 22 had one or more pre-existing conditions including: 9 hypertension, 5 obesity, 5 diabetes mellitus and 5 chronic kidney disease. Relative to the COVID-19 illness, 20 had concurrent rhabdomyolysis, 10

developed it after admission for COVID and 2 were admitted for rhabdomyolysis and the COVID-19 diagnosis was made after admission. There was not a clear link between severity of COVID-19 and of rhabdomyolysis. In 10, the rhabdomyolysis led to acute renal failure and dialysis was required. In 16 cases COVID-19 was severe with respiratory failure requiring ventilation. A fatal outcome occurred in 8 cases.

#### 4.4.3 Thyroiditis (Endocrine system - see Annex 13 and the Endocrine tab of the excel spreadsheet 'COVID Update Jan\_Nov13\_2020\_Final')

- Prior to August 8<sup>th</sup>: The first report of thyroiditis was found after May 2020 as part of the 1<sup>st</sup> quarterly update. There was a total of 5 case reports, 1 from Singapore and 4 from Italy. These were described in the 1<sup>st</sup> quarterly update. 1 case was Hashimoto's autoimmune thyroiditis involving a previously healthy man with onset 1 week after COVID-19 infection. The other four were all subacute thyroiditis involving women (18-69 years old) with onset 1 to 6 weeks after COVID-19. Muller compared thyroid function in 93 COVID positive patients and 101 pre-pandemic patients admitted to high intensity Italian ICUs in 2020 and 2019, respectively. Evidence of thyrotoxicosis was found in 15% of the COVID patients versus 1% of those admitted in 2019. Eight of the COVID patients were followed for several weeks post discharge and 2 were hypothyroid with features of autoimmune thyroiditis on scan.
- Aug 8 – Nov 13, 2020: Nine more cases of typical subacute thyroiditis were reported (7F/2M; age range 28-46 years). Most had mild COVID-19 illness managed at home; no severe cases but 1 admitted to hospital. Onset ranged from 9 days to 5 weeks after COVID-19 resolved. All responded quickly to oral prednisone or ibuprofen therapy; most were euthyroid within 6-10 weeks. Also, there was a single case of postpartum thyroiditis (Mizuno-Japan) 4.5 months following delivery and 9 days after discharge from hospital where she had spent 4 weeks for moderately severe COVID-19.

#### 4.4.3 Acute pancreatitis (previously Gastrointestinal system; now under Endocrine system - see Annex 13 and the Endocrine tab of the excel spreadsheet 'COVID Update Jan\_Nov13\_2020\_Final')

- Prior to August 8<sup>th</sup>: An early report from China (Wang F) noted that 17% of 52 COVID-19 patients had evidence of pancreatic injury, defined as any abnormality in amylase or lipase but did not comment on symptoms. In the 1<sup>st</sup> Quarter update, there were 14 case reports of acute pancreatitis, which was the presenting complaint for 5, concurrent with COVID19 infection in 2, onset after COVID-19 admission for 6 and couldn't be determined for 1. Known etiologic causes of pancreatitis (alcohol, gallstones, trauma, recent invasive procedures) were ruled out in most and all recovered. There was also a US study of 339 admissions for acute pancreatitis among whom 75 were tested for COVID (Dirweesh A). No other cause for pancreatitis was found among 57% of the 14 COVID confirmed cases versus only 2% of 61 COVID negative cases. Mortality was 21% and 2% respectively.
- Aug 8 – Nov 13, 2020: Two additional studies (Imandar, Akarsu) had similar findings to Dirweesh. Both compared acute pancreatitis among concurrently hospitalized COVID positive and negative cases during the pandemic. Imandar found that after ruling out known causes of pancreatitis, idiopathic cases were more frequent in COVID-19 positive (69%) than COVID-19 negative (21%) cases. In the Akarsu series, acute pancreatitis was found in 0 of 50 mild COVID-19 cases, 7.9% of 189 severe COVID-19 cases and 32.5% of 77 critical COVID-19 cases. Mortality was 32% of COVID-19 positive acute pancreatitis cases versus 8% of COVID-19 negative pancreatitis cases. There were an additional 22 new published case reports of pancreatitis associated with COVID-19.
- In total during the COVID-19 pandemic to November 13, there have been 36 case reports, 16 females and 20 males. Ages ranged from 7 to 76 years with a median of 38 years. In 14 cases there were no co-morbidities whereas 11 were obese, 8 had hypertension and 2 had diabetes mellitus. Several had more than one co-morbidity. Relative to the onset of COVID-19, 5 preceded it, 13

presented concurrently, 17 followed the COVID-19 presentation and 1 presented as pancreatitis and never developed typical COVID-19 symptoms but had a confirmed SARS-CoV-2 positive PCR. Two cases had a fatal outcome.

#### 4.4.4 **Pregnancy Outcomes:** Maternal, Fetal, Neonatal (see the Mixed clinical tab and the Pregnancy tab of the companion excel COVID Update Jan\_Nov13\_2020)

As per Table 2 there have been 152 new publications focused on various aspects of pregnancy outcomes from Aug 8 through Nov 13, 2020. As was the case in the September 2020 Quarterly update, the sheer volume of publications did not allow thorough review.

#### 4.4.5 **Chronic complications of COVID-19** (see Annex 14)

There is a growing understanding that COVID-19 complications extend beyond the acute illness. As shown in Table 2 there were 19 articles focusing on long term-complications published from August 8 to Nov 13, 2020. Long term pulmonary fibrosis has been the topic of some, but most are theoretical in nature focused on the potential for long-term neurologic complications such as parkinsonism. A single Egyptian study (Tolba) noted persisting symptoms for several months after recovering from COVID-19, with fatigue the most prominent. In their discussion they noted that similar findings occurred following SARS-CoV-1 outbreak. The term “Long-Haul syndrome” has been used to describe such cases where the predominant feature is clearly fatigue accompanied by a number of other general symptoms including depression, myalgia/arthritis, disordered sleep and so on. The current search strategy only identified the single Egyptian study and will need to be amended to focus on this entity.

### 4.4 Quarterly Review Workload

Completion of the December 2020 quarterly update required 10 hours for screening, 85.25 hours to read and summarize new citations and 27.75 hours to prepare and revise the deliverable.

## 5. Recommendations & discussion

The results of the second quarterly update for the COVID-19 AESI priority list have been presented above along with: a cumulative summary of publications since January focused on cardiovascular injury and coagulation disorders; as well as an overview of what has been seen since the start of the COVID-19 pandemic for acute liver injury, acute kidney injury, autoimmune hemolytic anemia, rhabdomyolysis, acute pancreatitis and subacute thyroiditis. Based on these results SPEAC has the following recommendations:

### 5.1 Regarding new AESI for the COVID-19 list

#### 5.1.1 Add the following entities to the AESI list: subacute thyroiditis, pancreatitis and rhabdomyolysis:

Subacute thyroiditis occurs predominantly as a post-infectious illness with onset several weeks after the acute COVID-19. In contrast pancreatitis and rhabdomyolysis are clearly part of acute COVID-19 illness, similar to acute cardiovascular, kidney and liver injuries. The mechanisms are unclear and while they could be considered part of the multi-organ dysfunction that is seen in COVID-19 it is also clearly the case that COVID-19 may present with features of either and in some cases not manifest the usual respiratory features of illness. Prior to prioritizing any of these to the list for new Brighton case definitions, a search for international standards will be made and adopted

if there are widely accepted case definitions. With the entities added to the AESI list, SPEAC will develop resources and tools related to each including background rates and risk factors, ICD-9 /10-CM and MedDRA codes.

**5.1.2** There is insufficient evidence to support the addition of acute hemolytic anemia to the AESI list.

## 5.2 AESI for COVID-19 and development of new Brighton case definitions

**5.2.1** Defer a decision related to acute cardiovascular injuries other than myocarditis/pericarditis until the case definition currently being developed is completed (expected by January 2021) in conjunction with further review of existing literature on the other entities.

**5.2.2** Proceed with development of a Brighton case definition for coagulation disorder involving bleeding and disseminated intravascular coagulation but align the prioritization with other CEPI target diseases for which this is an AESI (Lassa Fever, MERS, Rift Valley Fever).

**5.2.3** Acute Liver Injury (ALI): International consensus guidelines could not be found for acute liver injury. There are definitions for acute liver failure but that is rare in COVID-19. The meta-analysis by Ahmed and study of liver function tests in COVID-19 by Cai were presented in some detail in the results section above because they provide a basis for defining ALI used by many other authors publishing on ALI in COVID-19. Thus, it is proposed that the following definition of ALI be used:

- > 3-fold elevation above the upper normal limit for ALT or AST OR
- > 2-fold elevation above the upper normal limit for total serum bilirubin or GGT or ALP
- As done by Cai, measuring all 4 liver enzymes (ALT, AST, GGT, ALP) and total bilirubin will enable defining the pattern of injury as hepatocytic, cholangiocytic or mixed and further whether it is a type 1 ALI (ALT/AST > GGT/ALP) or Type 2 ALI (ALT/AST < GGT/ALP).

**5.2.4** Acute kidney injury (AKI): Several international guidelines exist and have been reviewed (Thomas ME, Blaine C, Dawnay A et al. The definition of acute kidney injury and its use in practice. *Kidney International* 2015; 87:62-73. Doi:10.1038/ki.2014.328). The Risk, Injury, Failure, Loss and End-stage renal disease (RIFLE) classification was developed in 2004 by the Acute Dialysis Quality Initiative Group. A modification was made by the Acute Kidney Injury Network (AKIN) in 2007 and then the two were merged in 2012 by the Kidney Disease Improving Global Outcomes (KDIGO) expert consensus group (see [www.kdigo.org](http://www.kdigo.org)). In the absence of a Brighton Case Definition, it is recommended to use the criteria for detecting AKI, as defined by KDIGO below:

- Increase in serum creatinine by  $\geq 0.3$  mg/dl ( $\geq 26.5$   $\mu\text{mol/l}$ ) within 48 hours; OR
- Increase in serum creatinine to  $\geq 1.5$  times baseline, which is known or presumed to have occurred within the prior 7 days OR
- Urine volume  $\leq 0.5$  ml/ kg/ hour for 6 hours

The Thomas review article also presents the modified pRIFLE criteria for defining AKI in children >1 month old. The article also discusses the relative merits and limitations of the KDIGO and other criteria.

## 5.3 Regarding a consolidation of the literature reviewed as part of the COVID-19 landscape analyses from January 1 through November 13, 2020

The appendices 2 through 14 provide a summary of the quantity, focus and publication type for all included citations. The full citations have been captured in the excel spreadsheet ‘COVID Update for Jan\_Nov13\_2020\_Final’ which is a companion to this deliverable.

## 5.4 Regarding the process to be followed for the next quarterly update of COVID-19

Reviewing of the literature is a time-consuming task. We recommend to:

- 5.4.1 Narrow the focus of the literature review to entities that need time to emerge specifically, pregnancy outcomes, manifestations of COVID-19 in children and the 'long haul COVID' and other chronic complications.
- 5.4.2 Conduct full text review of systematic reviews and meta-analyses already identified that focus on the diverse types of cardiovascular injury other than myocarditis and pericarditis in order to determine whether or not Brighton case definitions should be developed for one or more.

## 6 References

1. Global Advisory Committee on Vaccine Safety, 27-28 May 2020. WHO Weekly epidemiological record 2020; July 10. 28: 325-326. <http://www.who.int/wer>
2. COVID Update for Jan\_Nov13\_2020\_Final.xlsx (can be accessed via Developer's toolbox as well as the Brighton Collaboration website)

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# ANNEXES

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## Annex I

### Search Strategy for literature relevant to updates to the potential AESI list for covid-19 (used to retrieve articles from Aug 7 to Nov 13, 2020)

The only difference between this and the search strategy used for Quarter 1 updates since July 2020 was to exclude PMIDs from all previous searches, as a strategy to reduce the number of duplicates.

((("Coronavirus"[Mesh] OR "coronavirus"[ti] OR "nCoV"[ti] OR "COVID"[ti] OR "SARS-CoV-2"[ti]) AND English[lang] AND "2020/08/07 12.00"[MHDA]:"2020/01/01 15.00"[MHDA]) AND ("brain involvement"[ti] OR "neurological"[ti] OR "neurologic"[ti] OR "seizure"[ti] OR "seizures"[ti] OR "convulsion"[ti] OR "convulsions"[ti] OR "epilepsy"[ti] OR "status epilepticus"[ti] OR "leukoencephalopathy"[ti] OR "olfactory"[ti] OR "gustatory"[ti] OR "neuropathy"[ti] OR "paresthesia"[ti] OR "paraesthesia"[ti] OR "Miller Fisher"[ti] OR "smell"[ti] OR "taste"[ti] OR "nervous system"[ti] OR "stroke"[ti] OR "cerebrovascular"[ti] OR "myoclonus"[ti] OR Guillain\*[ti] OR "encephalitis"[ti] OR "encephalopathy"[ti] OR "encephalitic"[ti] OR "encephalomyelitis"[ti] OR "rhombencephalitis"[ti] OR "meningitis"[ti] OR "myelitis"[ti] OR "meningomyelitis"[ti] OR "meningoencephalitis"[ti] OR "anosmia"[ti] OR "hyposmia"[ti] OR "ageusia"[ti] OR "hypogeusia"[ti] OR "optic neuritis"[ti] OR "viral meningitis"[ti] OR "aseptic meningitis"[ti] OR "palsy"[ti] OR "cranial nerve"[ti] OR "dysphagia"[ti] OR "subarachnoid"[ti] OR "confusion"[ti] OR "confusional"[ti] OR "coma"[ti] OR "comatose"[ti] OR "unresponsive"[ti] OR "neuroinvasive"[ti] OR "neuroinvasion"[ti] OR "neurotropism"[ti] OR "neurotropic"[ti] OR "sensorineural hearing loss"[ti] OR "ataxia"[ti] OR "cerebellitis"[ti] OR "radiculitis"[ti] OR "neuritis"[ti] OR "polyneuritis"[ti] OR "polyneuropathy"[ti] OR "neuralgia"[ti] OR "weakness"[ti] OR "focal deficit"[ti]) OR ("inflammatory"[ti] OR "hyperinflammatory"[ti] OR "hyperinflammation"[ti] OR "hyper-inflammatory"[ti] OR "macrophage activation syndrome"[ti] OR "cytokine storm syndrome"[ti] OR "cytokine release syndrome"[ti] OR "kawasaki"[ti] OR "hemophagocytic lymphohistiocytosis"[ti] OR "haemophagocytic lymphohistiocytosis"[ti] OR "shock"[ti] OR "hyponatremia"[ti] OR "inflammation"[ti] OR "hyperferritinaemia"[ti] OR "hyperferritinemia"[ti] OR "hyperferritinaemic"[ti] OR "hyperferritinemic"[ti] OR "multisystem inflammatory syndrome"[ti] OR "inflammatory multisystem syndrome"[ti] OR "viral sepsis"[ti]) OR ("chilblain"[ti] OR "chilblains"[ti] OR "acral"[ti] OR "acroischemia"[ti] OR "urticaria"[ti] OR "urticarial"[ti] OR "rash"[ti] OR "rashes"[ti] OR "skin lesion"[ti] OR "skin lesions"[ti] OR "skin finding"[ti] OR "skin findings"[ti] OR "alopecia"[ti] OR "purpura"[ti] OR "purpuric"[ti] OR "vasculitis"[ti] OR "vasculitic"[ti] OR "angioedema"[ti] OR "Sweet's syndrome"[ti] OR "cutaneous"[ti] OR "Stevens-Johnson"[ti] OR "erythema multiforme"[ti] OR "pernio"[ti] OR "maculopapular"[ti] OR "varicella-like"[ti] OR "chickenpox-like"[ti] OR "papulovesicular"[ti] OR "exanthem"[ti] OR "exanthems"[ti] OR "exanthema"[ti] OR "exanthematous"[ti] OR "morbilliform"[ti] OR "erythema nodosum"[ti] OR "vesicular"[ti] OR "bullous"[ti] OR "bullae"[ti] OR "vesiculobullous"[ti] OR "livedoid"[ti] OR "livedo"[ti] OR "necrotic"[ti] OR "papule"[ti] OR "papules"[ti] OR "macule"[ti] OR "macules"[ti] OR "macular"[ti] OR "papular"[ti] OR "petechial"[ti] OR "petechiae"[ti] OR "gangrene"[ti] OR "erythroderma"[ti] OR "pustulosis"[ti] OR "pustular"[ti] OR "pustule"[ti] OR "pustules"[ti] OR "angioedema"[ti] OR "vesicle"[ti] OR "vesicles"[ti]) OR ("myocarditis"[ti] OR "cardiomyopathy"[ti] OR "infarction"[ti] OR "infarct"[ti] OR "infarcts"[ti] OR "cardiac arrest"[ti] OR "microangiopathy"[ti] OR "micro-angiopathy"[ti] OR "microvascular inflammation"[ti] OR "vascular inflammation"[ti] OR "cardiogenic"[ti] OR "cardiogenic shock"[ti] OR "right ventricular failure"[ti] OR "cor pulmonale"[ti] OR "aneurysm"[ti] OR "aneurysmal"[ti] OR "mediastinum"[ti] OR



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## Annex 2

### Cardiovascular System

Type of Reference	Review Period	Author	Country	Focus
1. Reviews	16May20	1. Akhmerov A	USA	COVID-19 and the heart
	16May20	2. Atri D	USA	COVID-19 for the cardiologist: current review
	16May20	3. Gupta AK	Multiple	Current perspectives on COVID-19 and CV disease; A white paper by JAHA editors
	16May20	4. Matsushita K	France	Impact of COVID-19 on the Cardiovascular System: a review
	16May20	5. Larson AS	USA	COVID-19 and Cerbro-Cardiovascular Systems: What do we know so far?
	16May20	6. Long B	USA	Cardiovascular complications of COVID-19
	16May20	7. Madjiid M	USA	Potential Effects of Coronaviruses on the cardiovascular system: Review
	16May20	8. Clerkin KJ	USA	COVID-19 and cardiovascular disease
	16May20	9. Bansal M	India	Cardiovascular disease and COVID-19
	16May20	10. Basu-Ray I	USA	Cardiac manifestations of COVID-19
	16May20	11. Kochi AN	Italy/Switz	Cardiac & arrhythmic complications in COVID-19
	16May20	12. Tan W	USA	The cardiovascular burden of COVID-19 (focus on congenital heart disease)
	16May20	13. Fried JA	USA	The variety of cardiovascular presentations of COVID-19
	16May20	14. Zhao M	China	Advances in relationship between coronavirus infection & cardiovascular diseases
	Q1 Update	16 new reviews	Multiple	For Q1 and Q2 updates see cardiac tab – COVID spreadsheet (subgroup 2=Review)
	Q2 update	14 new reviews	Multiple	
2. Meta-Analyses	16May20	1. Li JW	China/UK/Aus	Impact of COVID-19 on heart injury: systematic review and meta-analysis
	16May20	2. Lippi G	Italy/Spain/US	Cardiac troponin I in patients with COVID-19: Meta-analysis
	16May20	3. Krittanawong C	USA/China	COVID-19 & cardiovascular risk: meta-analysis
	Q1 update	4 New meta-analyses	Multiple	
	Q2 update	6 new meta-analyses	Multiple	For Q1/Q2 updates see cardiac tab – COVID spreadsheet (Subgroup 2=meta-analysis)

3. Pathogenesis / hypothesis	16May20	1. Cheng P	USA	Cardiovascular risks in COVID-19: Potential mechanisms and areas of uncertainty Arrhythmic risk and inflammation COVID-19 and inherited arrhythmia syndromes Hypoxia in acute cardiac injury of COVID-19. Lessons from pathological studies COVID-19, ACE2 and cardiovascular consequences Genetic susceptibility for COVID-19 associated sudden cardiac death in Afro-Americ. ACE2 expression in human heart: cause of post-pandemic wave of heart failure? SARS-CoV-2 and myocardial injury: Few answers, many questions. Pericyte vascular expression SARS-CoV-2 receptor ACE2 & microvascular inflammation For Q1/Q2 updates see cardiac tab – COVID spreadsheet (Subgroup 2=pathogenesis)
	16May20	2. Lazzerini PE	Italy/USA	
	16May20	3. Wu	Europe(7)	
	16May20	4. Nan J	---	
	16May20	5. South AM	USA	
	16May20	6. Giudicessi JR	USA	
	16May20	7. Thum T	Germany	
	16May20	8. Cremer PC	USA	
	16May20	9. He L	Sweden +multi	
	Q1 update	17 new publications	Multiple	
Q2 update	13 new publications	Multiple		
4. Guidelines or Registry	16May20	1. NICE	UK	COVID-19 rapid guideline: acute myocardial injury Recognizing COVID-19 related myocarditis: possible pathophysiology, Dx/Rx guideline Cardiovascular implications of the COVID-19 pandemic For Q1/Q2 updates see cardiac tab – COVID spreadsheet (Subgroup 2=guideline)
	16May20	2. Siripanthong B	UK/USA	
	16May20	3. Boukhris M	Global	
	Q1 update	3 guidelines/1registry	Multiple	
	Q2 update	1 new guideline	Multiple	
5. Studies	16May20	1. Zhou B	China	Clinical characteristic of myocardial injury in severe & very severe COVID-19 patients Suspected myocardial injury in patients with COVID-19 The ACE2 expression in human heart indicates new potential mechanism of injury Cardiovascular implications of fatal COVID-19 outcomes Analysis of heart injury lab parameters in 273 COVID-19 patients STEMI in patients with COVID-19: clinical and angiographic outcomes COVID-19 myocarditis and severity factors: an adult cohort study Characteristics_& clinical significance of myocardial injury in severe COVID-19 disease For Q1/Q2 updates see cardiac tab – COVID spreadsheet (Subgroup 2=study)
	16May20	2. Deng Q	China	
	16May20	3. Chen L	China	
	16May20	4. Guo T	China-Wuhan	
	16May20	5. Han H	China-Wuhan	
	16May20	6. Stefanini GG	Italy	
	16May20	7. Ma L	China	
	16May20	8. Shi S	China	
	Q1 update	32 new publications	Multiple	
	Q2 update	21 new publications	Multiple	
6. Case Reports/Series				
Arrhythmias	16May20	1. Kir D	USA	AV block in COVID-19 Atrial arrhythmias in a patient presenting with COVID-19 For Q1/Q2 updates see cardiac tab-COVID spreadsheet (subgroup1=arrhythmia; subgroup2=case reports)
	16May20	2. Seecheran R	Trinidad-Toba	
	Q1 update	6 more case reports	Multiple	
	Q2 update	16 more case reports	Multiple	

Cardiac injury / Endotheliitis	16May20 Q1 update Q2 update	1. Varga Z 4 more case reports 4 more case reports	Switz Multiple Multiple	Endothelial cell infection and endotheliitis in COVID-19 For Q1/Q2 updates see cardiac tab-COVID spreadsheet (subgroup1=injury or endothelial dysfunction; subgroup2=case reports)
Myocarditis	16 May20 16May20 16May20 16May20 16May20 16May20 16May20 16May20 16May20 16May20 Q1 update Q2 update	1. Farina A 2. Chen C 3. Cizgici H 4. Doyen D 5. Inciardi RM 6. Hu 7. Sala S 8. Zeng JH 9. Hua A 10. Luetkens JA 11. Craver R 31 more case reports 35 more case reports	Italy China Turkey France Italy China Italy China China Germany USA Multiple Multiple	SARS-CoV-2 detection in pericardial fluid of patient with cardiac tamponade SARS-CoV-2: A potential etiology of fulminant myocarditis COVID-19 myopericarditis Myocarditis in a patient with COVID-19 Cardiac involvement in a patient with COVID-19 Fulminant myocarditis saved with glucocorticoid and human Ig Acute myocarditis presenting as a reverse Tako-Tsubo syndrome in SARS-CoV2 First case of COVID-19 complicated with fulminant myocarditis Life threatening cardiac tamponade complicating myo-pericarditis in COVID-19 Diffuse myocardial inflammation in COVID19 detected by Cardiac MRI Fatal eosinophilic myocarditis in a healthy 17yr old male For Q1/Q2 updates see cardiac tab-COVID spreadsheet (subgroup1=myocarditis; subgroup2=case reports)
Heart Failure and Cardiogenic Shock	16May20 16May20 Q1 update Q2 update	1. Tavazzi G 2. Creel-Bulos C 5 more case reports 2 more case reports	Italy USA Multiple Multiple	Myocardial localization of Coronavirus in COVID-19 cardiogenic shock Cor Pulmonale in Critically Ill Patients For Q1/Q2 updates see cardiac tab-COVID spreadsheet (subgroup1=Heart failure; subgroup2=case reports)
Stress cardio-myopathy (Takotsubo Síndrome)	16May20 16May20 16May20 16May20 Q1 update Q2 update	1. Minhas AS 2. Jussela A 3. Roca E 4. Nguyen D 6 more case reports 12 more case reports	USA USA Italy Belgium Multiple Multiple	Takostubo syndrome in setting of COVID-19 COVID-19 related cardiomyopathy in pregnancy Takotsubo syndrome associated with COVID-19 A case of Takotsubo cardiomyopathy with COVID-19 For Q1/Q2 updates see cardiac tab-COVID spreadsheet (subgroup1=Takotsubo; subgroup2=case reports)
Acute Coronary Syndrome (ACS)	16May20 16May20 16May20 16May20 Q1 update Q2 update	1. Fernandez Gasso 2. Dominguez Erquic 3. Kumar K 4. Salido-tahoces L 3 more case reports 1 more case reports	Spain Spain USA Spain Multiple Multiple	Multivessel spontaneous coronary artery dissection in COVID19 Multivessel coronary thrombosis in patient with COVID-19 pneumonia Spontaneous coronary arter dissection in 48 yr old – presenting complaint of COVID Unusual presentation of ACS (plaque destabilization) in SARS-CoV2 infection For Q1/Q2 updates see cardiac tab-COVID spreadsheet (subgroup 1 = ACS; subgroup 2 = case reports)

STEMI	16May 20 Q1 update Q2 update	1. Bangalore S 13 more case reports 3 more case reports	USA Multiple Multiple	ST-Segment elevation in patients with COVID19 – case series. For Q1/Q2 updates see cardiac tab-COVID spreadsheet (subgroup 1 = STEMI; subgroup 2 = case reports)
MI / sudden death	Q1 update Q2 update	4 more case reports 2 more case reports	Multiple Multiple	For Q1/Q2 updates see cardiac tab-COVID spreadsheet (subgroup1=MI or sudden death; subgroup2=case reports)
Other	16May20 Q1 update Q1 update Q1 update Q1 update Q2 update Q2 update Q2 update	1. Tape 2. Birlutiu V 3. Powezka K 4. Shih M 5. Roncati L 6. Oda R 7. Kishore R 8. Balata D	USA Romania UK USA Italy Japan India Sweden	<p>Syncope as a presenting feature of COVID-19</p> <p>SARS-CoV-2 infection associated with micturition syncope</p> <p>Ruptured popliteal artery aneurysm complicated with ARDS</p> <p>Ruptured Abdominal aortic aneurysm in a patient with COVID-19</p> <p>Type 3 hypersensitivity in COVID-19 vasculitis</p> <p>Case of adult large vessel vasculitis after SARS-CoV-2 infection</p> <p>Dilated cardiomyopathy in a child with COVID-19</p> <p>Non-bacterial thrombotic endocarditis: a presentation of COVID19</p>

## Annex 3

## Neurologic System

Type of Reference	Review Period	Author	Country	Focus
1. Reviews	16May20	1. Asadi-Pooya AA	Iran, USA	CNS manifestations of COVID-19: a systematic review
	16May20	2. Troyer EA	USA	Neuropsychiatric sequelae of COVID-19 – potential immunologic mechanisms
	16May20	3. Wu Y	China	CNS involvement after infection with COVID19 and other coronaviruses
	16May20	4. Li H	China	Involvement of the Nervous System in SARS-CoV-2
	16May20	5. Daou BJ	USA	Neurologic implications of COVID19: lessons learned from prior epidemics
	16May20	6. Liu K	China	Neurologic manifestations of SARS-CoV-2
	16May20	7. Finsterer J	Austria	Update on the neurology of COVID-19
	Q1 update Q2 update	54 new reviews 59 new reviews	Multiple Multiple	For Q1/Q2 updates see COVID spreadsheet, neurologic tab (subgroup2=review)
2. Meta-Analyses	16May20	1. Tong JY	USA	Prevalence of olfactory & gustatory dysfunction in COVID19: SystRev/Meta-Analysis
	16May20	2. Aziz	USA	Taste Changes (Dysgeusia) in COVID-19: Systematic review/Meta-analysis.
	Q1 update	8 new meta-analyses	Multiple	For Q1/Q2 updates see COVID spreadsheet, neurologic tab (subgroup2=review)
	Q2 update	8 new meta-analyses	Multiple	
3. Pathogenesis / hypothesis	16May20	1. Baig AM	Pakistan	Tissue Distribution, Host-Virus interaction & proposed neurotropic mechanisms
	16May20	2. De Felice FG	Brazil,Canada	SARS-CoV-2 and the CNS
	16May20	3. Gandhi S	India	Is collapse of brain respiratory centre responsible for COVID resp breakdown
	16May20	4. Li Z	China, UK	Potential routes of SARS-CoV-2 neuroinvasion from periphery to the brain
	16May20	5. Paniz-Mondolfi P	USA	CNS involvement by SARS-CoV-2
	16May20	6. Steardo L	Italy, UK	Neuroinfection may contribute to pathophysiology/clinical manifestations
	16May20	7. Vaira LA	Multiple	Potential pathogenesis of ageusia and anosmia
	Q1 update Q2 update	23 new publications 45 new publications	Multiple	For Q1/Q2 updates see COVID spreadsheet, neurologic tab (subgroup2=pathogenesis)



				For Q1/Q2 updates: see COVID spreadsheet, neurologic tab (subgroup2=pathogenesis)
4. Guidelines / Registries	16May20 16May20 16May20 Q1 update Q2 update	1. Lao wP 2. Needham EJ 3. Soler ZM 4 new publications 1 new publication	USA UK, USA USA Multiple Multiple	Anosmia, hyposmia & dysgeusia as indicators for positive SARS-CoV-2 infection Neurological implications of COVID-19 infections A primer on viral-associated olfactory loss in the era of COVID19 For Q1/Q2 updates: see COVID spreadsheet, neurologic tab (subgroup2=Guideline)
5. Studies	16May20 16May20 16May20 16May20 16May20 16May20 16May20 16May20 16May20 16May20 16May20 16May20 16May20 16May20 16May20 16May20 16May20 16May20 16May20 Q1 update Q2 update	1. Kandemirli SG 2. Beltran-Corbellini 3. Giacomelli A 4. Hopkins C 5. Hopkins C 6. Jitaroon K 7. Klopfenstein T 8. Luers JC 9. Mao L 10. Moein ST 11. Spinato G 12. Yan CH 13. De Maria A 14. Lee Y 15. Lu L 16. Vaira LA 17. Kaye R 80 new studies 81 new studies	Turkey Spain Italy UK UK Thailand, USA France Germany China Iran, USA Italy, UK USA Italy Korea China Italy Multiple Multiple	Brain MRI findings in ICU patients with COVID-19 Acute-onset smell&taste disorders: pilot multicenter PCR based case-ctl study Self-reported olfactory & taste disorders in SARS-CoV-2: cross-sectional study Presentation of new anosmia during COVID-19 pandemic Early recovery following new onset anosmia: observational cohort study Evaluation of Incidence of other cranial neuropathies in patients with anosmia Features of anosmia in COVID-19 Olfactory & gustatory dysfunction in COVID-19 Neurologic manifestations of hospitalized patients with COVID-19 Smell dysfunction: a biomarker for COVID-19 Alterations in smell or taste in mildly symptomatic outpatients with SARS-CoV-2 Association of chemosensory dysfunction and COVID19 in patients with ILI High prevalence of olfactory and taste disorder during ARS-CoV-2 in outpatients Prevalence & Duration of acute loss of smell or Taste in COVID-19 patients New onset acute symptomatic seizure and risk factors in COVID-19 Validation of a self-administered olfactory & gustatory test Anosmia reporting tool: initial findings For Q1/Q2 updates: see COVID spreadsheet, neurologic tab (subgroup2=Study)
6. Case Reports/Series				
Encephalitis	16May20 16May20 16May20 16May20	1. Duong L 2. Huang YH 3. Moriguchi T 4. Ye M	USA USA Japan China	Meningoencephalitis without respiratory failure in young female patient Update to Duong L(1 above): Detection of SARS-CoV-2 in CSF by PCR A first case of meningitis / encephalitis associated with SARS-CoV-2 Encephalitis as a clinical manifestation of COVID-19

	16May20 Q1 update Q2 update	5. Bernard-Valnet R 26 new case reports 22 new case reports	Switzerland Multiple Multiple	Meningo-encephalitis concomitant to SARS-CoV-2 For Q1/Q2 updates: see COVID spreadsheet, neurologic tab (subgroup 1=encephalitis; subgroup2=case reports)
Encephalopathy	Q1 update Q2 update	21 new case reports 26 new case reports	Multiple Multiple	For Q1/Q2 updates: see COVID spreadsheet, neurologic tab (subgroup 1=encephalopathy; subgroup2=case reports)
Generalized convulsion	Q1 update Q2 update	12 new case reports 8 new case reports	Multiple Multiple	For Q1/Q2 updates: see COVID spreadsheet, neurologic tab (subgroup 1=seizure; subgroup2=case reports)
GBS	16May20	1. Scheidl E	Germany	GBS during SARS-CoV-2: case report and review of recent literature
	16May20	2. Alberti P	Italy	GBS related to COVID-19 infection
	16May20	3. Camedssanche JP	France	COVID-19 may induce GBS
	16May20	4. Gutierrez-Ortiz C	Spain	Miller Fisher syndrome and polyneuritis cranialis in COVID-19 (2 cases)
	16May20	5. El Otmani H	Morocco	COVID-19 and GBS: more than a coincidence
	16May20	6. Sedaghat Z	Iran	GBS associated with COVID19 infection: a case report
	16May20	7. Toscano G	Italy	GBS associated with SARS-CoV-2 – 5 cases reported
	16May20	8. Virani A	USA	GBS associated with SARS-CoV-2 infection
	16May20	9. Zhao H	China	GBS associated with SARS-CoV-2 infection: causality or coincidence
	16May20	10. Coen M	Switzerland	Fatal GBS after infection with SARS-CoV-2
	16May20	11. Ottoviani D	Italy	GBS in COVID-19: a case report
	16May20	12. Pfefferkorn	Germany	Acute polyradiculoneuritis with locked-in syndrome in a patient with COVID-19
	Q1 update Q2 update	34 new case reports 22 new case reports	Multiple Multiple	For Q1/Q2 updates: see COVID spreadsheet, neurologic tab (subgroup 1=GBS; subgroup2=case reports)
ADEM	Q1 update Q2 update	7 new case reports 3 new case reports	Multiple Multiple	For Q1/Q2 updates: see COVID spreadsheet, neurologic tab (subgroup 1=ADEM; subgroup2=case reports)
Myelitis	Q1 update Q2 update	4 new case reports 12 new case reports	Multiple Multiple	For Q1/Q2 updates: see COVID spreadsheet, neurologic tab (subgroup 1=myelitis; subgroup2=case reports)
CNS bleed	16May20	1. Sharifi-Razavi A	Iran	COVID-19 and intracerebral haemorrhage: causative or coincidental
	16May20	2. Poyiadii N	USA	COVID-19 associated Acute Hemorrhagic Necrotizing Encephalopathy
	16May20	3. Muhammad S	Germany	Severe brain haemorrhage and concomitant COVID-19
	Q1 update Q2 update	12 new case reports 11 new case reports	Multiple Multiple	For Q1/Q2 updates: see COVID spreadsheet, neurologic tab (subgroup 1=CNS bleed; subgroup2=case reports)

Anosmia/ Ageusia	16May20 16May20 16May20 16May20 16May20 Q1 update Q2 update	1. Gane SB 2. Galougahi MK 3. Oilarves-Carrerro 4. Gilani S 5. Hjelmesaeth J 15 new case reports 11 new case reports	UK Iran Spain Iran Norway Multiple Multiple	Isolated sudden onset anosmia in COVID-19 infection: A novel syndrome? Olfactory Bulb MRI in SARS-CoV2 induced anosmia: the first report Anosmia in a healthcare worker with COVID-19 in Madrid Spain COVID-19 and anosmia in Tehran, Iran Loss of smell or taste as the only symptom of COVID-19 For Q1/Q2 updates: see COVID spreadsheet, neurologic tab (subgroup 1=smell/taste; subgroup2=case reports)
Other Cranial Nerve abnormalities	16May20 16May20 Q1 update Q2 update	1. Dinkin M 2. Kaya Y 8 new case reports 17 new case reports	USA Turkey Multiple Multiple	COVID-19 infection presenting with ophthalmoparesis from cranial nerve palsy Transient cortical blindness in COVID-19 pneumonia For Q1/Q2 updates: see COVID spreadsheet, neurologic tab (subgroup 1=cranial nerve-other; subgroup2=case reports)
Peripheral neuropathy	16May20 Q2 update	Abdelnour L Denes E	UK France	COVID-19 infection presenting as a motor peripheral neuropathy Temporal+Spatial concomitance of exantema and dysesthesia in pt with COVID-19
Meningitis	Q1 update Q2 update Q2 update Q2 update Q2 update	Cebrian J Naz S Yousefi K Khodamoradi Z De Oliveira FAA	Spain Pakistan Iran Iran Brazil	Headache and impaired consciousness level associated with SARS-CoV-2 in CSF Meningitis as an Initial Presentation of COVID-19: A Case Report Viral meningitis associated with covid-19 in a 9-year-old child COVID-19 meningitis with positive cerebrospinal fluid PCR Headache and pleocytosis in CSF associated with COVID-19
Myoclonus	Q1 update Q2 update Q2 update Q2 update Q2 update Q2 update Q2 update Q2 update Q2 update	Rabano-Suarez Schellekens Borroni B Anand P Dijkstra F Muccioli L Ros-Castella V Shah PB Sanguinetti S	Spain Netherlands Italy USA Belgium Italy Spain India USA	Generalized myoclonus in COVID-19 Reversible Myoclonus-Ataxia as a Postinfectious Manifestation of COVID-19 Diaphragmatic myoclonus due to SARS-CoV-2 infection Myoclonus in Patients With Coronavirus Disease 2019: A Multicenter Case Series Myoclonus and cerebellar ataxia following Coronavirus Disease 2019 (COVID-19) Subcortical myoclonus in COVID-19: comprehensive evaluation of a patient Post-hypoxic myoclonus after COVID-19 infection recovery Opsoclonus myoclonus ataxia syndrome (OMAS) in the setting of COVID-19 infection Opsoclonus Myoclonus Ataxia Syndrome Related to COVID-19
SIADH	16May20 Q1 update Q1 update	Yousaf Z Habib MB Ho KS	Qatar Qatar USA	COVID-19 associated SIADH: a clue in the times of pandemic Acute symptomatic hyponatremia in setting of SIADH SIADH as the initial presentation of COVID-19
CNS Vasculitis	Q1 update Q1 update	Hanafi R Pinto AA	France UK	COVID-19 Neurologic Complication with CNS Vasculitis-Like Pattern. CNS inflammatory vasculopathy with anti-myelin oligodendrocyte glycoprotein

	Q1 update Q2 update Q2 update Q2 update	Brun G De Sousa G Vaschetto R Chia KX	France Brazil Italy UK	White matter & globus pallidum lesions: Demyelination or small-vessel vasculitis? Vasculitis-related stroke as a presenting feature CNS vasculitis in a COVID-19 patient with pneumonia Possible affective cognitive cerebellar syndrome with CNS vasculopathy and stroke
Other	16May20 Q1 update Q1 update Q1 update Q1 update Q1 update Q1 update Q1 update Q1 update Q2 update Q2 update Q2 update Q2 update Q2 update Q2 update	Zanin L Noro F Chaumont H Coolen T Diezma-Marten Vitale JA Allard N Eshak N Dorgalaleh A Saleh AO Cunha P Sia J Tony AA Klein S	Italy Brazil France Belgium Spain Italy France USA Iran France Qatar Canada Egypt USA	SARS-CoV-2 can induce brain and spine demyelinating lesions Benign intracranial hypertension: A case report Mixed central and peripheral nervous system disorders Early postmortem brain MRI findings in COVID-19 non-survivors. Tremor and ataxia in COVID-19. Is disruption of sleep quality a consequence of severe Covid-19 infection? Acute hypothermia in Covid 19 Dysautonomia in a Critically ill COVID-19 Patient Persistent hiccups in a patient with mild congenital factor V deficiency Urinary Retention and Severe Hyponatremia Movement disorders as a new neurological clinical picture in severe SARS-CoV-2 Dizziness can be an early sole clinical manifestation for COVID-19 infection COVID-19-associated sleep disorders: A case report COVID 19 Presenting with Tremors and Gait Disturbance

## Annex 4

## Hematologic System

Type of Reference	Review Period	Author	Country	Focus
1. Reviews	16May20 Q1 update Q2 update	1. Giannis D 26 new reviews 39 new reviews	USA + more Multiple Multiple	Coagulation disorders in coronavirus infected patients (COVID/SARS/MERS) For Q1/Q2 update see COVID spreadsheet, Hematologic tab (Subgroup2=Review)
2. Meta-Analyses	16May20 16May20 Q1 update Q2 update	1. Lippi G 2. Xiong M 6 new meta-analyses 13 new meta-analyses	Italy China Multiple Multiple	Thrombocytopenia Changes in blood coagulation For Q1/Q2 update see COVID spreadsheet, Hematologic tab (Subgroup2=Meta-analysis)
3. Pathogenesis / hypothesis	16May20 16May20 Q1 update Q2 update	1. Gavrilaki E 2. Xu P 38 new publications 31 new publications	Greece/US China Multiple Multiple	COVID and thrombotic microangiopathy Mechanism of thrombocytopenia in COVID19 patients For Q1/Q2 update see COVID spreadsheet, Hematologic tab (Subgroup2=pathogenesis)
4. Guidelines	16May20 16May20 16May20 Q1 update Q2 update	1. Bikdeli B 2. Castelli R 3. Zhai Z No new publications No new publications	Multiple Italy China	COVID19 thromboembolic disease: implications_prevention_therapy_follow-up Abnormal hemostatic parameters/risk of TE Prevention/treatment of TE: Consensus statement
5. Studies	16May20 16May20 16May20 16May20 16May20 16May20 16May20 16May20	1. Cui S 2. Fogarty H 3. Klok FA 4. Han H 5. Helms J 6. Llitjos JF 7. Lodigiani C 8. MiddeldorpS	China Ireland Holland China France France Italy Holland	Prevalence of venous Thromboembolism Coagulopathy in Caucasian patients Incidence of thrombotic complications in critically ill ICU patients Prominent changes in blood coagulation Multicentre prospective cohort: High risk of thrombosis High incidence of venous thromboembolic events in anticoagulated patients Venous & arterial thromboembolic complications Incidence of venous thromboembolism in hospitalized

	16May20	9. Panigada M	Italy	Hypercoagulability of COVID19 patients in ICU
	16May20	10. Ranucci M	ItalyUSA(2)	Procoagulant pattern of patients with ARDS
	16May20	11. Spiezia L	Italy	Severe hypercoagulability in ICU pts with respiratory failure
	16May20	12. Tang N	China	Anticoagulant therapy associated with decreased mortality
	16May20	13. Yang X	China	Thrombocytopenia association with mortality
	16May20	14. Zou Y	China	Analysis of coagulation parameters
	16May20	15. Thomas W	UK	Thrombotic complications of patients admitted to ICU with COVID-19
	16May20	16. Wichmann D	Germany	Autopsy findings and venous thromboembolism in patients with COVID-19
	16May20	17. Yaghi S	USA	SARS-CoV-2 and Stroke in New York healthcare system
	16May20	18. Tejada Meza H	Spain	Ischaemic stroke in the time of COVID-19
	Q1 update	42 new studies	Multiple	
	Q2 update	104 new studies	Multiple	For Q1/Q2 update see COVID spreadsheet, Hematologic tab (Subgroup2=Study)
<b>6. Case Reports/Series</b>				
Coagulopathy /Microvascular Injury	16May20	1. Zhang Y	China	Coagulopathy and antiphospholipid antibodies
	16May20	2. Magro C	USA	Complement associated microvascular injury and thrombosis
	Q1 update	7 new case reports	Multiple	For Q1/Q2 update see COVID spreadsheet, Hematologic tab (Subgroup 1 =
	Q2 update	10 new case reports	Multiple	coagulopathy; Subgroup2=case reports)
Stroke	16May20	1. Avula A	USA	COVID-19 presenting as stroke (4 cases)
	16May20	2. Beyrouti R	UK	Characteristics of ischemic stroke (6 cases)
	16May20	3. Oxley TJ	USA	Large-vessel stroke as presenting feature in the young
	16May20	4. Viguier A	France	Acute ischemic stroke complicating common carotid artery thrombosis
	16May20	5. Bruggemann R	Netherlands	Arterial and venous thromboembolic disease in a patient with COVID-19
	16May20	6. Hughes C	UK	Cerebral venous sinus thrombosis as a presentation of COVID-19
	16May20	7. Zhou B	China	Acute Cerebral Infarction and deep vein thrombosis concomitant with COVID-19
	16May20	8. Tunc A	Turkey	Coexistence of COVID-19 & acute ischemic stroke – 4 cases
	16May20	9. Zayet S	France	Acute cerebral stroke with multiple infarctions & COVID-19
	16May20	10. Gunasekaran K	USA	Stroke in a young COVID-19 patient
	16May20	11. Morassi M	Italy	Stroke in patients with SARS-CoV-2 infection: case series (6)
	Q1 update	40 new case reports	Multiple	For Q1/Q2 update see COVID spreadsheet, Hematologic tab (Subgroup 1 = stroke;
Q2 update	56 new case reports	Multiple	Subgroup2=case reports)	

Pulmonary Embolus (PE)	16May20 16May20 16May20 Q1 update Q2 update	1. Fabre O 2. Poissy J 3. Polat V 32 new case reports 26 new case reports	France France Turkey Multiple Multiple	Severe acute proximal PE Increased prevalence of PE in COVID19 patients Sudden death due to acute PE in a young woman with COVID-19 For Q1/Q2 update see COVID spreadsheet, Hematologic tab (Subgroup 1 = PE; Subgroup2=case reports)
Other Thrombotic Disease	16May20 16May20 16May20 16May20 16May20 16May20 Q1 update Q2 update	1. Griffin DO 2. Beccara A 3. Besutti G 4. Poggiali E 5. Schultz K 6. Bellosta R 44 new case reports 71 new case reports	USA Italy Italy Italy USA Italy Multiple Multiple	Arterial thromboembolic complications in prophylaxed low risk patients Arterial Mesenteric Thrombosis as a complication of SARS-CoV-2 Abdominal Visceral Infarction in 3 patients with COVID-19 Deep Vein Thrombosis and Pulmonary Embolism: 2 complications of COVID-19 Digital Ischemia in COVID-19 patients Acute limb ischemia in patients with COVID-19 pneumonia (20 cases) For Q1/Q2 update see COVID spreadsheet, Hematologic tab (Subgroup 1 = thrombosis OR TE OR ischemia; Subgroup2=case reports)
Thrombocytopenia / ITP	16May20 16May20 Q1 update Q2 update	1. Ahmed MZ 2. Zulfiqar AA 20 new case reports 15 new case reports	UK France Multiple Multiple	Thrombocytopenia as an initial manifestation (3 cases) Idiopathic thrombocytopenic purpura (ITP) For Q1/Q2 update see COVID spreadsheet, Hematologic tab (Subgroup 1 = tcp; Subgroup2=case reports)
Autoimmune hemolytic anemia	16May20 16May20 Q1 update Q2 update	1. Lopez C 2. Lazarian G 5 new case reports 1 new case report	USA France Multiple	Simultaneous onset of COVID 19 and AHA AHA associated with COVID19 For Q1/Q2 update see COVID spreadsheet, Hematologic tab (Subgroup 1 = AHA, Subgroup2=case reports)
Other	16May20 16May20 Q2 update Q2 update	1. Mitra A 2. Li G 3. Jensen CE 4. Faisal H	USA China USA USA	Leukoerythroblastic reaction in patient with COVID19 Covid-19 presenting with hematochezia Cold agglutinin síndrome as a complication of COVID-19 in two cases Unexplained methemoglobinemia in COVID-19: a case report

## Annex 5

## Dermatologic System

Type of Reference	Review Period	Author	Country	Focus
1. Reviews	16May20	1. Wollina U	Germany	Cutaneous signs in COVID-19 patients
	16May20	2. Sachdeva M	Italy	Cutaneous manifestations of COVID-19: report of 3 cases and review of literature
	16May20	3. Tang K	China	Cutaneous manifestations of COVID-19: a brief review
	16May20	4. Almutairi N	USA	COVID-19 with Dermatologic Manifestations & implications: an unfolding Conundrum
	16May20	5. Young S	USA	Skin manifestations of COVID-19
	Q1 update	6. Elmas AF	Turkey	Cutaneous manifestations of COVID19
	Q1 update	7. Jia JL	USA	Cutaneous manifestations of COVID19-preliminary review
	Q1 update	8. Marzano AV	Italy	Cutaneous manifestations in patients with COVID19 – preliminary review
	Q1 update	9. Gisondi P	Italy	Cutaneous manifestations of SARS-CoV-2: clinical update
	Q1 update	10. Kaya G	Switz	Clinical&Histopathological Features_Potential Pathologic mechanisms
	Q1 update	11. Matar S	France	Cutaneous manifestations in COVID19: French experience and syst review
	Q1 update	12. Potekaev NN	Russia	Clinical characteristics of dermatologic manifestations; Case series & review
	Q1 update	13. Zhao Q	China	COVID19 and cutaneous manifestations: systematic review
	Q1 update	14. Criado PR	Brazil	Lessons from dermatology about inflammatory responses in COVID19
	Q1 update	15. SeirafianpourF	Iran	Cutaneous manifestations and considerations in COVID19: Syst review
	Q1 update	16. Rahimi MA	Iran	Comprehensive review of Cutaneous manifestations
	Q1 update	17. Ladha MA	Canada	Approach to Chilblains during COVID19 pandemic
	Q1 update	18. Massey PR	USA	Going viral: a brief history of chilblain-like lesions (“COVID toes”
	Q1 update	19. Gottlieb M	USA	Dermatologic manifestations and complications of COVID19
	Q2 update	20. Balestri R	Italy	Do we have serologic evidences that chilblain-like lesions are related to SARS-CoV2
	Q2 update	21. Almutairi A	SaudArab	Dermatologic manifestations: systematic review
	Q2 update	22. DaneshgaranG	USA	Cutaneous manifestations of COVID19: evidenc-based review
	Q2 update	23. Li H	China	Cutaneous, skin histopathologic manifestations and relationship to COVID19
	Q2 update	24. MarrahaF	Morocco	Review of Dermatologic manifestations of COVID19



	Q2 update	25. Nieto-BenitoLM	Spain	Histopathologic findings in COVID19 induced cutaneous lesions: clinicopathology
	Q2 update	26. AlgaadiSA	SaudiArab	Urticaria and COVID19: review
	Q2 update	27. AndinaD	Global	Skin manifstations of COVID19 in children: Part 1 (focus on chilblain like lesions)
	Q2 update	28. Andina D	Global	Skin manifstations of COVID19 in children: Part 2
	Q2 update	29. Garduno-SotoM	Mexico	Dermatologic aspects of SARS-CoV-2: mechanisms and manifestations
	Q2 update	30. MirzaFN	USA	Dermatologic manifestations of COVID019: comprehensive syst review
	Q2 update	31. MawhirtSL	USA	Cutaneous manifestations in adult pts with COVID19
	Q2 update	32. SinghH	USA	Cutaneous manifestations of COVID19: systematic review
2. Meta-Analyses	Q2 update	1. Bandhala R	India	Trend of cutaneous lesions during COVID19 pandemic: meta-anal & syst review
3. Pathogenesis / hypothesis	Q1 update	1. Criado PR	Brazil	Are cutaneous manifestations during or due to COVID-19 frequent or not?
	Q2 update	2. Criado PR	Brazil	Potential interactions of SARSCoV2 with human cell receptors in the skin
	Q2 update	3. Allegra A	Italy	Urticaria and coronavirus infection: a lesson from the pandemic
	Q2 update	4. Magro C	USA	Doced SARSCoV2 proteins within cutaneous/subcutaneous microvasculature
4. Guidelines	Q1 update	1. Ortega-QuijanoD	Spain	Algorithm for the classification of COVID19 rashes
5. Studies	16May20	1. Galvan Casas C	Spain	Classification of the cutaneous manifestations of COVID-19
	16May20	2. Recalcati S	Italy	Cutaneous manifestations in COVID-19: a first perspective
	16May20	3. Bouaziz	France	Vascular skin symptoms in COVID-19: French observational study
	16May20	4. Young S	USA	Skin manifestations of COVID19
	Q1 update	5. Docampo-Simon	Spain	Are chilblain-like acral skin lesions really indicative of COVID19
	Q1 update	6. ElHachem M	Italy	Clinical, histopath and lab study of 19 Italian children with chilblain-like lesions
	Q1 update	7. Reymundo A	Spain	Clinical and histologic characterization of late macpap eruptions in COVID19
	Q1 update	8. Freeman EE	USA	Pernio-like skin lesions in COVID19: 318pts from 8 countries
	Q1 update	9. Hughes M	UK	Furter evidence that chilblains are a cutaneous manifestation of COVID19
	Q1 update	10. Kanitakis J	France	Chilblain-like acral lesions: histology, immunofluorescence, immunohistochemistry
	Q1 update	11. Mahieu R	France	No antibody respons in acral cutaneous manifestations associated with COVID19
	Q1 update	12. Piccolo V	Italy	Acral findings during COVID19
	Q1 update	13. SaenzAguirre A	Spain	Novel outbreak of acral lesions in times of COVID19: 74 cases – Spain
	Q1 update	14. Battesti G	France	New insights in COVID19 associated chilblains: comparison with chilblain LE
	Q1 update	15. Colmenero I	Spain	SARS-CV2 endothelial infection causes chilblains: histopah/IHC/ultrastructure-7child.
	Q1 update	16. ColonnaC	Italy	Outbreak of chilblain like acral lesions in Milan

Q1 update	17. Fernandez-Nieto	Spain	Characterization of acute acral skin lesions in non-hsp pts – case series 132 pts
Q1 update	18. Hubiche T	France	Negative SARS-CoV2 PCR in patients with chilblain-like lesions
Q1 update	19. LeCleach L	France	Most chilblains observed during COVid19 outbreak occur in PCR/serology neg
Q1 update	20. Lesort C	France	COVID19 and outbreak of chilblains: related?
Q1 update	21. Navarro L	Spain	Dermoscopy features of COVID19 related chilblains in children and adolescents
Q1 update	22. Rizzoli L	Italy	Chilblain-like lesions during COVID-19 pandemic: a serological study on a case series.
Q1 update	23. Rouanet J	France	Outbreak of chilblain-like lesions not directly related with SARS-CoV-2 infection.
Q1 update	24. Hebert V	France	Lack of association: chilblains&SARS-CoV-2: histological and serological findings
Q1 update	25. Bitar C	USA	Cutaneous manifestations of hospitalized COVID19: biopsy & in situ hybridization
Q2 update	26. Magro C	USA	Diff pathophysiologies in COVID-19 perniosis & thrombotic retiform purpura
Q2 update	27. Denina M	Italy	All that glisters is not COVID: low SARS-CoV-2 seroconversion in ped Chilblain-like
Q2 update	28. Ko CJ	USA	Anti-SARS-CoV-2 S protein&RNA staining in pernioitic lesions
Q2 update	29. Stavert R	USA	SARS-CoV-2 antibodies in 24 patients with chilblains-like lesions
Q2 update	30. Occidental M	USA	Dermatologic Spectrum in COVID-19 Severely Ill Patients - A Series of Four Cases
Q2 update	31. Baeck M	Belgium	Chilblains and COVID-19: further evidence against a causal association
Q2 update	32. Roses-Gilbert P	Spain	Acral lesions in ped popn: case series (36) from a single hospital in Spain
Q2 update	33. Piccolo V	Italy	Dermoscopy of chilblain-like lesions: A multicenter study on 10 patients
Q2 update	34. Docampo-Simon	Spain	No SARS-CoV-2 antibody response in 25 patients with pseudo-chilblains
Q2 update	35. Feito-Rodriquez	Spain	Chilblain-like lesions & covid-19: a prospective observational Spanish study
Q2 update	36. Fabbrocini	Italy	New dermoscopic pattern for Chilblain-COVID-like skin lesion in the adolescent
Q2 update	37. Diociaiuti	Italy	Meaning of SARS-CoV-2 IgA Abs in ped pts with chilblain-like lesions
Q2 update	38. Kluger N	Finland	Why are chilblains underreported in Nordic countries
Q2 update	39. Fertitta L	France	Immunological & virological profile of children with chilblain-like lesions
Q2 update	40. Gomez-Fernandez	Spain	High prevalence of cryofibrinogenemia in patients with chilblains
Q2 update	41. Sohier P	France	Histopathological features of Chilblain-like lesions
Q2 update	42. Caselli D	Italy	No evidence of SARS-CoV-2 by PCR/serology in children with pseudo-chilblain
Q2 update	43. DeGiorgi V	China/Italy	Cutaneous manifestations in COVID-19: A prospective study from China and Italy
Q2 update	44. Guarneri C	Italy	Diversity of clinical appearance of cutaneous manifestations in COVID-19
Q2 update	45. Rubio0Muniz CA	Spain	Dermatological manifestations in COVID-19. Clinical&histopathology – 34 cases
Q2 update	46. Ruggiero G	Italy	Reply to: "acute acro-ischemic lesions in non-hsp pts (132 case series)
Q2 update	47. Freeman EE	USA	Spectrum of COVID-19 dermatologic manifestations: Intl registry(716pts/31countries)
Q2 update	48. Askin O	Turkey	Cutaneous manifestations in hospitalized patients diagnosed as COVID-19.

	Q2 update	49. Gionotti R	Italy	Similar Cutaneous Histopath Patterns: COVID-19-pos&COVID-19 High-risk Pts
	Q2 update	50. Perez-Suarez B	Spain	Skin findings in the COVID-19 pandemic in the Region of Murcia
	Q2 update	51. Rerknimitr P	Thailand	Skin manifestations in COVID-19: The tropics experience
	Q2 update	52. Avancini J	Brazil	Absence of specific cutaneous manifestations of SARS-Cov-2 in a Brazil ref center
	Q2 update	53. MendezMaestro I	Spain	Skin manifestations in COVID-19: a cross-sectional study in a tertiary hospital
	Q2 update	54. Nuno-Gonzalez A	Spain	Mucocutaneous_oral_palmoplantar findings in 666 Spanish pts with COVID-19
	Q2 update	55. Punyaratabandhu	Thailand	Cutaneous eruption in COVID-19-infected patients in Thailand
	Q2 update	56. Miot HA	Brazil	Self-reported skin manifestations in 1,429 Brazilian COVID-19 patients
	Q2 update	57. Strom MA	USA	Cutaneous findings in critically-ill patients with COVID-19: case series(15)
	Q2 update	58. Giavedoni P	Spain	Skin Manifestations in COVID-19: Prevalence & Relationship with Disease Severity
	Q2 update	59. Freeman EE	USA	Timing of PCR/Ab Testing in Pts with COVID-19 associated skin manifestations
	Q2 update	60. Dursun R	Turkey	Clinics of HHV-6 infection in COVID-19 pandemic: Pityriasis rosea & Kawasaki disease
	Q2 update	61. Duong TA	France	Did Whatsapp(®) reveal a new cutaneous COVID-19 manifestation?
	Q2 update	62. Herrero-Moyano	Spain	A clinicopath study of 8 pts with COVID-19 pneumonia & late-onset exanthema
	Q2 update	63. Catalia A	Spain	Maculopap eruptions associated to COVID-19: a subanalysis of COVID-Piel study
	Q2 update	64. Pangti R	India	COVID19 Recognizable vascular skin changes uncommon in pts with skin-of-color
<b>6. Case Reports/Series</b>				
Rash – general or multiple forms	16May20	1. Najarian DJ	USA	Morbiliform exanthema associated with COVID-19
	16May20	2. Gianotti R	Italy	Cutaneous clinicopathological findings in 3 COVID-19 positive patients
	Q1 update	3. Anunziata MC	Italy	Cutaneous involvement during COVID19 pandemic
	Q1 update	4. GoldustM	China	Fever with Rash in COVID19: viral exanthema or secondary lesions
	Q1 update	5. Ho WYB	Singapore	Two cases of cutaneous eruptions due to COVID19 in Singapore
	Q1 update	6. Amatore F	France	SARS-CoV2 infection presenting as a febrile rash
	Q1 update	7. Jimenez-Cauhe J	Spain	Enanthem in patients with COVID19 and skin rash
	Q1 update	8. Rossi E	Italy	Acute macpap eruption in a COVID19 patient
	Q1 update	9. Patel N	UK	Polymorphic cutaneous manifestations of COVID19 infection in a single host
	Q1 update	10. Mizutani Y	Japan	Late onset cutaneous manifestations in a patient with severe COVID19
	Q1 update	11. Avellana Moreno	Romania	Cutaneous manifestation of COVID 19 in images: a case report
	Q2 update	12. Tatu AL	Spain	Familial clustering of COVID19 skin manifestations
	Q1 update	13. Bursal Duramaz	Turkey	3 Case presentations of Pediatric COVID with rash
	Q1 update	14. Klimach A	UK	Rash as a presenting complaint in a child with COVID19
	Q1 update	15. Olisova OY	Russia	Cutaneous manifestations in COVID19: a skin rash in a child

	Q1 update Q2 update Q2 update Q2 update Q2 update Q2 update Q2 update	16. Estabanez A 17. Aragao MT 18. Oksum Solak E 19. Redondo-Sendino 20. Kulkarni RB 21. Farabi B 22. Serafini A	Spain Brazil Turkey Spain USA Turkey Italy	Cutaneous manifestations in COVID19 COVID19 presenting as an exanthematic disease: case report COVID19 accompanies by maculopapular rash Skin manifestations associated with COVID19 Morbilliform rash: an uncommon herald of SARS CoV2 Isolated maculopapular eruption Itchy erythematous papular skin rash as a possible early sign of COVID19
Chilblain like lesions	16May20 16May20 16May20 16May20 16May20 16May20 16May20 Q1 update Q2 update	1. Locatelli AG 2. Andina D 3. Lopez-Robles J 4. Suarez-Valle A 5. Alramthan A 6. Garcia-Lara G 7. Piccolo V 8. Landa N 16 more case reports 13 more case reports	Italy Spain Spain Spain Middle East Spain Italy Spain Multiple Multiple	Histologic features of long lasting chilblain-like lesions in a pediatric COVID-19 patient Chilblains in children in the setting of COVID19 pandemic Chilblain-like lesions: case series of 41 patients during COVID19 pandemic Acro-ischemia in hospitalized COVID-19 patients COVID19 presenting with chilblain – like disease Chilblain-like lesions in pediatric dermatologic outpatients Chilblain-like lesions during COVID19 epidemic: preliminary stud on 63 patients Chilblain-like lesions on feet and hands during COVID-19 pandemic See literature spreadsheet, dermatologic tab See literature spreadsheet, dermatologic tab
Livedo +/-or purpura	16May20 Q1 update Q1 update Q1 update Q1 update Q1 update Q1 update Q1 update Q1 update Q1 update Q2 update Q2 update Q2 update Q2 update Q2 update	1. Conforti C 2. Bosch-Amate X 3. Novara E 4. Verheyden M 5. Kappel C 6. Wollina U 7. Llamas-Velasco 8. Droesch C 9. Karaca Z 10. Larrondo J 11. Trellu LT 12. Khalil S 13. Martino GP 14. Rotman JA 15. Wang JS	Italy Spain Italy Belgium Canada Germany Madrid USA Turkey Chile Switz USA Italy USA USA	COVID-Mask: an atypical livedoid manifestation of COVID-19 Retiform purpura as a dermatologic sign of COVID19 coagulopathy Severe acute dried gangrene in COVID19 – Case Report Relapsing symmetric livedo reticularis in a patient with COVID19 A case of possible Fournier’s gangrene associated with proning in COVID19 ARDS Schamberg-like purpuric eruptions and tonsillitis in mild COVID19 Thrombotic occlusive vasculopathy in skin biopsy from a livedoid lesion Livedoid and purpuric skin eruptions associated with coagulopathy A unilateral purpuric rash in a patient with COVID19 infection Papular-purpuric exanthem in a COVID19 patient Livedo reticularis as a presenting sign of SARS-CoV-2 infection COVID fingers: another severe vascular manifestation Concomitant calciphylaxis and COVID19 associated thrombotic retiform purpura Digital gangrene as a sign of catastrophic COVID19 related microangiopathy Large sacral/buttocks ulcerations in the setting of coagulopathy

	Q2 update Q2 update Q2 update Q2 update Q2 update Q2 update Q2 update Q2 update	16. Young S 17. Garcia-Gil MF 18. Tusheva I 19. Zinder R 20. Shehi E 21. Karagounis TK 22. Beaupre R 23. Heald M	USA Spain Macedonia USA USA USA USA USA	Livedo reticularis and acrocyanosis as late manifestations of COVID19 Unilateral livedo reticularis in COVID19 patient – case with fatal outcome COVID-19 wounds: unusual lower extremity bullae Microthrombi on skin biopsy in COVID19 patient Acrofacial purpura and necrotic ulcerations in COVID19 Mixed purpuric and maculopapular lesions in COVID 19 – Case Report\ Mixed purpuric and maculopapular lesions in a COVID 19 patient Skin manifestations of COVID19 resembling acute limb ischemia
Petechial rash	16May20	1. Diaz-Guimaraens	Spain	Petechial skin rash associated with SARS-CoV2
Vesiculo-bullous varicella-like	16May20 16May20 16May20 16May20 Q1 update Q1 update Q1 update Q1 update Q2 update Q2 update	1. Marzano AV 2. Martin Carreras 3. Genovese G 4. Fernandez-Nieto 5. Mahe A 6. Aghazadeh 7. Dadras MS 8. Goudarzi S 9. Soares CD 10. Boix-Vilanova J	Italy Spain Italy Spain France Iran Iran Iran Brazil Spain	Varicella like exanthema as a specific COVID19 associated skin manifestation: 22 cases Oral vesiculobullous lesions associated with SARS-CoV-2 infection Varicella-like exanthema associated with COVID-19 in an 8 year old girl Clinical and histological characterization of vesicular COVID-19 rashes Histology of skin lesions establishes that COVID vesicular rash is not varicella like Oral vesicles and acral erythema Probable atypical skin manifestation of COVID19 infection (necrotic ‘spider bite’ like) Cystic painful lesion in a case with positive SARS-CoV2 Oral vesiculobullous lesions as an early sign: detection of SARS-CoV-2 spike protein Grover-like skin eruption: another cutaneous manifestation in COVID19
Pustulosis / erythema multiforme like	16May20 16May20 16May20 Q1 update Q1 update Q1 update Q2 update Q2 update Q2 update Q2 update	1. Robustelli Test 2. Janah H 3. Jimenez-Cauhe J 4. Torello A 5. Gargiulo L 6. Labe P 7. Ayatollahi A 8. SanchezVelazquez 9. Reguero-DelCura 10. Hartmann M	Italy Morocco Spain Spain Italy France Iran Spain Spain Germany	Acute generalized exanthematous pustulosis with erythema multiforme-like lesions Atypical erythema multiforme palmar plaques lesions due to SARS-CoV-2 Erythema multiforme-like eruption in patients with COVID-19: clinical/histological Erythema multiforme-like lesions in children and COVID19 Fatal case of COVID19 presenting with erythema multiforme like eruption & fever Erythema multiforme and Kawasaki disease associated with COVID19 in children Late onset AGEP like skin pustular eruption following COVID19 Erythema multiforme in the context of COVID19 Onset of Erythema multiforme like lesions with COVID symptom recurrence COVID19 rash – erythema multiforme like
Urticaria / angioedema	16May20 16May20	1. Naziroglu T 2. Rodriguez-Jimen	Turkey Spain	COVID-19 pneumonia presenting with acute urticarial Urticaria-like lesions in COVID19 are not really urticaria: case with clinicopath

	16May20 Q1 update Q1 update Q1 update Q1 update Q1 update Q1 update Q1 update Q1 update Q1 update Q1 update Q1 update Q1 update Q1 update Q1 update Q2 update Q2 update Q2 update Q2 update	3. Gunawan C 4. Cepeda-Valdes R 5. Diotallevi F 6. Falkenhain-Lopez 7. Najafzadeh M 8. Azmy V 9. Henry D 10. Hassan K 11. Sousa Gonzales C 12. Lockey RF 13. Proietti I 14. Van Damme C 15. Proietti I 16. Adelino R 17. Elhag SA 18. Grewal E 19. Rotulo GA	Indonesia Mexico Italy Spain UK USA France UK Portugal USA Italy Belgium Spain UAR USA Italy Italy	Urticarial eruption in COVID-19: a case report Family cluster of urticarial rash Skin involvement in SARS-CoV2 infections – case series SARS-CoV-2 and acute urticaria Urticaria (angioedema) and COVID19 infection Idiopathic nonhistaminergic acquired angioedema in a patient with COVID19 Urticarial eruption in COVID19 infection Urticaria and angioedema as a prodromal cutaneous manifestation of COVID19 Erythematous papular rash: dermatologic feature of COVID19 COVID19 associated urticaria with angioedema in a morbidly obese male Polymorphic eruption of pregnancy as a possible COVID 19 manifestations Urticaria in an infant with SARS-CoV2 positivity Acute urticaria with pyrexia as first manifestation of COVID19 infection Acute urticaria with angioedema in the setting of COVID19 Angioedema and urticaria in a COVID19 patient: case report and review of literature Angioedema, ACE inhibitor and COVID19 Giant urticaria and acral peelin in a child with COVID19
Vasculitic	16May20 Q1 update Q1 update Q1 update Q1 update Q1 update Q1 update Q1 update Q1 update Q1 update Q1 update Q2 update Q2 update Q2 update Q2 update	1. Castelnovo L 2. De Perosanz-Lobo 3. Dominguez-Santas 4. Mayor-Ibarguren 5. Ordieres-Ortega L 6. Papa A 7. Taskin B 8. Allez M 9. Caputo V 10. Negrini S 11. Suter P 12. Sipfle DON 13. Tahir A 14. Adekiigbe R 15. Camprodon G	Italy Spain Spain Spain Spain Italy Turkey France Italy Italy Switz USA Dubai USA Spain	Symmetric cutaneous vasculitis in COVID-19 pneumonia Urticarial vasculitis in COVID19 infection: vasculopathy related symptom? Cutaneous small-vessel vasculitis associated with COVID19 Cutaneous small vessel vasculitis secondary to COVID19 Atypical erythema nodosum in a patient with COVID19 pneumonia Painful cutaneous vasculitis in a SARS-CoV-2 IgG positive child COVID 19 presenting with Atypical Sweets syndrome COVID19 related IgA vasculitis Generalized purpuc eruption with histopath of leucocytoclastic vasculitis Unusual case of bullous hemorrhagic vasculitis Erythema nodosum as a cutaneous manifestations of COVID19 Erythema nodosum-like rash in a COVID19 patient. Widespread cutaneous small vessel vasculitis secondary to COVID19 Hispanic man with cutaneous vasculitis lesions and gangrene of toes Leukocytoclastic vasculitis with positive SARS-CoV2 PCR in skin biopsy

	Q2 update	16. Kosters K	Germany	Cutaneous vasculitis in COVID19
	Q2 update	17. Tammaro A	Italy	Cutaneous endothelial dysfunction and complement deposition in COVID19
Alopecia	Q1 update	1. Wambier CG	USA	Androgenetic alopecia and hospital outcomes in COVID19: Gabrin sign
	Q2 update	2. Sgubbi P	Italy	Alopecia areata in a patient with SARS-CoV-2 infection
Other	16May20	1. Joob B	Thailand	COVID-19 can present with a rash and be mistaken for Dengue
	Q1 update	2. De Medeiros VLS	Brazil	Follow-up of skin lesions during evolution of COVID19
	Q1 update	3. Krajewski PK	Poland	Cutaneous hyperesthesia: novel manifestation of COVID 19
	Q1 update	4. Putra BE	Indonesia	Viral exanthem with “spins and needles sensation” on extremities
	Q1 update	5. Tehranchinia Z	Iran	Lichenoid eruptions with interface dermatitis and necrotic subepidermal blister
	Q1 update	6. Skroza N	Italy	Late onset widespread skin rash: viral or multidrug
	Q1 update	7. Dertlioglu SB	Turkey	Skin manifestations in COVID 19: 5 Case Reports
	Q2 update	8. Farouk	Egypt	Cutaneous manifestations of COVID 19
	Q1 update	9. Mendez-Flores S	Mexico	COVID19 and nail manifestations: be on the lookout for the red half-moon nail sign
	Q2 update	10. Ng SM	UK	Prolonged skin manifestations 4 wks after COVID recovery in a child(pityriasis?)
	Q2 update	11. Altayeb A	UK	2 cases of skin manifestations prior to the onset of COVID respiratory symptoms
	Q2 update	12. Martin Enguix D	Spain	Pityriasis rosea Gibert type rash in asymptomatic COVID+ case
	Q2 update	13. Alpalhao M	Portugal	Seborrheic dermatitis in COVID19: a case report
	Q2 update	14. Tammaro A	Italy	Severe palmar hyperkeratosis and hematochezia in COVID19
	Q2 update	15. Glick LR	USA	Unilateral laterothoracic exanthem in association with COVID19
	Q2 update	16. Danarti R	Indonesia	Follicular eruption as a cutaneous manifestation in COVID19
	Q2 update	17. Brin C	France	An isolated peculiar Gianotti-Crosti rash in the course of a COVID19 episode



## Annex 6

## Gastrointestinal System (for Liver see Annex 7; for Pancreatitis see Annex 13)

Type of Reference	Review Period	Author	Country	Focus
1. Reviews	May16/20	1. Tian Y	China	GI features in COVID-19 and the possibility of faecal transmission
	May16/20	2. Lee IC	China	GI and liver manifestations in patients with COVID-19
	May16/20	3. Patel KP	China/USA	Gastrointestinal, hepatobiliary and pancreatic manifestations of COVID-19
	Q1 update	4. Cha MH	Taiwan	GI and hepatic manifestations of COVID-19: a comprehensive review
	Q1 update	5. D'Amico F	China	Diarrhea with COVID19: Pathogenesis, epidemiology, prevention, mgmt
	Q2 update	6. Amorin Dos Santos	Brazil	Oral manifestations in COVID-19: a living systematic review
2. Meta-Analyses	May16/20	1. Cheung KS	China	GI manifestations of COVID-19 & fecal virus load
	Q1 update	2. Mao R	CHina	Manifestations and prognosis of GI & liver involvement
	Q1 update	3. Kumar VCS	USA	Novelty in the gut: a syst rev and meta-anal of GI manifestations of COVID-19
	Q1 update	4. Rokkas T	Greece	GI involvement in COVID-19: syst review and meta-analysis
	Q1 update	5. Tariq R	USA	Prevalence and mortality fo COVID-19 patients with GI symptoms
3. Pathogenesis / hypothesis	May16/20	1. Liang W	China	Diarrhoea may be underestimated: a missing link in COVID-19
	Q1 update	2. Kopel J	USA	Clinical insights into the GI manifestations of COVID-19
	Q2 update	3. Galanopoulos M	Greece	COVID-19 pandemic: pathophysiology and manifestations from the GI tract
4. Guidelines				
5. Studies	May 16/20	1. Jin X	China	Epidemiologic, clinical, virologic characteristics of 74 cases with GI symptoms
	May16/20	2. Lin L	China	GI symptoms of 95 cases
	May16/20	3. Wei XS	China	Diarrhea is associated with prolonged symptoms and viral carriage
	May16/20	4. Hajifathalian K	USA	GI and hepatic manifestations of COVID-19 in large Ney York cohort
	Q1 update	5. Kaafarani HMA	USA	GI complications in critically ill patients with COVID-19
	Q1 update	6. Ferm S	USA	Analysis of GI and Hepatic Manifestations: 892 patients in Queens NY
	Q2 update	7. Laszkowska M	USA	Course/outcomes of COVID-19 among hospitalized patients with GI symp/signs
	Q2 update	8. El Moheb M	USA	GI complications in critically ill patients with and without COVID-19
	Q2 update	9. Elmunzer BJ	USA	Digestive manifestations in patients hospitalized with COVID-19



6. Case Reports/Series				
Hematochezia	May16/20	1. Guotao L 2. Li G	China China	SARS-CoV-2 presenting with hematochezia SARS-CoV-2 infection presenting with hematochezia
Enteritis/ Colitis	Q1 update	1. Sattar T	USA	Three cases of COVID-19 disease with colonic manifestations
	Q1 update	2. Amarpurkar AD	India	Haemorrhagic enteritis and COVID-19: causality or coincidence
	Q1 update	3. Carnevale S	Italy	Direct endothelial damage & vasculitis due to SARS-CoV-2 in small bowel
	Q1 update	4. Carvalho A	USA	COVID GI infection causing hemorrhagic colitis
	Q1 update	5. Chan KH	USA	COVID-19 and ischemic colitis: an under-recognized complication
	Q1 update	6. Rehman M	USA	Neutropenic enterocolitis & rapid spontaneous resolution of portal venous gas
	Q2 update	7. Gonzalez Lazaro P	Spain	Ischemic colitis and short bowel disease due to COVID-19
	Q2 update	8. Brunet E	Spain	Ileitis as the exclusive manifestation of COVID-19
	Q2 update	9. Paul T	Qatar	Ischemic colitis in severe COVID-19 pneumonia
	Q2 update	10. Jaijakul S	USA	Colitis as a sole presentation of SARS-CoV-2
Ischemia	Q1 update	1. Farina D	Italy	Bowel ischemia in a suspected COVID-19 patient
	Q1 update	2. Ignat M	France	Small bowel ischemia and SARS-CoV2 infection: underdiagnosed
	Q1 update	3. Norsa L	Italy	Intestinal ischemia in the COVID-19 era
	Q1 update	4. Mitchell JM	USA	Ischemic enteritis secondary to superior mesenteric artery thrombosis
	Q1 update	5. Norsa L	Italy	Poor outcome of intestinal ischemic manifestations of COVID-19
	Q1 update	6. Bruni A	Italy	Histopathologic findings in COVID with ischemic gangrenous cholecystitis
	Q1 update	7. English WJ	UK	Coagulopathy and mesenteric ischaemia in severe COVID
	Q1 update	8. Ofosu A	USA	Portal vein thrombosis in a patient with COVID-19
	Q1 update	9. Cheung S	USA	Superior mesenteric artery thrombosis and acute intestinal ischemia
	Q2 update	10. Low SW	USA	Gastric ischemia and portal vein thrombosis in a COVID-19 patient
	Q2 update	11. Khesrani LS	Algeria	Intestinal ischemia secondary to COVID-19
	Q2 update	12. Sehhat S	Iran	Acute mesenteric ischemia in a patient with COVID-19
	Q2 update	13. Thuluva SK	India	29 year old male from India with isolated superior mesenteric vein thrombosis
	Q2 update	14. Singh B	USA	Acute intestinal ischemia in a patient with COVID-19 infection
	Q2 update	15. Chiu CY	USA	COVID-19 related ischemic bowel disease
	Q2 update	16. Almeida Vargas A	Spain	Severe colon ischemia in patients with severe COVID-19
Acute abdomen	Q1 update	1. De nardi P	Italy	Bowel perforation in a COVID19 patient: case report
	Q1 update	2. Cabrero-HernandezM	Spain	SARS-CoV-2 infection in children with suspected acute abdomen

	Q1 update Q1 update	3. Alsuwailem AB 4. Ahmed AOE	Saudi Arabia Qatar	Complicated appendicitis in a pediatric patient with COVID-19 COVID-19 masquerading as an acute surgical abdomen
Cholecystitis	Q1 update Q2 update Q2 update	1. Ying M 2. Mattone E 3. Cirillo B	China Italy Italy	COVID19 with acute cholecystitis: case report Acute acalculous cholecystitis in a COVID-19 patient Acalculous hemorrhagic cholecystitis
Oral lesions	Q1 update Q1 update Q2 update Q2 update Q2 update	1. Ansari R 2. Kahraman FC 3. Riad A 4. Riad A 5. Riad A	Iran Turkey Czech Czech Czech	Oral cavity lesions as a manifestation of COVID-19 Mucosal involvement in a COVID-19 positive patient Manifestation of oral mucositis in COVID-19 patients: case series Angular cheilitis of COVID-19 patients: case series and literatura review Tongue ulcers associated with SARS-CoV-2 infection: case series
Other	Q1 update Q2 update Q2 update Q2 update Q2 update Q2 update	1. Ekbatani MS 2. Ibrahim YS 3. Moazzam Z 4. Mobayen M 5. Karki S 6. Bolia R	Iran Qatar Pakistan Iran Nepal India	Atypical and novel presentations of COVID-19: 3 children Paralytic ileus: potential extrapulmonary manifestation of severe COVID-19 Intussusception in an infant as a manifestation of COVID-19 Presentation of spontaneous splenic ruptura in a COVID-19 patient Spontaneous hemoperitoneum in COVID-19 patient Recognising the gastrointestinal manifestations of pediatric COVID-19

## Annex 7

## Liver

Type of Reference	Review Period	Author	Country	Focus
1. Reviews	May 16/20	1. Li J	China	Characteristics & Mechanism of Liver injury in COVID-19
	May 16/20	2. Lee IC	Taiwan	GI & Liver manifestations in COVID-19
	May 16/20	3. Xu L	China	Liver injury during highly pathogenic human coronavirus infections
	May 16/20	4. Zhang C	China	Liver injury in COVID-19: management and challenges
	Q1 update	5. Alqahtani SA	Saudi Arabia	Liver injury in COVID-19: the current evidence
	Q1 update	6. Cha MH	USA	GI and hepatic manifestations of COVID-19: a comprehensive review.
	Q1 update	7. Debes JD	Poland	Systematic analysis of acute liver injury during SARS-CoV-2 infection
	Q1 update	8. Kukla M	USA	COVID-19, MERS and SARS with concomitant liver injury-Systematic Review
	Q1 update	9. Reddy KR	USA	SARS0CoiV02 and the liver: considerations in Hepatitis B and Hepatitis C infections
	Q1 update	10. Ali N	Bangladesh	Liver injury in severe COVID-19 infection: current insights and challenges
	Q2 update	11. Ali N	Bangladesh	Relationship between COVID-19 infection and liver injury: a Review of Recent Data
	Q2 update	12. Garland V	USA	GI & Hepatic manifestations of COVID-19: evolving recognition re vulnerable popns
	Q2 update	13. Ghoda A	India	Liver injury in COVID-19 infection: a systematic review
	Q2 update	14. Papadopoulos	Greece	COVID-19 and liver injury: where do we stand
	Q2 update	15. Zhou YH	China	Abnormal liver enzymes in children and infants
	Q2 update	16. Cheong J	USA	GI and liver manifestations of COVID-19
	Q2 update	17. Farshidpour M	USA	A brief review of liver injury in patients with COVID-19
	Q2 update	18. Zhong P	China	COVID19 associated GI and liver injury: clinical features & potential mechanisms
	Q2 update	19. Bin Arif T	Pakistan	Incidence, patterns, risk factors and histopathology of liver injury in COVID19
	Q2 update	20. Zhao JN	China	Liver injury in COVID-19: a minireview
2. Meta-Analyses	May 16/20	1. Parohan M	Iran	Liver injury associated with severe COVID19: systematic review and meta-analysis
	Q1 update	2. Kunutsor SK	England	Markers of liver injury and clinical outcomes in COVID-19 patients: Syst rev & MA
	Q1 update	3. Mao R	China	Manifestations and prognosis of GI and liver involvement: syst rev & meta-analysis
	Q1 update	4. Wang H	China	Liver injury and GI symptoms in COVID19: syst review and meta-analysis

	Q1 update Q1 update Q1 update Q1 update Q1 update Q1 update Q1 update Q2 update Q2 update Q2 update Q2 update Q2 update Q2 update Q2 update	5. Youssef M 6. Kumar MP 7. Kunutsor SK 8. Samidoust P 9. Xin S 10. Kulkarni AV 11. Wijarnpreecha K 12. Ahmed J 13. Labenz C 14. Wong YJ 15. Kumar A 16. Liu C 17. Wu ZH 18. Merola E	Egypt India England Iran China India USA Pakistan Germany Singapore India China China Italy	COVID-19 and liver dysfunction: syst rev and meta-analysis of retrospective studies COVID-19 and the liver: a comprehensive syst rev and meta-analysis Hepatic manifestations and complications of COVID-19: syst rev and meta-anal Risk of hepatic failure in COVID-19 patients. A systematic review & meta-analysis Abnormal LFTs with COVID-29 in mainland China: Syst review & meta-analysis Systematic review with meta-analysis: liver manifestations & outcomes in COVID19 COVID-19 and liver injury: a meta-analysis COVID-19 and liver injury: a systematic review and meta-analysis Liver injury in patients with SARS-CoV-2: a systematic review and meta-analysis A systematic review and meta-analysis of the COVID-19 associated liver injury GI and hepatic manifestations of COVID-19 and their relationship to severe course Liver injury could be associated with severe disease in COVID-19 patients A meta-analysis of the impact of COVID-19 on liver dysfunction Prevalence of live injury in patients with COVID19: syst rev & meta-analysis
3. Patho- genesis	May 16/ 20	1. Li Y	China	Hepatic involvement in COVID-19: pathology, pathogenesis, clinical implications
4. Guidelines	May 16/20 May 16/20 May 16/20	1. Musa S 2. Su TH 3. Sun J	Egypt Taiwan China, Italy	Hepatic and GI involvement in COVID-19: what do we know till now? Clinical manifestations & management of COVID-19 related liver injury COVID-19 and liver disease
5. Studies	May 16/20 May 16/20 May 16/20 Q1 update Q1 update Q1 update Q1 update Q1 update Q2 update Q2 update Q2 update Q2 update	1. Xie H 2. Zhang Y 3. Hajifathalian K 4. Huang H 5. Phipps MM 6. Wang Q 7. Schattenberg JM 8. Jiang S 9. Yip TC 10. Anastasiou OE 11. Bernal-Monterde V 12. Effenberger M 13. Lei P	China China USA China USA China Germany China China Germany Spain Austria China	Clinical characteristics of non-ICU hospitalized patients with COVID-19 liver injury Liver impairment in COVID-19 patients: 115 cases from single centre in Wuhan GI and hepatic manifestations of COVID19 in large Ney York cohort The association between markers of liver injury and clinical outcomes COVID-Wuhan Acute liver injury in COVID19: prevalence and outcomes in large US cohort Patterns of liver injury in adult patients with COVID19: retrospective analysis–105 cases Patterns of liver injury in COVID19 – a German case series Liver injury in critically and non-critically ill COVID-patients: multict observ study Liver injury is independently associated with adverse clinical outcomes Mild vs severe liver injury in SARS-CoV-2 infection SARS-CoV-2 infection induces a dual response in LFTs: association with mortality Systemic inflammation as fuel for acute live injury in COVID-19 Liver injury in COVID-19: clinical profiles, CT findings, correlation with severity

	Q2 update	14. Uchida Y	Japan	Significance of live dysfunction in Japanese patients with severe COVID19
	Q2 update	15. Zhang H	China	Clinical characteristics and risk factors for liver injury in COVID – in Wuhan
	Q2 update	16. Abe K	Japan	Clinical features and liver injury in patients with COVID19: in Japanese population
	Q2 update	17. Brito CA	Brazil	Mechanisms and consequences of COVID-19 associated liver injury: what can we affirm
	Q2 update	18. Chen VL	USA	Hepatic steatosis I associated with increased disease severity and injury
	Q2 update	19. Guo H	China	Analysis of live injury factors in 332 patients with COVID-19 in Shanghai
	Q2 update	20. Suresh Kumar VCS	USA	Transaminitis is an indicator of mortality in patients with COVID19
	Q2 update	21. Wang M	China	Clinical characteristics/risk factors of liver injury in COVID19: retrospect Wuhan cohort
	Q2 update	22. Wang J	China	Risk factors of liver injury in COVID19 in Jiangu, China: retrospective multictr study
	Q2 update	23. Kaneko S	Japan	Liver injury with COVID-19 based on GI symptoms and pneumonia severity
	Q2 update	24. Sikkema BJB	Netherlands	No association between COVID19 related liver injury and course of disease
	Q2 update	25. Schmit G	Belgium	The liver in COVID19 related death: protagonist or innocent bystander
	Q2 update	26. Fu L	China	Liver dysfunction and its association with the risk of death in COVID19 pts
	Q2 update	27. Chen F	China	Clinical features & risk factors of COVID19 associated liver injury & function: 830 cases
	Q2 update	28. Tsutsumi T	Japan	Association of coagulopathy with liver dysfunction in patients with COVID19
<b>6. Case Reports/Series</b>				
Acute liver injury	May 16/20	1. Cardoso FS	Portugal	Liver injury in critically ill patients with COVID-19: case series
	Q1 update	2. Li X	China	Severe COVID-19 patients wtih liver injury: a seven case series
	Q1 update	3. Kudravalli P	USA	Case series and review of liver dysfunction in COVID-19 patients
	Q2 update	4. Makarem J	Iran	Case Report of progressive liver failure inappropriate to decompensated Heart failure
Acute hepatitis	May 16/20	1. Lagana SM	USA	COVID-19 associated hepatitis complicating living donor liver transplantations
	May 16/20	2. Wander P	USA	COVID-19 presenting as acute hepatitis
	Q1 update	3. Aldhaleei WA	Abu Dhabi	COVID-19 induced Hepatitis B virus reactivation: novel case from United Arab Emirates
	Q1 update	4. Fraga M	Swiss	Hepatocellular type II Fibrinogen inclusions in patient with severe COVID-19 & hepatitis
	Q2 update	5. Bongiovanni M	Italy	Acute hepatitis caused by asymptomatic COVID-19 infection
	Q2 update	6. Melquist S	USA	COVID-19 presenting as fulminant hepatic failure: Case report
	Q2 update	7. Haji E Memar EHE	Iran	Fulminant hepatic failure: rare and devastating manifestation of COVID19 in 11yo boy

## Annex 8

## Kidney

Type of Reference	Review Period	Author	Country	Focus
1. Reviews	Q1 update	1. Chan VW	China	Syst Rev: COVID-19 urological manifestations and viral RNA detection
	Q1 update	2. Moitinho MS	Brazil	AKI in patients with COVID-19: integrative review
	Q1 update	3. Qian JY	China	AKI in 2019 Novel coronavirus disease
	Q2 update	4. Kellum JA	USA	Targeting AKI in COVID-19
	Q2 update	5. Nogueira SAR	Brazil	Renal changes and AKI in Covid-19: a systematic review
	Q2 update	6. Prasad N	India	COVID-19 and AKI
	Q2 update	7. Ostermann M	England	What every intensivist should know about COVID-19 associated AKI
	Q2 update	8. Parmar MS	Canada	AKI assoc with COVID19-cumulative evidence & rationale against direct injury
	Q2 update	9. Mallhi TH	Saudi Arabia	Stratification of AKI in COVID19
	Q2 update	10. Nadim MK	US/Europe	COVID19 assoc AKI: Consensus report-25 <sup>th</sup> Acute disease quality initiative WG
2. Meta-Analyses	16May20	1. Ali H	Egypt	Survival rate in AKI in COVID-19 patients: systematic review & meta-analysis
	16May20	2. Ng JJ	Singapore	AKI in hospitalized patients with COVID-19
	Q1 update	3. Wang Y	China	AKI associated with mortality of COVID-19
	Q1 update	4. Brienza N	Italy	AKI in COVID-19 infected: a Meta-analytic study
	Q1 update	5. Chen YT	Taiwan	Incidence of AKI in COVID-19
	Q1 update	6. Gabarre P	France	AKI in critically ill patients with COVID-19
	Q1 update	7. Yang X	China	Prevalence and impact of acute renal impairment on COVID-19
	Q1 update	8. Chen YT	Taiwan	Mortality rate of AKI in SARS, MERS and COVID-19 infection
	Q1 update	9. Hansrivijit P	USA	Incidence of AKI and its association with mortality in COVID-19
	Q1 update	10. Kunutsor SK	Finland	Renal complications in COVID-19
	Q1 update	11. Shao M	China	AKI is associated with severe infection and fatality in patients with COVID-19
	Q2 update	12. Oliveira CB	Brazil	High burden of AKI in COVID-19 pandemic
	Q2 update	13. Pan XW	China	AKI during the COVID-19 outbreak
	Q2 update	14. Robbins-Juarez	USA	Outcomes for patients with COVID-19 and AKI

	Q2 update	15. Ouyang L	China	Association of AKI with severity & mortality of SARS-CoV-2: meta-analysis
3. Pathogenesis / hypothesis	16May20	1. Soleimani M	USA	AKI in SARS-CoV2: Direct effect of virus on kidney proximal tubule cells
	Q1 update	2. Pan XW	China	Identification of potential mechanism of AKI: single-cell transcriptome analysis
	Q1 update	3. Battle D	USA	AKI in COVID-19: Emerging Evidence of a distinct pathophysiology
	Q2 update	4. Braun F	Germany	SARS-CoV-2 renal tropism associates with AKI
	Q2 update	5. Izzedine H	France	AKI in patients with COVID-19: an update on the pathophysiology
	Q2 update	6. Chueh TI	China	Novel evidence of AKI in COVID-19
4. Guidelines	Q1 update	1. Selby NM	England	COVID-19 and AKI in hospital: summary of NICE guidelines
5. Studies	16May20	1. Wang L	China	COVID-19 doesn't result in AKI: 116 hospitalized patients-Wuhan
	16May20	2. Su H	China	Renal histopathological analysis of 26 postmortem findings
	16May20	3. Cheng Y	China	Kidney disease is associated with in-hospital death of COVID19 patients
	Q1 update	4. Gaetano A	Italy	Incidence, risk factors, mortality: single centre observational study
	Q1 update	5. Chan L	USA	AKI in hospitalized patients with COVID-19
	Q1 update	6. Hirsch JS	USA	AKI in patients hospitalized with COVID-19
	Q1 update	7. Lim JH	S Korea	Fatal outcomes of COVID-19 in patients with severe AKI
	Q1 update	8. Sun DQ	China	Subclinical AKI in Covid-19 patients: Retrospective cohort study
	Q1 update	9. Dudoignon E	France	Activation of the renin-angiotensin-aldosterone system associated with AKI
	Q1 update	10. Pelayo J	USA	Clinical characteristics&Outcomes of community and hospital acquired AKI
	Q1 update	11. Stewart DJ	England	Renal dysfunction in hospitalized children with COVID-19
	Q1 update	12. Golmai P	USA	Histopathologic and Ultrastructural findings in pm kidney biopsy material (n-12)
	Q1 update	13. Na KR	S Korea	AKI and kidney damage in COVID-19 patients
	Q1 update	14. Sharma P	USA	COVID-19 associated kidney injury: case series of kidney biopsy findings
	Q1 update	15. Cui X	China	AKI in patients with COVID-19: multicenter study
	Q1 update	16. Hong D	China	Kidney manifestations of mild/mod/severe COVID-19: retro cohort study
	Q1 update	17. Husain-Syed F	Germany	AKI and urinary biomarkers in hospitalized patients with COVID-19
	Q1 update	18. Kormann R	France	COVID-19: acute Fanconi syndrome precedes AKI
	Q1 update	19. Rubin S	France	Characterization of AKI in critically ill patients with severe COVID-19
	Q1 update	20. Santoriello D	USA	Postmortem kidney pathology findings in patients with COVID-19.
	Q2 update	21. Frithiof R	Sweden	Presence of SARS-CoV-2 in urine is rare and not associated with AKI in critically ill
	Q2 update	22. Lee JR	USA	AKI in hospitalized COVID-19 patients in an urban academic center
	Q2 update	23. Naar L	USA	AKI in Critically ill COVID patients; single center experience-206 consecutive pts

	Q2 update	24. Ng JH	USA	Outcomes among patients hospitalized with COVID-19 and AKI
	Q2 update	25. Russo E	Italy	Kidney disease & all-cause mortality in COVID patients hospitalized in Genoa
	Q2 update	26. Zahid U	USA	AKI in COVID-19: inner city hospital experience and policy implications
	Q2 update	27. Zheng X	China	Prevalence of AKI and associations with critical illness and death
	Q2 update	28. Chaibi K	France	Severe AKI in COVID-19 patients with ARDS
	Q2 update	29. Joseph A	France	AKI in patients with SARS-CoV2 infection
	Q2 update	30. Liu L	China	Potential proximal tubular dysfunction in hospitalized patients
	Q2 update	31. Nimkar A	USA	Incidence and risk factors for AKI and effect on mortality
	Q2 update	32. Portoles J	Spain	Chronic kidney disease and AKI in COVID-19 Spanish outbreak
	Q2 update	33. Taher A	Bahrain	AKI in COVID-19 pneumonia: single-center experience in Bahrain
	Q2 update	34. Wang J	China	Risk factors of COVID-19 related AKI: single center retro cohort study
	Q2 update	35. Watchorn J	England	Critically ill patients with AKI have reduced renal blood flow and perfusion
	Q2 update	36. Werion A	Belgium	SARS-CoV2 causes a specific dysfunction of the Kidney proximal tubule
	Q2 update	37. Xia P	China	Clinicopath features/outcomes of AKI in critically ill: retrosp cohort
	Q2 update	38. Chaudhri I	USA	Proteinuria & hematuria with AKI and mortality in hospitalized patients
	Q2 update	39. Bjornstad EC	USA	AKI in critically ill children: Multicenter cross-sectional analysis
	Q2 update	40. Hamilton P	UK	Characteristics & Outcomes of hospitalized with AKI & COVID19
	Q2 update	41. Kolhe NV	UK	AKI associated with COVID19: retrospective cohort study
	Q2 update	42. Akilesh S	USA	Multicenter clinicopath correlation of kidney biopsies in COVID AKI or proteinuria
<b>6. Case Reports/Series</b>				
Acute kidney injury	16May20	1. Gopalakrishnan	USA	Fulminant acute kidney injury in a young patient with COVID-19
	Q1 update	2. Post A	Netherlands	Kidney infarction in patients with COVID19
	Q1 update	3. Rossi GM	Italy	Kidney biopsy findings: case against SARS CoV2 nephropathy
	Q1 update	4. Chenna A	USA	AKI in Case Series-Role of ACE2 and RAS blockade
	Q1 update	5. Wang Y	China	AKI in 2 patients with pre-existing chronic renal disease
	Q1 update	6. Zhu D	China	Progressive renal impairment in an older patient
	Q2 update	7. DiMauro M	Italy	AKI in COVID-19: a case report
	Q2 update	8. Patel N	USA	COVID-19 associated AKI: a case series
	Q2 update	9. Ammous A	USA	Renal infarction in a COVID19 patient
Hematuria	16May20	1. Almeida FJ	Brazil	Hematuria associated with SARS-CoV-2 infection in a child
Virus in tissue	Q1 update	1. Ren JG	China	Positive RT-PCR in urine from asymptomatic patient



Collapsing Glomerulo- pathy	Q2 update Q2 update	1. Nlandu YM 2. Tancredi T	DR Congo USA	1st case of COVID-19 assoc collapsing glomerulopathy in Sub-Saharan Africa Renal US findings in COVID related collapsing focal segmental glomerulosclerosis
Vasculitis	Q2 update Q2 update	1. Suso AS 2. Uppal NN	Spain USA	IgA vasculitis with nephritis (HSP) in a COVID patient De Novo ANCA-associated vasculitis with glomerulonephritis in COVID-19
Hyper- natremia	Q2 update	1. Zimmer MA	Germany	Hypernatremia: A manifestation of COVID-19 – a case series

## Annex 9

## Multisystem Inflammatory Syndromes

Type of Reference	Review Period	Author	Country	Focus
1. Reviews	16May20	1. Zhang Y	China	New understanding of the damage of SARS-CoV-2 infections outside the respiratory system.
	Q1 update	2. Gomez-Pastora	USA	Hyperferritinemia in critically ill COVID-19 patients: product of inflammation or mediator?
	Q1 update	3. Soy M	Turkey	Hemophagocytic lymphohistiocytosis: a review inspired by COVID-19 pandemic
	Q1 update	4. Singh-Grewal D	Aust/NZ	Update on COVID-19 MIS-C
	Q2 update	5. Upadhyay J	India	Role of inflammatory markers in COVID-19 patients
	Q2 update	6. Santos BSD	Brazil	Clinical-epidemiological relation between SARS-CoV-2 and Kawasaki disease
	Q2 update	7. Abrams JY	USA	MIS-C associated with SARS-CoV-2: systematic review
	Q2 update	8. Sperotto F	USA	Cardiac manifestations in SARS-CoV2 associated MIS-C
	Q2 update	9. Loomba RS	USA	COVID-19 and MIS-C: Kawasaki disease with macrophage activation syndrome in disguise?
	Q2 update	10. Sims JT	US/UK/Italy	Characterization of the cytokine storm reflects hyperinflammatory endothelial dysfunction
	Q2 update	11. Goncalves LF	Brazil	Kawasaki and COVID-19 disease in children
	Q2 update	12. Rife E	USA	Kawasaki disease: an update
	Q2 update	13. Simon Jr H	Brazil	MIS associated with COVID-19 from pediatric emergency physician's point of view
	Q2 update	14. Kaushik A	USA/India	Systematic review of MIS-C
	Q2 update	15. Aronoff SC	USA	Natural history of SARS-CoV-2 related MIS-C: systematic review
	Q2 update	16. Lami F	Italy	"Perfect storm": current evidence on MIS-C during SARS-CoV-2 pandemic
	Q2 update	17. Sarzaeim M	Iran	Kawasaki disease and MIS-C
	Q2 update	18. Bustos BR	Chile/Colum	MIS-C associated with SARS-CoV-2: case series quantitative systematic review.
	Q2 update	19. Berardicurti O	Italy	Wide spectrum of Kawasaki-like disease associated with SARS-CoV-2 infection.
	Q2 update	20. Lawrensia S	Indonesia	MIS-C associated with SARS-CoV-2
	Q2 update	21. Carter MJ	UK	MIS-C temporally-associated with SARS-CoV-2 infection: overview
	Q2 update	22. Cavallo F	Italy	An outbreak of Kawasaki-like Disease in children during SARS-CoV-2: no surprise?
2. Meta-Analyses	Q1 update	1. Feng X	China	Immune-inflammatory parameters in COVID-19 cases: Systematic review & meta-analysis
	Q2 update	2. Jiang L	Canada	COVID-19 and MIS-C

	Q2 update	3. Leisman DE	USA	Cytokine elevation in severe, critical COVID-19: rapid systematic review & meta-analysis
3. Pathogenesis / hypothesis	16May20	1. Colafrancesco S	Italy	COVID19 gone bad: New character in the spectrum of hyperferritinemic syndrome?
	16May20	2. Calabrese LH	USA	Cytokine storm and prospects for immunotherapy with COVID-19.
	16May20	3. McGonagle D	UK	COVID-19 induced pneumonia and macrophage activation syndrome-like disease.
	16May20	4. Ruscitti P	Italy	Cytokine storm syndrome in severe COVID-19.
	16May20	5. Amiral J	France	COVID-19 induced activation of hemostasis & immune reactions: Auto-immune reaction?
	16May20	6. Alunno A	Italy	Storm, typhoon, cyclone or hurricane in COVID-19? Beware_same storm_different origin.
	16May20	7. Li H	China	SARS-CoV-2 and viral sepsis: observations and hypotheses.
	Q1 update Q2 update	22 new publications 20 new publications	Multiple Multiple	For Q1/Q2 update see COVID spreadsheet, 'Multisystem Inflammatory Synd' tab; (Subgroup 2 = pathogenesis)
4. Guidelines	16May20	1. ECDC	Europe	Pediatric inflammatory multisystem syndrome & SARS-CoV-2: rapid risk assessment
	16May20	2. RCPCH	UK	Pediatric multisystem inflammatory syndrome temporally associated with COVID-19
	16May20	3. WHO	Global	Multisystem inflammatory syndrome in children and adolescents with COVID-19
	16May20	4. CDCP	USA	Multisystem Inflammatory Syndrome in Children (MIS-C) Associated with COVID-19
5. Studies	16May20	1. Verdoni L	Italy	Outbreak of severe Kawasaki-like disease at Italian COVID epicenter: observational cohort
	16May20	2. Belhadjer Z	France	Acute heart failure in multisystem inflammatory syndrome in children
	Q1 update	3. Grimaud M	France	Acute myocarditis and MIS-C following SARS-CoV-2 infection
	Q1 update	4. Toubiana J	France	Kawasaki-like MIS-C during covid-19 pandemic in Paris: prospective observational study
	Q1 update	5. Belot A	France	SARS-CoV-2-related MIS-C: an epidemiological study, France
	Q1 update	6. Pouletty M	France	MIS-C mimicking Kawasaki disease (Kawa-COVID-19): a multicentre cohort.
	Q1 update	7. Kaushik S	USA	MIS-C: A Multi-institutional Study from New York City.
	Q1 update	8. Capone CA	USA	Characteristics, Cardiac involvement, and Outcomes of MIS-C
	Q1 update	9. Perez-Toledo	UK	Serology confirms SARS-CoV-2 infection in PCR-negative MIS-C
	Q1 update	10. McElvaney OJ	Ireland	Characterization of Inflammatory Response to Severe COVID-19 Illness.
	Q1 update	11. Wang W	China	Definition & Risks of Cytokine Release Syndrome in 11 Critically Ill Patients with Pneumonia:
	Q1 update	12. Chen TH	Taiwan/USA	Gastrointestinal involvements in children with MIS-C
	Q1 update	13. Ouldali N	France	Emergence of Kawasaki disease related to SARS-CoV-2: a time-series analysis France.
	Q1 update	14. Prilutskiy A	USA	SARS-CoV-2 Infection-Associated Hemophagocytic Lymphohistiocytosis
	Q1 update	15. Fraser DD	USA	Inflammation Profiling of Critically Ill COVID-19 Patients
	Q1 update	16. Dufort EM	USA	MIS-C in New York State
	Q1 update	17. Feldstein LR	USA	MIS-C in U.S. Children and Adolescents
	Q1 update	18. Bhandari S	India	Inflammatory Markers in COVID-19

Q1 update	19. Diorio C	USA	MIS-C & COVID-19 are distinct presentations of SARS-CoV-2
Q1 update	20. Blumfield E	USA	Imaging Findings in MIS-C
Q2 update	21. Losocco GG	Italy	HScore for secondary HLH, calculated without marrow biopsy is low in COVID-19
Q2 update	22. Choe SA	S Korea	No temporal association: human coronavirus & Kawasaki disease: South Korea
Q2 update	23. Lio K	Japan	Kawasaki or Kawasaki-like disease: influence of SARS-CoV-2 infections in Japan
Q2 update	24. Theocharis P	UK	Multimodality cardiac evaluation MIS-C
Q2 update	25. Carter MJ	UK	Peripheral immunophenotypes in MIS-C
Q2 update	26. Davies P	UK	Intensive care admissions for MIS-C in UK: a multicentre observational study
Q2 update	27. De Farias ECF	Brazil	MIS-C: Multi-centered Study - Brazil
Q2 update	28. Dhanalakshmi	India	Epidemiological & Clinical Profile of MIS-C in Indian Children
Q2 update	29. Godfred-Cato	USA	MIS-C: United States, March-July 2020
Q2 update	30. Jain S	India	MIS-C: Mumbai, India
Q2 update	31. Mamishi S	Iran	MIS-C in 45 Children: 1st Report from Iran
Q2 update	32. Matsubara D	USA	Echocardiographic Findings in MIS-C in the United States
Q2 update	33. Rostad CA	USA	Quantitative SARS-CoV-2 Serology in Children With MIS-C
Q2 update	34. Sadiq M	Pakistan	MIS-C: Pakistan
Q2 update	35. Torres JP	Chile	MIS-C: clinical & epidemiological characteristics Santiago de Chile
Q2 update	36. Pereira MFB	Brazil	Severe clinical spectrum with high mortality in MIS-C
Q2 update	37. Webb Bj	USA	Clinical criteria for COVID-19-associated hyperinflammatory syndrome: a cohort study
Q2 update	38. Hutchings SD	UK	Microcirculatory/Endothelial/Inflammatory Responses: COVID-19 vs Septic Shock
Q2 update	39. Minocha PK	USA	Cardiac Findings in MIS-C
Q2 update	40. Zeichner SL	USA	MIS-C and SARS-CoV-2 Serology
Q2 update	41. Bordet J	France	MIS-C: filling the gap between myocarditis and Kawasaki?
Q2 update	42. Grazioli S	Switzerland	Immunological assessment of MIS-C
Q2 update	43. Valverdi I	Europe	Acute Cardiovascular manifestations in 286 European children with MIS-C
Q2 update	44. Garcia-Salido	Spain	CD64, CD11a and CD18 leukocytes expression: MIS-C vs Kawasaki disease
Q2 update	45. Caro-Paton GL	Spain	Shock and Myocardial Injury in Children With MIS-C: case series & review
Q2 update	46. Sethuraman U	USA	MIS-C in Michigan
Q2 update	47. Antunez-Montes	Multiple	MIS-C in Latin American Children: A Multinational Study
Q2 update	48. OkarskaNapierat	Poland	MIS-C in Poland during Months with Low COVID-19 Prevalence: Registry
Q2 update	49. Deep A	UK	Acute Kidney Injury in MIS-C: United Kingdom experience
Q2 update	50. Dionne A	USA	Atrioventricular Block in MIS-C

	Q2 update	51. Clark KEN	UK	Assessment of HLH HScore in COVID-19 patients
	Q2 update	52. Corwin DJ	USA	Distinguishing MISC from Kawasaki Disease and benign inflammatory illnesses
	Q2 update	53. Ece I	Turkey	Assessment of cardiac arrhythmic risk in children with COVID-19
	Q2 update	54. Gaitonde M	USA	COVID-19 related MISC affects LVent function & global strain compared with Kawasaki
	Q2 update	55. Hakim NN	USA	Secondary HLH versus cytokine release syndrome in severe COVID-19
	Q2 update	56. Pang J	UK	SARS-CoV-2 polymorphisms and MIS-C
<b>6. Case Reports/Series</b>				
MIS-C (Children)	16May20	1. Licciardi F	Italy	SARS-CoV-2 induced Kawasaki-like hyperinflammatory Syndrome: novel child phenotype
	16May20	2. Acharyya	India	Novel Coronavirus mimicking KD in an infant.
	16May20	3. Patel PA	USA	Severe pediatric COVID-19 presenting with respiratory failure and severe thrombocytopenia
	16May20	4. Riphagen S	UK	Hyperinflammatory shock in children during COVID-19 pandemic
	16May20	5. Chiotos K	USA	MIS-C in children during COVID-19 pandemic: case series
	Q1 update	39 new case reports	Multiple	For Q1/Q2 update see COVID spreadsheet, 'Multisystem Inflammatory Synd' tab; (Subgroup 1=pediatric, Subgroup2=case reports))
	Q2 update	43 new case reports	Multiple	
MIS-A (Adult)	Q1 update	1. Wang C	China	Alveolar macrophage dysfunction and cytokine storm in two fatal COVID-19 cases
	Q1 update	2. Chhetri S	Oman	Fatal COVID-19: metabolic acidosis followed by cytokine storm
	Q1 update	3. Haberman R	USA	COVID-19 in immune mediated inflammatory diseases: New York case series
	Q1 update	4. Bonnet M	France	Endomyocardial biopsy findings in Kawasaki-like disease associated with SARS-CoV-2
	Q1 update	5. Moghadam P	France	MIS-A with particular cutaneous lesions
	Q2 update	6. Chowdhary A	UK	MIS in an adult with SARS-CoV-2 infection
	Q2 update	7. Cogan E	Belgium	MIS-A With Complete Kawasaki Disease Features
	Q2 update	8. Feng Y	USA	Novel case of an adult with toxic shock syndrome following COVID-19 infection
	Q2 update	9. Lidder AK	USA	An adult with COVID-19 kawasaki-like syndrome and ocular manifestations
	Q2 update	10. Lolachi S	Switzerland	Macrophage activation syndrome: A case report
	Q2 update	11. Chau VQ	USA	Cardiogenic Shock and Hyperinflammatory Syndrome in Young Males with COVID-19
	Q2 update	12. Morris SB	UK	Case Series of MIS-A: UK and USA March-August 2020
	Q2 update	13. Kofman AD	USA	MIS-A: a case report
	Q2 update	14. Abdollahi A	Iran	Possibility of hemophagocytic lymphohistiocytosis in COVID-19 patients
	Q2 update	15. Othenin-Girard A	Switzerland	MIS-A with refractory cardiogenic shock, acute myocarditis & mononeuritis multiplex
	Q2 update	16. Burgi Vieira C	Portugal	Kawasaki-like Syndrome as an Emerging Complication in Young Adults
	Q2 update	17. Nicol M	France	Delayed acute myocarditis and COVID-19-related MIS
	Q2 update	18. Hekimian G	France	COVID-19 acute myocarditis and MIS in Adult intensive and cardiac care units

Kawasaki Disease & Kawasaki-like syndromes	16May20 16May20 Q1 update Q2 update Q2 update	1. Jones VG 2. Rivera-Figueroa 3. Charif MY 4. To KK 5. Rehman S	USA USA USA China Saudi Arabia	COVID-19 and Kawasaki Disease: novel virus and novel case Incomplete Kawasaki Disease in a child with COVID-19. COVID-19 related Kawasaki-like disease in an adult False positive SARS-CoV-2 serology in 3 children with Kawasaki disease Syndrome resembling Kawasaki disease in COVID-19 asymptomatic children
HLH	Q1 update Q1 update Q1 update Q2 update Q2 update	1. Radmanesh F 2. Dewaele K 3. Ruscitti P 4. VonderThusen J 5. Amaral LTQ	USA Belgium Italy Netherlands Brazil	Severe cerebral involvement in adult-onset hemophagocytic lymphohistiocytosis (HLH) HLH in SARS-CoV-2 infection Lung involvement in macrophage activation síndrome and severe COVID-19 Fatal combination of HLH with extensive pulmonary microvascular damage in COVID-19 Hemophagocytic síndrome: a potential COVID-19 complication

## Annex 10

## Musculoskeletal System

Type of Reference	Review Period	Author	Country	Focus
1. Reviews	Q1 update	Cipollaro L	Italy	Musculoskeletal symptoms in COVID-19 patients
	Q1 update	Schett G	Germany	COVID-19 revisiting inflammatory pathways of arthritis
	Q1 update	Disser NP	USA	Musculoskeletal consequences of COVID-19
2. Meta-Analyses				
3. Pathogenesis				
4. Guidelines				
5. Studies				
6. Case Reports/Series				
Myositis	16May20	1. Beydon M	France	Myositis as a manifestation of SARS-CoV-2
	Q1 update	2. Zhang H	USA	COVID-19 associated myositis with severe proximal and bulbar weakness
	Q2 update	3. Mehan WA	USA	Paraspinal myositis in patients with COVID-19
	Q2 update	4. Almadani M	USA	Compartment syndrome secondary to viral myositis as initial COVID-19 presentation
	Q2 update	5. Ishkanian A	USA	Clinical conundrum: Dysphagia in patient with COVID-19 & progressive muscle weakness
Rhabdo-myolysis	16May20	1. Jin M	China	Rhabdomyolysis as potential late complications associated with COVID-19
	16May20	2. Suwanwongse K	USA	Rhabdomyolysis as a presentation of COVID-19
	Q1 update	3. Chan KH	USA	Weakness & elevated creatinine kinase as initial presentation of COVID-19
	Q1 update	4. Gefen AM	USA	Pediatric COVID-19-associated rhabdomyolysis: a case report
	Q1 update	5. Borku Uysal B	Turkey	A COVID-19 Patient Presenting with Mild Rhabdomyolysis.
	Q1 update	6. Rivas Garcia S	Spain	Rhabdomyolysis as the main manifestation of COVID-19
	Q1 update	7. Valente-Acosta B	Mexico	Rhabdomyolysis as an initial presentation of COVID-19.
	Q1 update	8. Zhang Q	USA	COVID-19 Induced Viral Myositis & Subsequent Rhabdomyolysis.
	Q1 update	9. Chedid NR	USA	COVID-19 and Rhabdomyolysis
	Q1 update	10. Mukherjee A	USA	Rhabdomyolysis in a Patient With COVID-19

	Q1 update	11. Samies NL	USA	Rhabdomyolysis and Acute Renal Failure in an Adolescent with COVID-19
	Q1 update	12. Husain R	USA	Rhabdomyolysis as a manifestation of a severe case of COVID-19
	Q2 update	13. Alrubaye R	USA	Severe Rhabdomyolysis in a 35-Year-old Woman with COVID-19
	Q2 update	14. He YC	China	Rhabdomyolysis as Potential Late Complication Associated with COVID-19
	Q2 update	15. Taxbro K	Sweden	Rhabdomyolysis and acute kidney injury in severe COVID-19 infection
	Q2 update	16. Chong WH	USA	SARS-CoV-2 with Rhabdomyolysis and Acute Kidney Injury
	Q2 update	17. Meegada S	USA	Coronavirus Disease 2019-Induced Rhabdomyolysis
	Q2 update	18. Singh B	USA	Rhabdomyolysis in COVID-19: Report of Four Cases
	Q2 update	19. Tram N	Belgium	Rhabdomyolysis & Acute Kidney Injury as COVID-19 Presentation in an Adolescent
	Q2 update	20. Murillo F	Peru	SARS-CoV-2 Infection Rhabdomyolysis and Probable Myocarditis
	Q2 update	21. Shanbhag A	USA	COVID-19 Presenting as Severe Rhabdomyolysis With Normal Renal Function
	Q2 update	22. Buckholz AP	USA	Clinical Characteristics/Diagnosis/Outcomes of 6 Patients With COVID-19 Rhabdomyolysis
	Q2 update	23. Anklesaria Z	USA	Fatal Rhabdomyolysis in a COVID-19 Patient on Rosuvastatin
	Q2 update	24. Gilpin S	USA	Rhabdomyolysis as the Initial Presentation of SARS-CoV-2 in an Adolescent
Arthritis +/- Arthralgia	16May20	1. Joob B	Thailand	Arthralgia as an initial presentation of COVID-19
	Q1 update	2. Lopez-Gonzalez	Spain	Case series of acute arthritis during COVID-19 admission
	Q1 update	3. Alivernini S	Italy	Comparative analysis of sinovial inflammation after SARS-CoV-2 infection
	Q1 update	4. De Stefano L	Italy	Transient monoarthritis and psoriatic skin lesions following COVID-19
Other	Q2 update	1. Van Aerde N	Belgium	Intensive care unit acquired muscle weakness in COVID-19 patients



## Annex 11

### Ocular System

Type of Reference	Review Period	Author	Country	Focus
1. Reviews	16May20	1. Hu K	USA	Ophthalmic manifestations of COVID-19
	16May20	2. Seah I	Singapore	Can COVID-19 affect the eyes
	Q1 update	3. Douglas KAA	US/Greece	Ocular Manifestations of COVID-19: Critical Review of Current Literature
	Q1 update	4. Ho D	Singapore	COVID-19 and the Ocular Surface: Review of Transmission/Manifestations
	Q2 update	5. Torres BRS	Brazil	Ocular manifestations of COVID-19: a literature review
	Q2 update	6. Bertoli F	Italy	Ocular Findings in COVID-19: Review of Direct Manifestations & Indirect Effects
	Q2 update	7. Tisdale AK	USA	Neuro-ophthalmic manifestations of COVID-19
	Q2 update	8. Sanghi P	UK	Ocular Complications in the Prone Position in the Critical Care Setting
	Q2 update	9. Luis ME	Portugal	Review of Neuro-Ophthalmological Manifestations of Human Coronavirus Infection
2. Meta-Analyses	16May20	1. Ulhaq ZS	Indonesia	Prevalence of ophthalmic manifestations in COVID-19; diagnostic value of ocular fluid
	Q2 update	2. Aggarwal K	India/Sing	Ocular Surface manifestations of COVID-19: systematic review and meta-analysis
	Q2 update	3. Ling XC	Taiwan	Ocular manifestations/comorbidities and detection of SARS-CoV-2 in conjunctiva
3. Pathogenesis/hypothesis				
4. Guidelines	16May20	1. Siedlecki J	Germany	Ophthalmological aspects of the SARS-CoV-2 global pandemic
5. Studies	16May20	1. Wu P	China	Characteristics of ocular findings of patients with COVID-19
	Q1 update	2. Chen L	China	Ocular manifestations/clinical characteristics: 535 cases in Wuhan, China
	Q1 update	3. Bostanci CB	Turkey	Ocular manifestations of COVID-19
	Q1 update	4. Valente P	Italy	Ocular manifestations & viral shedding in tears of pediatric patients with COVID-19
	Q1 update	5. Abrishami M	Iran	Ocular Manifestations of Hospitalized Patients with COVID-19 in Northeast of Iran.
	Q1 update	6. Landecho MF	Spain	COVID-19 retinal microangiopathy as an in vivo biomarker of systemic vascular disease?
	Q2 update	7. Lee YH	Korea	Ocular Manifestations of Patients with COVID-19 in Daegu Province, Korea
	Q2 update	8. Ma N	China	Ocular Manifestations & Clinical Characteristics of Children With Confirmed COVID-19

	Q2 update	9. Sawant OB	USA	Prevalence of SARS-CoV-2 in human post-mortem ocular tissues
6. Case Reports/Series				
Conjunctivitis	16May20	1. Cheema M	Canada	Keratoconjunctivitis as initial presentation of COVID-19
	16May20	2. Chen L	China	Ocular manifestations of a hospitalized patient with confirmed COVID-19
	Q1 update	3. Guo D	China	Relapsing viral keratoconjunctivitis in COVID-19
	Q1 update	4. Ozturker ZK	Turkey	Conjunctivitis as sole symptom of COVID-19: case report and review of literature
	Q2 update	5. Lim LW	Singapore	Acute onset of bilateral follicular conjunctivitis in two patients
Uveitis and/or retinitis	Q1 update	1. Virgo J	UK	Paracentral acute maculopathy & acute macular neuroretinopathy after COVID-19
	Q1 update	2. Bettach E	Israel	Bilateral anterior uveitis as part of a COVID-19 multisystem inflammatory syndrome
	Q1 update	3. QuintanaCastanedo	Spain	Concurrent chilblains and retinal vasculitis in a child with COVID-19.
	Q2 update	4. Benito-Pascual	Spain	Panuveitis and Optic Neuritis as Possible Initial Presentation of COVID-19
	Q2 update	5. Gascon P	France	Covid-19-Associated Retinopathy: A Case Report
	Q2 update	6. Ortiz-Seller A	Spain	Ophthalmic & Neuro-ophthalmic Manifestations of COVID-19
Other	Q1 update	1. Stevens DV	USA	Complications of Orbital Emphysema in a COVID-19 Patient
	Q1 update	2. Mendez Mangana C	Spain	Episcleritis as an ocular manifestation in a patient with COVID-19
	Q1 update	3. Ruiy W	Taiwan	COVID-19 mimicking dengue fever with retro-orbital pain
	Q1 update	4. Insausti-Garcia A	Spain	Papillophlebitis in a COVID-19 patient: Inflammation and hypercoagulable state
	Q2 update	5. Khan AW	Pakistan	Ischemic stroke leading to bilateral vision loss in COVID-19 patient
	Q2 update	6. Otaif W	SaudiArab	Episcleritis as a possible presenting sign of the novel coronavirus disease
	Q2 update	7. D'Aloisio R	Italy	Bilateral macular hemorrhage in a patient with COVID-19
	Q2 update	8. Sriwastava S	US/India	New onset ocular myasthenia gravis in COVID-19: novel case report & literature review

## Annex 12

## Respiratory System

Type of Reference	Review Period	Author	Country	Focus
1. Reviews	Q1 update	1. Shelmerdine SC	Europe	COVID-19 in children: systematic review of imaging findings
	Q1 update	2. Baksh M	India/Pakist	Systematic review of ARDS in COVID-19
	Q1 update	3. Anapat.hrc	Spain	First COVID-19 autopsy in Spain
	Q2 update	4. Kadyrova A	Kyrgyz	Identifying pulmonary manifestations of COVID-19 on CT
2. Meta-Analyses				
3. Pathogenesis / hypothesis	16May20	1. Gattinoni L	Italy	COVID-19 Does not lead to a “typical” ARDS
	16May20	2. Gattinoni L	Italy/Germany	COVID19 pneumonia: ARDS or not?
	Q2 update	3. Lin SH	China	COVID-19: cytokine storms, hyper-inflammatory phenotypes, ARDS
	Q2 update	4. Painter JD	USA	Role of Autophagy in Lung Inflammation
	Q2 update	5. Sadegh Beigee	Iran	Diffuse alveolar damage/thrombotic microangiopathy main lung biopsy finding
	Q2 update	6. Holter JC	Norway	Systemic complement activation associated with respiratory failure in COVID-19
	Q2 update	7. Ronit A	Denmark	Compartmental immunophenotyping in COVID-19 ARDS
	Q2 update	8. Bussani R	Italy/UK	Viral RNA persistence/pneumocyte syncytia/thrombosis: hallmarks of COVID-19
	Q2 update	9. Notz Q	Germany	Pro&Anti-Inflammatory Responses in Severe COVID-19 ARDS
	Q2 update	10. Stukas S	Canada	Association of Inflammatory Cytokines in COVID-19 Respiratory Failure
	Q2 update	11. Quan C	China	Immunopathogenesis of COVID-19 ARDS
	Q2 update	12. Thachil J	UK/India	Hemostatic Lung Abnormality in COVID-19: Thrombosis or Embolism?
4. Guidelines				
5. Studies	16May20	1. Mo P	China	Clinical characteristics of refractory COVID-19 pneumonia in Wuhan
	Q1 update	2. Carsana L	Italy	Pulmonary post-mortem findings in COVID-19: case series from Italy
	Q2 update	3. Kangas-Dick A	USA	Clinical characteristics and outcome of pneumomediastinum in COVID-19
	Q2 update	4. Jalobe OMP	UK	Implications of COVID-19 related pneumomediastinum
	Q2 update	5. Jones E	UK	Subcutaneous emphysema/pneumomediastinum/pneumothorax in COVID19

	Q2 update	6. Morrone KA	USA	Acute chest syndrome in setting of COVID-19: case series from the Bronx
	Q2 update	7. Martinelli AW	UK	COVID-19 and pneumothorax: multicentre retrospective case series
	Q2 update	8. Marsico S	Spain	Spontaneous pneumothorax in COVID-19 patients
	Q2 update	9. Zantah M	USA	Pneumothorax in COVID-19 disease – incidence and clinical characteristics
	Q2 update	10. Wang XH	China	High incidence and mortality of pneumothorax in COVID-19 critically ill.
Case Reports/Series				
Spontaneous pneumothorax	16May20	1. Rohailla S	Canada	SARS-CoV-2 infection associated with spontaneous pneumothorax
	Q1 update	12 new reports	Multiple	For Q1/Q2 update see COVID-19 spreadsheet – respiratory tab, subgroup 1 = pneumothorax, subgroup 2 = case reports
	Q2 update	21 new reports	Multiple	
Pneumomediastinum +/- Pneumothorax	16May20	1. Zhou C	China	COVID-19 with spontaneous pneumomediastinum
	16May20	2. Kolani S	Morocco	Spontaneous pneumomediastinum in SARS-CoV02 infection 23yo F
	Q1 update	14 new reports	Multiple	For Q1/Q2 update see COVID-19 spreadsheet – respiratory tab, subgroup 1 = pneumomediastinum, subgroup 2 = case reports
	Q2 update	19 new reports	Multiple	
3. Other	16May20	1. Shi F	China	COVID 19 pneumonia with hemoptysis as the initial symptom
	16May20	2. Beerkens F	USA	COVID -19 pneumonia as cause of acute chest syndrome in adult sickle cell patient
	16May20	3. Sivakorn C	Thailand	Walking pneumonia in COVID-19: mild symptoms with marked CT abnormalities
	Q1 update	4. Suess C	Switzerland	Gross and histopathologic pulmonary findings in COVID-19 death in self-isolation.
	Q1 update	5. Chen Y	China	Large pulmonary cavity in COVID-19 cured patient case report.
	Q1 update	6. Nyholm S	Sweden	Invasive mechanical ventilation in a former preterm infant with COVID-19.
	Q1 update	7. Renaud-Picard	France	Delayed pulmonary abscess following COVID-19 pneumonia: A case report.
	Q1 update	8. Borghesi A	italy	COVID-19 Pneumonia: Three Thoracic Complications in the Same Patient
	Q1 update	9. Schwensen HF	Denmark	Fatal pulmonary fibrosis: a post-COVID-19 autopsy case
	Q1 update	10. Amaral LTW	Brazil	Lung cavitation in COVID-19: co-infection complication or rare evolution?
	Q2 update	11. Mughal MS	USA	Hilar lymphadenopathy, novel finding in COVID-19
	Q2 update	12. Longo C	Italy	Platypnea-orthodeoxia after fibrotic evolution of COVID-19 interstitial pneumonia.
	Q2 update	13. Venn AMR	USA	A case series of pediatric croup with COVID-19
	Q2 update	14. Lari A	Kuwait	Caution against precaution: A case report on silent hypoxia in COVID-19
	Q2 update	15. Berhane S	UK	Bullous lung disease in a patient with severe COVID-19 pneumonitis
	Q2 update	16. Widysanto A	Indonesia	Happy hypoxia in critical COVID-19 patient: A case report in Tangerang, Indonesia
	Q2 update	17. Peys E	Belgium	Haemoptysis as the first presentation of COVID-19: a case report

## Annex 13

### Endocrine System

Type of Reference	Review Period	Author	Country	Focus
1. Reviews	16May20	1. Patel KP	China/USA	Gastrointestinal, hepatobiliary and pancreatic manifestations of COVID-19
	Q2 update	2. Kralicka AL	Poland	Hyponatremia in infectious diseases: a literature review
	Q2 update	3. Halboub E	Saudi Arabia	Orofacial manifestations of COVID-19: brief review
	Q2 update	4. Juhasz MF	Hungary	Insufficient etiologic workup of COVID associated acute pancreatitis:SystReview
2. Meta-Analyses				
3. Pathogenesis / hypothesis				
4. Guidelines				
5. Studies	16May20	1. Wang F	China	Pancreatic injury patterns in patients with COVID-19 pneumonia
	Q1 update	2. Dirweesh A	USA	Clinical outcomes of acute pancreatitis in patients with COVID-19
	Q1 update	3. Muller I	Italy	SARS-CoV-2 related atypical thyroiditis
	Q2 update	4. Inamdar S	USA	Prevalence/risk factors/outcomes of acute pancreatitis with COVID19
	Q2 update	5. Achua JK	USA	Histopathology and ultrastructural findings of fatal COVID-19 on Testis
	Q2 update	6. Akarsu C	Turkey	Association between acute pancreatitis and COVID-19
	Q2 update	7. Lui DTW	China	Thyroid dysfunction relative to COVID immune profile & outcome: 191 cases
6. Case Reports/Series				
1. Thyroiditis	Q1 update	1. Asfuoglu Kalkan E	Turkey	A case of subacute thyroiditis associated with Covid-19 infection
	Q1 update	2. Brancatella A	Italy	Subacute Thyroiditis After Sars-COV-2 Infection
	Q1 update	3. Ippolito S	Italy	SARS-CoV-2: potential trigger for subacute thyroiditis?
	Q1 update	4. Ruggeri RM	Italy	Subacute thyroiditis: endocrine complication linked to the COVID-19
	Q1 update	5. Tee LY	Singapore	COVID-19 complicated by Hashimoto's thyroiditis
	Q2 update	6. Brancatella A	Italy	Is Subacute Thyroiditis an Underestimated Manifestation of SARS-CoV-2
	Q2 update	7. Mattar SAM	Singapore	Subacute thyroiditis associated with COVID-19

	Q2 update	8. Campos-Barrera E	Mexico	Subacute Thyroiditis Associated with COVID-19
	Q2 update	9. Rotondi M	Italy	SARS-CoV-2 receptor ACE-2 mRNA in thyroid cells-clue for thyroiditis?
	Q2 update	10. Mizuno S	Japan	A case of postpartum thyroiditis following SARS-CoV-2 infection
	Q2 update	11. Ruano R	Spain	Subacute thyroiditis might be a complication triggered by SARS-CoV-2
	Q2 update	12. Chong WH	USA	Subacute Thyroiditis in the Setting of Coronavirus Disease 2019
2. Pancreatitis	May16/20	1. Hadi A	Denmark	COVID-19 with severe acute pancreatitis: case report on 3 family members
	Q1 update	2. Anand ER	UK	Acute pancreatitis in a COVID19 patient
	Q1 update	3. Aloysius MM	USA	COVID19 presenting as acute pancreatitis
	Q1 update	4. Miao Y	France	First case of acute pancreatitis related to SARS-CoV-2 infection
	Q1 update	5. Meireles PA	Portugal	Acalculous acute pancreatitis in a COVID19 patient
	Q1 update	6. Pinte L	Romania	Pancreatic involvement in SARS CoV2: case report and living review
	Q1 update	7. Alloway BC	USA	Suspected case of COVID19-associated pancreatitis in a child
	Q1 update	8. Karimzadeh S	Iran	COVID19 presenting as acute pancreatitis: lessons from a patient in Iran
	Q1 update	9. Gadiparthi C	USA	Hyperglycemia, Hypertriglyceridemia and acute pancreatitis in COVID infection
	Q1 update	10. Ali Bokhari SMMA	Pakistan	Case report: novel coronavirus – a potential cause of acute pancreatitis
	Q1 update	11. Al Mazrouei SSA	UAE	COVID19 associated acute pancreatitis: a rare cause of acute abdomen
	Q1 update	12. Brikman S	Israel	Acute pancreatitis in a 61 year old man with COVID19
	Q2 update	13. Alves AM	Brazil	SARS-CoV-2 leading to acute pancreatitis: an unusual presentation
	Q2 update	14. Kurihara Y	Japan	Pancreatitis in a Patient with Severe COVID Pneumonia treated with ECMO
	Q2 update	15. Lakshmanan S	USA	Acute Pancreatitis in Mild COVID-19 Infection
	Q2 update	16. Purayil N	Qatar	COVID-19 Presenting as Acute Abdominal Pain: A Case Report
	Q2 update	17. Wang K	China	Acute Pancreatitis as the PC in 2 Cases of COVID-19 in Wuhan, China
	Q2 update	18. Cheung S	USA	Recurrent Acute Pancreatitis in a Patient with COVID-19 Infection
	Q2 update	19. Gonzalo-Voltas A	Spain	Acute pancreatitis in a patient with COVID-19 infection
	Q2 update	20. Gupta V	India	COVID-19 and Acute Pancreatitis: What Do Surgeons Need to Know
	Q2 update	21. Kataria S	USA/Pakistan	COVID-19 Induced Acute Pancreatitis: Case Report & Literature Review
	Q2 update	22. Kumaran NK	UK	COVID-19 associated with acute necrotising pancreatitis (ANP)
	Q2 update	23. Tollard C	France	Inaugural diabetic ketoacidosis with acute pancreatitis during COVID-19
	Q2 update	24. Meyers Mh	USA	A Case of COVID-19-Induced Acute Pancreatitis
	Q2 update	25. Shinohara T	Japan	Acute Pancreatitis During COVID-19 Pneumonia
	Q2 update	26. Samies NL	USA	Pancreatitis in Pediatric Patients with COVID-19
	Q2 update	27. Fernandes DA	Brazil	SARS-CoV-2 and acute pancreatitis: a new etiological agent?

	Q2 update	28. Szatmary P	UK	Emerging Phenotype of severe SARS-CoV 2-associated Pancreatitis
3. Hyper-glycemia	Q1 update	1. Armeni E	UK	Protracted ketonaemia in COVID hyperglycaemic emergencies: case series
	Q1 update	2. Hoe Chan K	USA	Clinical & Outcome in Pts with COVID19 DKA: Hospital case series
	Q1 update	3. Oriot P	Belgium	Euglycemic DKA in a patient with type 1 diabetes & COVID pneumonia
	Q2 update	4. Gianniosis M	USA	Clinical dilemma of DKA and Covid-19 infection: A case report
	Q2 update	5. Hollstein T	Germany	Autoantibody-negative type1 diabetes after SARS-CoV-2 infection
	Q2 update	6. Meza JL	Columbia	DKA Precipitated by COVID-19 in Patients Without Respiratory Symptoms
	Q2 update	7. Alsadhan I	Saudi Arabia	DKA precipitated by COVID-19 infection: Case series (all prior DMtype 2)
4. Adrenal Injury	Q1 update	1. Iuga AC	USA	Adrenal Vascular Changes in COVID-19 Autopsies.
	Q1 update	2. Zinserling VA	Europe	Inflammatory Cell Infiltration of Adrenals in COVID-19.
	Q1 update	3. Alvarez-Troncoso J	Spain	Case Report: COVID-19 with Bilateral Adrenal Hemorrhage
	Q1 update	4. Frankel M	Israel	Bilateral adrenal hemorrhage in Coronavirus disease 2019 patient
	Q2 update	5. Freire Santana M	Spain	Case Report: Adrenal Pathology Findings in Severe COVID-19: An Autopsy Study
	Q2 update	6. Heidarpour M	Iran	Adrenal insufficiency in coronavirus disease 2019: a case report
	Q2 update	7. Kumar R	UK	A case of adrenal infarction in a patient with COVID 19 infection
5. Parotitis	Q1 update	1. Capaccio P	Italy	Acute parotitis: possible precocious clinical manifestation of SARS-CoV2
	Q1 update	2. Fisher J	USA	COVID19 associated parotitis: case report
	Q2 update	3. Chern A	USA	Sialadenitis: possible early manifestation of COVID19
	Q2 update	4. Afsal AS	India	Inflammation of papillae of Wharton's duct in COVID – a debatable entity
5. Male Reproductive tract	Q2 update	1. Bridwell RE	USA	COVID-19 patient with bilateral orchitis: A case report
	Q2 update	2. Shoar S	USA	Late COVID-19 Complication: Male Sexual Dysfunction
	Q2 update	3. Duarte SAC	Brazil	Prostate infarction & acute urinary retention: complication of severe COVID
6. Other	Q2 update	1. Dixit NM	USA	Sudden Cardiac Arrest in a Patient With Myxedema Coma and COVID-19

## Annex 14

## Long Haul Syndrome and other COVID chronic complications

Body System	Review Period	Author	Country	Focus
Systemic				
Reviews	Q2 update	Bektas A	USA	Do hyper-inflammatory syndromes accelerate short- and long-term inflammaging?
Studies	Q2 update Q2 update	Ramani C Tolba M	USA Egypt	Post-Intensive Care Unit COVID-19 Outcomes-a Case Series Assessment and Characterization of Post-COVID-19 manifestations
Case reports	Q2 update	Novak P	USA	Orthostatic cerebral hypoperfusion síndrome & small fiber neuropathy
Neurologic				
Reviews:	Q2 update Q2 update Q2 update Q2 update Q2 update	4. Wang F 5. McClafferty B 6. Riederer P 7. Schirinzi T 8. Nami M	USA USA Den/Ger Italy Multiple	Long-Term Respiratory and Neurological Sequelae of COVID-19 Critical illness myopathy and polyneuropathy in older SARS-CoV-2 patients Coronaviruses: a call for extended human postmortem brain analyses COVID-19: dealing with a potential risk factor for chronic neurological disorders Interrelation of COVID19 Neurological & Psychological Symptoms: Risks & Remedies
Pathogenesis and Hypothesis	Q2 update Q2 update Q2 update Q2 update Q2 update	9. Tavassoly O 10. Alpert O 11. Mohammadi 12. Shiers S 13. Wijeratne T	Can/USA USA Iran USA Australia	Brain Protein Aggregation by SARS-CoV-2 as a Possible Long-Term Complication Cytokine storm induced new onset depression in patients with COVID-19. Immunologic Characteristics/Mechanisms of Neurologic Manifestations of SARS-CoV-2 ACE2 & SCARF expression in human DRG nociceptors & COVID CNS effects Post-COVID 19 Neurological Syndrome (PCNS); novel síndrome&global challenges
Studies	Q2 update	14. Sollini M	Italy	Vasculitis changes in COVID-19 survivors with persistent symptoms (PET/CT scan)
Case reports	Q2 update	15. Faber I	Brazil	Covid-19 and Parkinsonism: A non-post-encephalitic case
Respiratory				
Reviews	Q2 update	1. Wang F	USA	Long-Term Respiratory and Neurological Sequelae of COVID-19



		2. Shaw B	Italy	Update on long-term pulmonary consequences of COVID-19
Case Reports	Q2 update	1. Scelfo C	Italy	Early Lung Fibrosis Following COVID-19 Pneumonia - Case Reports
Endocrine				
Pathogenesis	Q2 update	1. Achua JK	USA	Histopathology and ultrastructural findings of fatal COVID19 infections on testis