



LEIDRAAD pre-operatieve diagnostische work up

Practice guideline

Pre-operative work-up for COVID-19 infection in asymptomatic patients scheduled for surgery under general anesthesia

Leidraad

Pre-operatieve diagnostiek naar COVID-19 bij asymptomatische patiënten ingepland voor chirurgie onder algehele anesthesie

Disclaimer

This practice guideline is drafted to address the need for advice about pre-operative COVID-19 screening in patients reporting no symptoms of COVID-19 after thorough history taking. The utility of COVID-19 screening in asymptomatic patients is highly dependent on the background prevalence of SARS-CoV-2 infection among the tested population. Due to the acute and dynamic nature of the pandemic and the lack of accurate estimates of COVID-19 prevalence among the Dutch population, it is rather difficult to generalize the expected results of the proposed screening for the entire country. Therefore, hospitals may deviate from this practice guideline based on a locally-formulated multidisciplinary statement if they observe a low background prevalence of COVID-19 infection within their community and hospital populations, while being notified that there is no exact definition of 'low prevalence' nor exact knowledge of the number of transmission of one undetected infection within a hospital population.

The committee prospectively collected data on the performed nasopharyngeal swabs and chest CTs. These results have been analyzed and used to alter this version of the practice guidelines. The collection of data on de nasopharyngeal swabs will be continued. Bi-weekly evaluation of the guideline by the committee, utilizing these and other results, will also be continued.

Introduction

The SARS-CoV-2 pandemic has rapidly altered the practice of medicine globally and in the Netherlands. This practice guideline was initiated by the Dutch Surgical Association (NVvH) and drafted by relevant medical specialists' associations under the auspices of the Dutch Association of Medical Specialists (FMS), and is a preliminary guide for how to perform a pre-operative COVID-19 workup for patients reporting no symptoms of COVID-19 who are awaiting elective or emergency surgery under general anesthesia.

The first filter in the diagnostic assessment of presence or absence of COVID-19 disease is history taking. This practice guideline specifically concerns patients who are asymptomatic based on a thorough history of current illness (no shortness of breath, cough, rhinorrhea, anosmia, etc.) [see Appendix 1] and without signs of fever or hypoxia on physical exam. When patients show any signs of infection, they should be considered as COVID-19 suspect and treated accordingly, thus not based on this guideline.

The aim of this practice guideline is to provide a flowchart for the pre-operative workup of patients reporting no symptoms of COVID-19 (after thorough history taking) and awaiting surgery under general anesthesia with the best available current evidence-base, while acknowledging the limitations of this knowledge base and minimizing the risks of unnecessary radiologic diagnostic tests.

Methods

A multidisciplinary working group was formed with representatives from surgery, radiology, anesthesiology, pulmonary medicine, infectious diseases and microbiology. The databases [Medline (via OVID), Embase (via Embase.com) and Google Scholar] were searched with relevant search terms until April 27, 2020. The detailed search strategies are depicted in Appendix 2. Both scientific literature and clinical considerations formed the flowchart.

Summary of the literature

COVID-19 has a median incubation time of 5 days with a range of 1 to 14 days (Wu, 2020). Following this incubation period, patients can develop mild to moderate symptoms, with clinical deterioration and severe disease usually occurring 5-10 days after symptom onset (Wu, 2020; Guan, 2020; Chan, 2020). Patients reporting no symptoms of COVID-19 after thorough history taking may be either without infection, asymptomatic or pre-symptomatic. An asymptomatic patient carries the SARS-CoV-2 virus but never experiences noticeable symptoms. A pre-symptomatic patient experiences no symptoms of COVID-19 at the time of evaluation, but will go on to subsequently develop COVID-19 symptoms in the future. When a patient reports no symptoms of COVID-19 during pre-operative screening, it is therefore impossible to make a clinically-relevant distinction between the three categories of without COVID-19 infection, asymptomatic COVID-19 infection, or pre-symptomatic COVID-19 infection. This means that patients who are initially asymptomatic, presymptomatic or mildly symptomatic can subsequently develop moderate to severe COVID-19 disease, placing them at significant risk for adverse post-operative outcomes i.e. ICU admittance or increased mortality (Aminian, 2020; Kluytmans, 2020; Lei, 2020; Li, Y, 2020; NVvH webinar, 2020). Comorbidities that are common to surgical populations, including hypertension, cardiovascular disease, COPD, asthma, and malignancies also place patients at significantly higher risk of severe COVID-19 disease (Yang, 2020; Zou, 2020). Effective screening of patients is therefore necessary to prevent post-operative development of severe COVID-19 disease in a vulnerable patient population.

In addition to the risk that COVID-19 poses to patients, COVID-19 may also pose a risk to health care workers and other hospitalized patients who are vulnerable to adverse COVID-19 outcomes (Heinzerling, 2020; Heneghan, 2020; Li, 2020). For example, one study reported that an undetected COVID-19 patient who underwent thoracic surgery may have infected six healthcare workers and five patients (Li Y, 2020). Another study reported that an undetected COVID-19 patient who underwent multiple aerosolizing procedures in 4 days of hospitalization may have infected 43 (35%) of 120 exposed hospital personnel (Heinzerling A, 2020). The understanding of this disease is rapidly evolving, but much remains unknown about the transmission of disease. However, growing evidence shows that, in contrast to SARS-CoV-1 and MERS, a significant proportion of COVID-19 infections may be highly infectious in periods that they are without symptoms or have mild symptoms, and that even persistently asymptomatic individuals shed SARS-CoV-2 and are capable of infecting other individuals who can subsequently develop severe disease (Arons, 2020; Chen, 2020; Chan, 2020; Du, 2020; Hu, 2020; Kimball, 2020; Kluytmans van den Bergh, 2020; Li P, 2020; Li R, 2020; Moriary, 2020; Qian, 2020; Rothe, 2020; Tong, 2020; Wei, 2020; Xia, 2020; Ye, 2020, Zhang, 2020). Serial evaluation of SARS-CoV-2 viral load in the nasopharynx also show highest levels of infectious viral shedding early in the disease, just prior to or at onset of symptomatology (To, 2020; Zou, 2020, Wolfel, 2020; Xia, 2020). A serial point prevalence survey in a skilled nursing facility showed that viral loads were similar between residents who tested positive before typical symptom onset and those who tested positive seven or more days after typical symptom onset. (Arons, 2020). Viable virus was isolated from specimens collected 6 days before to 8 days after the first evidence of typical symptoms. The authors speculated that impaired immune responses associated with aging and the high prevalence of underlying conditions, such as cognitive impairment and chronic cough, likely made it difficult to recognize early signs and symptoms in this population, as is likely the case in numerous nursing home and hospital settings in the Netherlands. To date, it is largely unknown what proportion of the total transmissions are caused by asymptomatic or presymptomatic carriers. One prospective study including 2147 patients concluded that virus infection rates of close contacts was 6.3% for symptomatic transmission and 4.1% for asymptomatic transmission. A prospective cohort study of 4950 close contacts showed that the proportion of asymptomatic and mild infections account for almost half of the confirmed cases among close contacts. The household contacts were the main transmission mode, and clinically more severe cases were more likely to pass the infection to their close contacts. Generally, the secondary cases were clinically milder than those of source cases (Luo, 2020). One study reported a mean probability of presymptomatic transmission of 37% (95% CI: 27.5% - 45%), which can be interpreted as the fraction of presymptomatic transmission events out of presymptomatic plus symptomatic transmission events (Ferretti et al, 2020). This is in line with estimates of 48% of transmission being presymptomatic in Singapore and 62% in Tianjin, China (Ganyani et al, 2020), and 44% in transmission pairs from various countries (He X., 2020). The infectiousness model of Ferretti et al suggests that the total contribution to R0 from presymptomatics is 0.9 (0.2 - 1.1), almost enough to sustain an epidemic on its own. (Ferretti, 2020). These results may have been affected by different types of bias, including recall bias. If the infector does not probably recall symptom onset, the incubation period would be overestimated resulting in an inflated proportion of presymptomatic transmissions (He X, 2020). Nonetheless, these data suggest that asymptomatic/mildly symptomatic SARS-CoV-2 patients pose a realistic risk to health-care workers, particularly during aerosol generating procedures (i.e. mask ventilation, intubation, bronchoscopy) and surgical procedures, and to other vulnerable hospitalized patients, through droplet and contact transmission in health-care settings. Transmission risks for asymptomatic/presymptomatic to mildly symptomatic patients are therefore of significantly higher consequence in the hospital compared to the community setting.

Identification of SARS-CoV-2 in patients without symptoms or limited symptoms is challenging and sensitivity and specificity of existing and new diagnostics are rapidly evolving. Nasopharyngeal swabs for SARS-CoV2 in symptomatic patients are prone to sampling error and have demonstrated diminished sensitivity in comparison to chest CT in a meta-analysis (Kim, 2020). Interpretation of this study, however, is limited by suboptimal reference tests, selection bias and heterogeneity. To date, there are no studies that report the sensitivity of CT in comparison to PCR or the yield of CT in addition to PCR in patient without symptoms. A relatively large proportion of PCR+ patients without symptoms appear to have changes on pulmonary CT. 12 of 19 (63%) asymptomatic patients from the Diamond Princess cruise ship in Japan had CT changes (vs 80% of symptomatic patients) (Hu, 2020; Inui, 2020). Another study reported that 37 out of 55 asymptomatic patients (67%) showed CT abnormalities (Wang Y, 2020). These data are limited by confirmation bias, however, they also suggest that CT may be a useful but under-characterized adjunct to PCR in peri-operative screening of asymptomatic patients with pulmonary involvement.

Conclusion

COVID-19 screening in asymptomatic surgery patients is important for three main reasons:

- 1. Patients may be in the incubation period of a COVID-19 infection and subsequently develop COVID-19 post-operatively, placing them at risk for adverse post-operative outcomes.
- 2. Patients may be asymptomatic/mildly symptomatic carriers and shedders of SARS-CoV-2 and place hospital workers at risk, particularly during aerosol generating procedures.
- 3. Patients may be asymptomatic/mildly symptomatic carriers and shedders of SARS-CoV-2 and place other hospitalized patients at risk, who are often in higher age groups with co-morbidities and at higher risk of severe COVID-19 disease.

Preliminary results of prospectively-collected data evaluating the diagnostic yield of pre-operative SARS-CoV-2 screening with SARS-CoV-2 PCR of nasopharyngeal swabs and chest CT

Since the publication of this practice guideline on April 2nd, 15 centers in the Netherlands have participated in the prospective collection of data on the diagnostic yield of nasopharyngeal swabs and chest CT (SCOUT-1 study, Principal investigators: Prof. dr. J. Stoker, Dr. H. Gietema, Prof. Dr. J. Prins, Dr. S. Gisbertz, Prof. Dr. M. Besselink & Prof. Dr. M. Boermeester). On April 23rd an interim analysis was performed on the first 900 patients without signs of infection awaiting surgery. Combined testing showed results indicative for COVID disease in 1-2% of the tested patients (positive PCR and/or CO-RADS 4-5 on chest CT). The percentage of positive patients solely based on chest CT was limited. The added value of chest CT when combined with nasopharyngeal swabs was low (0.3-0.4%).

Considerations

The committee's primary aim for the work-up for COVID-19 is to identify COVID-19 positive cases (high sensitivity) in order to limit transmission by rescheduling surgery, if possible, or allowing necessary precautions to be taken. Therefore, the committee initially advised that all adult patients requiring a surgical procedure under general anesthesia undergo pre-operative screening for COVID-19 infection through the use of SARS-CoV-2 PCR of a deep nasopharyngeal swab in conjunction with a low-dose chest CT (without iv contrast).

Preliminary data show that 1-2% Covid-19 infection among preoperative patients reporting no symptoms of COVID-19. This may seem to be a low percentage, however operative health care workers undergo repeated exposure during aerosol generating procedures or other risk baring procedures. Therefore, the cumulative exposure to SARS-CoV-2 positive patients for these HCW through aerosolization is assumed to be high. In addition, transmission to other patients remain an unknown risk factor. The committee's opinion is that this percentage justifies preoperative testing through the use of SARS-CoV-2 PCR of a deep nasopharyngeal swab.

However, the added value of chest CT is low. Therefore, the committee is of the opinion that there is no longer an indication for the use of chest CT in preoperative testing of asymptomatic patients. Therefore, the advice given by the committee on April 2nd has been adjusted.

Elective patients

The committee advises to test elective patients within 48 hours prior to surgery in an outpatient clinic setting, starting by thorough history taking and in Covid-19-symptom negative patients followed by Covid-19 screening using SARS-CoV-2 PCR.

In addition, we strongly recommend advising patients to comply with general directions regarding social distancing as stated by the government since this will likely lower the risk for COVID-19 disease at the time of operation.

Semi-acute and acute patients

It takes several hours (depending on the local setting) to get the results of PCR testing on nasopharyngeal swabs. The committee advises evaluation of options to increase the speed and availability of test results. First and foremost, it is important to perform PCR testing immediately when there is a surgical indication. One might consider testing in patients in whom surgery is expected, but not decided yet (i.e. test patients with suspicion of appendicitis immediately on presentation).

Second, the committee advises evaluation with local microbiology and laboratory departments to determine if PCR testing is possible via a faster diagnostic method in order to reduce the waiting time. If the results of PCR testing are unavailable at the time of surgery, the committee recommends that the patient be treated as highly suspect for COVID-19 and take precautions according to local protocol.

Should patients with COVID-19 be identified with PCR, the committee advises delaying elective surgery for at least 2 weeks in quarantine and to consider alternatives to surgery for (semi-)acute surgery if at all possible. Should surgery proceed in a COVID-19 patient, then appropriate peri-operative and operative hospital infectious disease / strict personal protective equipment (PPE) precautions should be used.

Pregnant women

This guideline does not apply to pregnant women.

Children

This guideline does not apply to children. Currently, a working group is working on a guideline for preoperative work-up in children.

Availability of PPE resources

In developing the recommendation, the committee has also weighed the limited availability of PPE in formulating recommendations. Currently, the limited availability of PPE in the Netherlands makes other solutions, such as increased use of isolation of patients and more general use of PPE, not possible in the evolving pandemic.

Policy after postponed surgery due to a positive test result

Should a patient have a positive nasopharyngeal swab or chest CT test result, the committee recommends postponing surgery for at least 14 days. If the patient remains asymptomatic in these 14 days, the committee recommends that the patient be considered negative and not undergo new testing. If the patient developed symptoms, the committee advises to discuss possible surgery or delay of surgery in a multidisciplinary meeting involving the treating surgical physician, infectious disease specialist, pulmonary physician and anesthesiologist before scheduling the patient for surgery.

Policy in case of repeat surgery

The committee advises testing a patient only once in case multiple surgeries within a short period of time is needed and, if the patient was admitted to the hospital and likely to be unexposed to potentially infected persons.

Legitimacy of the practice guideline

In adjusting the recommendations, the committee recognizes the continued limited evidence and an urgent need for more information about the utility of PCR in pre-operative screening. The committee also recognizes that the COVID-19 pandemic is dynamic with changes in background prevalence over time and by region. The parallel multi-center coordinated study to evaluate the utility of these diagnostics in identifying asymptomatic COVID-19 positive patients will continue and this data will be used to further evaluate the current guideline.

Recommendations/Aanbevelingen

The committee advises performing preoperative diagnostic testing in adult patients, reporting no symptoms indicative for COVID-19 infection (based on thorough history taking), prior to a surgical procedure under general anesthesia for COVID-19 infection using a deep nasopharyngeal swab for SARS-CoV-2 PCR testing (see flowchart).

De commissie adviseert om bij volwassenen zonder klachten die passen bij een mogelijke COVID-19 infectie (op basis van grondige anamnese) die een operatie onder algehele anesthesie ondergaan preoperatief onderzoek naar de mogelijke aanwezigheid van een COVID-19 infectie te verrichten door een diepe nasopharyngeale swab voor SARS-CoV-2 PCR (zie stroomschema).

Disclaimer 1

Hospitals may deviate from this practice guideline based on a locally-formulated multidisciplinary statement if they observe a low background prevalence of COVID-19 infection within their community and hospital populations, while being notified that there is no exact definition of 'low prevalence' nor exact knowledge of the number of transmission of one undetected infection within a hospital population.

Disclaimer 2

All associations involved have taken the greatest possible care in formulating the content of this Practice Guideline. Nevertheless, they accept no liability for any inaccuracies in this document, for any damages or for other consequences arising from or related to the use of this Practice Guideline.

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Appendix 1 Example history taking COVID-19

<u>Klachten</u>

'Ja' in als patiënt de afgelopen <u>48 uur</u> klachten heeft gehad van:

Hoesten: ja / nee / onbekend Dyspnoe: ja / nee / onbekend Koorts (≥38,0): ja / nee / onbekend Algehele malaise: ja / nee / onbekend Algehele spier- of gewrichtspijn: ja / nee / onbekend Hoofdpijn: ja / nee / onbekend Extreme vermoeidheid (nieuw): ja / nee / onbekend Keelpijn: ja / nee / onbekend Verkouden: ja / nee / onbekend Verlies van reuk: ja / nee / onbekend Buikpijn: ja / nee / onbekend Diarree: ja / nee / onbekend Braken: ja / nee / onbekend

Worden beschreven klachten beschouwd als mogelijk passend bij een COVID-19 infectie? ja / nee

Is patiënt recent (<2 weken) in het buitenland geweest? ja / nee / zo ja, welk land Heeft patiënt contact gehad met iemand die een bewezen COVID-19 infectie heeft? ja / nee / onbekend

Items based on history taking used in SCOUT study

Appendix 2 Search strategies

Search	Query
<u>#9</u>	Search #3 AND #8 AND #6
<u>#8</u>	Search ("COVID-19"[Supplementary Concept] OR "severe acute respiratory syndrome coronavirus 2"[Supplementary Concept] OR (("Coronavirus"[MeSH Terms] OR "Coronavirus Infections"[Mesh:NoExp] OR pneumonia virus*[tiab] OR cov[tiab]) AND (outbreak[tiab] OR wuhan[tiab] OR novel[all] OR 19[tiab] OR 2019[tiab] OR epidem*[tiab] OR epidemy[all] OR epidemic*[all] OR pandem*[all] OR new[tiab])) OR coronavirus*[tiab] OR corona virus*[tiab] OR ncov[tiab] OR 2019ncov[tiab] OR covid19[tiab] OR "covid 19"[tiab] OR "sars cov 2"[tiab] OR sars2[tiab] OR "ncov 2019"[tiab] OR "sars coronavirus 2"[tiab] OR "sars corona virus 2"[tiab] OR "severe acute respiratory syndrome cov 2"[tiab] OR "severe acute respiratory syndrome cov2"[tiab] OR severe acute respiratory syndrome cov*[tiab] OR cov2[tiab]) AND ("2019/12"[Date - Entrez] : "3000"[Date - Entrez]) Sort by: Best Match
<u>#7</u>	Search #4 AND #6

Search	Query
<u>#6</u>	Search #2 OR #5
<u>#5</u>	Search "Aerosols" [Mesh] OR "Disease Transmission, Infectious" [Mesh] OR "Cross Infection" [Mesh] OR "Safety" [Mesh] OR nosocomial infection* [tiab] OR cross infection* [tiab] OR hospital infection* [tiab] OR disease transmission [tiab] OR infection transfer [tiab] OR "infection transmission" [tiab] OR "infectious transmission" [tiab] OR "transmission of infection" [tiab] OR "transmission of infections" [tiab] OR "transmission of infectious disease" [tiab] OR "transmission of infectious diseases" [tiab] OR contamination* [tiab] OR infection risk* [tiab] OR occupational hazar* [tiab] OR virus transmission [tiab] OR viral transmission[tiab] OR infection risk* [tiab] OR safe* [tiab] OR shed* [tiab] OR aerogenic transmission[tiab] OR aerosol* [tiab]
<u>#4</u>	Search ("Severe Acute Respiratory Syndrome"[Mesh] OR "SARS Virus"[Mesh] OR "COVID- 19"[Supplementary Concept] OR "severe acute respiratory syndrome coronavirus 2"[Supplementary Concept] OR (("Coronavirus"[MeSH Terms] OR "Coronavirus Infections"[Mesh:NoExp] OR pneumonia virus*[tiab] OR cov[tiab]) AND (outbreak[tiab] OR wuhan[tiab] OR novel[all] OR 19[tiab] OR 2019[tiab] OR epidem*[tiab] OR epidemy[all] OR epidemic*[all] OR pandem*[all] OR new[tiab])) OR coronavirus*[tiab] OR corona virus*[tiab]) AND ("2019/12"[Date - Entrez] : "3000"[Date - Entrez]) OR (ncov[tiab] OR 2019ncov[tiab] OR covid19[tiab] OR "covid 19"[tiab] OR sars*[tiab] OR severe acute respiratory syndrome[tiab] OR sudden acute respiratory syndrome[tiab] OR mers[tiab] OR middle east respiratory syndrome[tiab])
<u>#2</u>	Search "Asymptomatic Diseases"[Mesh] OR asymptomatic[tiab] OR pre-symptomatic*[tiab] OR presymptomatic[tiab] OR mild*[tiab] OR no sign[tiab] OR no signs[tiab]

Search	Query
<u>#23</u>	Search #22 AND #17
<u>#22</u>	Search ((coronavirus*[tiab] OR corona virus*[tiab] OR pneumonia virus*[tiab] OR cov[tiab] OR ncov[tiab]) AND (outbreak[tiab] OR wuhan[tiab])) OR covid19[tiab] OR "covid 19"[tiab] OR ((coronavirus*[tiab] OR corona virus*[tiab]) AND 2019[tiab]) OR "sars cov 2"[tiab] OR sars2[tiab] OR new coronavirus*[tiab] OR new corona virus*[tiab] OR "ncov 2019"[tiab] OR "sars coronavirus 2"[tiab] OR "sars corona virus 2"[tiab] OR "severe acute respiratory syndrome cov 2"[tiab] OR "severe acute respiratory syndrome cov2"[tiab] Filters: Publication date from 2019/12/01
<u>#21</u>	Search ((coronavirus*[tiab] OR corona virus*[tiab] OR pneumonia virus*[tiab] OR cov[tiab] OR ncov[tiab]) AND (outbreak[tiab] OR wuhan[tiab])) OR covid19[tiab] OR "covid 19"[tiab] OR ((coronavirus*[tiab] OR corona virus*[tiab]) AND 2019[tiab]) OR "sars cov 2"[tiab] OR sars2[tiab] OR new coronavirus*[tiab] OR new corona virus*[tiab] OR "ncov 2019"[tiab] OR "sars coronavirus 2"[tiab] OR "sars corona virus 2"[tiab] OR "severe acute respiratory syndrome cov 2"[tiab] OR "severe acute respiratory syndrome cov2"[tiab]
<u>#20</u>	Search #18 AND #19
<u>#19</u>	Search "Sensitivity and Specificity"[MeSH] OR specificit*[tw] OR screening[tw] OR accura*[tw] OR reference value*[tw] OR false positive[tw] OR false negative[tw] OR predictive value*[tw] OR roc[tw] OR likelyhood*[tw] OR likelihood*[tw]
<u>#18</u>	Search #1 AND #17
<u>#17</u>	Search #10 OR #12 OR #11 OR #16
<u>#16</u>	Search "Polymerase Chain Reaction"[Mesh] OR polymerase chain reaction[tiab] OR pcr[tiab]
<u>#12</u>	Search ("Tomography, X-Ray Computed"[Mesh] OR computed tomograph*[tiab] OR ct[tiab] OR cts[tiab] OR cat scan*[tiab] OR computer assisted tomograph*[tiab] OR computerized

Search	Query
	tomograph*[tiab] OR computerised tomograph*[tiab] OR computed x ray tomograph*[tiab] OR computed xray tomograph*[tiab]) AND ("Thorax"[Mesh] OR thorax[tiab] OR thorac*[tiab] OR chest[tiab])
<u>#11</u>	Search (Ultrasonography"[Mesh] OR "diagnostic imaging"[Subheading] OR ultraso*[tiab] OR sonograph*[tiab] OR echograph*[tiab] OR echocardiograph*[tiab] OR echotomograph*[tiab]) AND ("Thorax"[Mesh] OR thorax[tiab] OR thorac*[tiab] OR chest[tiab])
<u>#10</u>	Search "Radiography, Thoracic"[Mesh] OR "X-thorax"[tiab] OR thoracic radiograph*[tiab]
<u>#1</u>	Search "Severe Acute Respiratory Syndrome"[Mesh] OR "SARS Virus"[Mesh] OR "COVID- 19"[Supplementary Concept] OR "severe acute respiratory syndrome coronavirus 2"[Supplementary Concept] OR 2019ncov[tiab] OR 2019 ncov[tiab] OR novel coronavirus*[tiab] OR novel corona virus*[tiab] OR ((coronavirus*[tiab] OR corona virus*[tiab] OR pneumonia virus*[tiab] OR cov[tiab] OR ncov[tiab]) AND (outbreak[tiab] OR wuhan[tiab])) OR covid19[tiab] OR covid 19[tiab] OR ((coronavirus*[tiab] OR corona virus*[tiab]) AND 2019[tiab]) OR sars*[tiab] OR new coronavirus*[tiab] OR new corona virus*[tiab] OR ncov 2019[tiab] OR "sars corona virus"[tiab] OR "sars-like cov"[tiab] OR "sars-like coronavirus"[tiab] OR sars-related cov[tiab] OR sars-related coronavirus[tiab] OR sars-cov[tiab] OR "severe acute respiratory syndrome-like coronavirus"[tiab] OR "severe acute respiratory syndrome-related coronavirus[tiab] OR hcov-sars[tiab] OR human sars coronavirus[tiab] OR sars cov[tiab] OR sars associated coronavirus"[tiab] OR sars coronavirus[tiab] OR sars virus[tiab] OR sars-cov[tiab] OR sars-cov[tiab] OR sars-cov[tiab] OR sars cov[tiab] OR sars-associated coronavirus[tiab] OR sars virus[tiab] OR sars cov[tiab] OR sars-associated coronavirus[tiab] OR severe acute respiratory syndrome coronavirus[tiab] OR sars-associated coronavirus[tiab] OR sars coronavirus[tiab] OR sars virus[tiab] OR sars-associated coronavirus[tiab] OR severe acute respiratory syndrome coronavirus[tiab] OR mers-cov[tiab] OR middle east respiratory syndrome coronavir*[tiab] OR severe acute respiratory infection*[tiab]
In addit	ion to abovementioned search specific strategies, on a daily basis all pre-prints are screened

In addition to abovementioned search specific strategies, on a daily basis all pre-prints are screened with the relevant terms for COVID-19 (covid19|"covid 19"|2019ncov|"2019 ncov|cov|coronavirus"| "2019 novel|new coronavirus|cov"| "wuhan coronavirus|cov|ncov|outbreak"| "wuhan*coronavirus|cov|ncov|outbreak"|

"wuhan**coronavirus|cov|ncov|outbreak"|"coronavirus|cov|ncov*wuhan")

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