



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 will prospectively collect data on the performed nasopharyngeal swabs and chest CTs. If these results show that the proposed strategy has no or limited value, the practice guideline will be changed. For the next few weeks, there will be a weekly evaluation by the committee to evaluate the obtained results.

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) 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 14, 2020. The detailed search strategies are depicted in Appendix 1. 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 (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). 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. It is likely that PCR sensitivity is higher in earlier stages of disease when shedding peaks and that patients with severe disease have higher viral loads than those with asymptomatic/mild disease (Liu Y, 2020, Wolfel R, 2020). A relatively large proportion of PCR+ patients without symptoms appear to have changes on pulmonary CT. 12 of 19 (63%) asymptomatic patients reported CT abnormalities in a Chinese cohort and 44 of 82 (54%) 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 comorbidities and at higher risk of severe COVID-19 disease.

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 take necessary precautions. Therefore, the committee advises 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).

In general, the utility of CT scans for pre-operative screening is dependent upon the local background prevalence of COVID-19 disease. This data is currently lacking and therefore we are unable to determine a minimum rate of infections among the population or health care workers which could guide us in deciding when testing every patient scheduled for surgery would be beneficial. Currently, there is a clear difference in prevalence of SARS-CoV-2 in different parts of the Netherlands. The rapid changes in prevalence rates of COVID-19 during the spread of SARS-CoV-2 makes adjustment for known prevalence in recommendations challenging.

The risks of false positive and false negative findings on CT, exposure of pre-operative patients to potentially contaminative environment of the CT room, and radiation exposure must be weighed against the risk of missing COVID-19 infections for patients, health care workers, and hospitalized patients. If an optimized scanning protocol on a modern CT scanner is used, a dose-length-product (DLP) below 190 mGy·cm on average is feasible. This corresponds with an effective dose less than 5 mSv. There is no need for high-dose, high-resolution CT or the use of iv contrast in this setting. The latter eliminates contrast allergy issues and risk of renal damage.

Elective patients

The committee advises to test elective patients within 48 hours prior to surgery in an outpatient clinic setting. One may consider starting with PCR testing await the test result and withhold a chest CT if the PCR is positive for a COVID-19 infection. However, this might have severe logistical implications (patients need to visit the hospital repeatedly) and joint testing of PCR and CT may be a more desirable and practical approach, depending on the local situation.

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 patients

In semi-acute patients (those whose surgery can be postponed for more than 24 hours) who are admitted to the hospital, one can choose to start with PCR testing and cancel chest CT in SARS-CoV-2 PCR+ patients.

Acute patients

In acute patients (those who need surgery immediately) PCR testing will, in contrast to a chest CT, not provide a test result before the surgical procedure will be executed. However, it is deemed valuable to know PCR status for the postoperative phase, in continuing or ceasing contact and droplet precautions. Therefore, we advise, also in acute patients, to perform PCR testing in conjunction to chest CT. Of course, chest CT should only be performed in acute situations if the clinical condition of the patient is stable enough to undergo this procedure.

One should realize that a CO-RADS 1-2 chest CT in an asymptomatic patient does not fully exclude a COVID-19 infection in these patients and careful treatment according to local protocol remains imminent. If history of present illness is not possible (i.e. trauma-patient in severe condition) or there

is minimal doubt regarding symptoms, it is advisable to consider the patient COVID-19 positive and take precautions accordingly.

The committee does recognize that hospitals may differ in their access to testing resources (like PCR test availability or CT capacity), however, in the committee's opinion, peri-operative COVID-19 infections should be minimized as much as possible. If new evidence appears indicating that a more restrictive policy is justified, the committee will adjust the current standpoint.

Should patients with COVID-19 be identified with PCR or chest CT, the committee advises to delay 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

In children avoidance of CT is wanted. 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.

CO-RADS

The CO-RADS grading system as proposed by the Dutch Society of Radiology, should reflect the impression of the reporting radiologist's level of suspicion on CT imaging characteristics alone (without clinical parameters) (COVID working group of the Dutch Radiological Society, 2020). This score is based on international CT findings in COVID-19 patients. However, the score is not validated nor properly tested in asymptomatic populations. It is likely that an increasing number of false positive CO-RADS 3 scores will be seen in populations with a low pretest probability of COVID-19 and in patients without symptoms. Therefore, the working group advises to discuss CO-RADS 3 patients in a multidisciplinary team to determine the level of precautions. This multidisciplinary team should ideally include the respective surgeon, anesthesiologist, pulmonary physician, microbiologist, infectious disease specialist and a radiologist. In addition, it is likely that an increasing number of false negative CT scores (CO-RADS 1 > 2) will be seen in patients without symptoms, as CT scans can be negative within the first days of the disease (Bernheim, 2020) or in patients without lung involvement. Hence, chest CT should be performed in addition to nasopharyngeal SARS-CoV-2 PCR testing.

The COVID working group of the Dutch Radiological Society advises to scan asymptomatic patients on a non-COVID CT scanner, if one has the availability of a dedicated COVID-CT scan.

Table 1. CO-RADS level of suspicion COVID-19 infection (COVID working group of the Dutch Radiological Society, 2020)

	Chance of COVID-19	CT findings
CO-RADS 1	Very low	Normal or non-infectious abnormalities
CO-RADS 2	Low	Abnormalities consistent with infections
		other than COVID-19
CO-RADS 3	Unsure	Unclear whether COVID-19 is present

CO-RADS 4	High	Abnormalities suspicious for COVID-19
CO-RADS 5	Very high	Typical COVID-19

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.

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.

Legitimacy of the practice guideline

In developing the recommendations, the committee recognizes that there is currently insufficient evidence and an urgent need for more information about the utility of CT and PCR in pre-operative screening. There is a parallel multi-center coordinated study to evaluate the utility of these diagnostics in identifying asymptomatic COVID-19 positive patients and this data will be used to re-evaluate the current guideline within one month's time.

Recommendations/Aanbevelingen

Adults

The committee advises to perform diagnostic testing in adult patients prior to a surgical procedure under general anesthesia for COVID-19 infection using a deep nasopharyngeal swab for SARS-CoV-2 PCR testing as well as a low-dose chest CT without contrast (see flowchart).

Children

The committee advises to perform diagnostic testing in pediatric patients prior to a surgical procedure under general anesthesia for COVID-19 infection using a deep nasopharyngeal swab for SARS-CoV-2 PCR testing. The committee advises against the use of low-dose CT.

Volwassenen

De commissie adviseert om bij volwassenen 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 en lowdose CT-thorax zonder contrast (zie flowchart).

Kinderen

De commissie adviseert om bij kinderen 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.

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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Literature:

Aminian, A., Safari, S., Razeghian-Jahromi, A., Ghorbari, M., Delaney, C.P. (2020) COVID-19 Outbreak and Surgical Practice: Unexpected Fatality in Perioperative Period. Annals of Surgery

Bao, L., Deng, W., Gao, H., Xiao, C., Liu, J., Xue, J., ... & Qi, F. (2020). Reinfection could not occur in SARS-CoV-2 infected rhesus macaques. bioRxiv.

Bernheim, A., Mei, X., Huang, M., Yang, Y., Fayad, Z. A., Zhang, N., ... & Li, S. (2020). Chest CT findings in coronavirus disease-19 (COVID-19): relationship to duration of infection. Radiology, 200463.

Chen, Y., Wang, A., Yi, B., Ding, K., Wang, H., Wang, J., ... & Xu, G. (2020). The epidemiological characteristics of infection in close contacts of COVID-19 in Ningbo city. *Chinese Journal of Epidemiology*, 41(0), 0-0.

Chan, J. F. W., Yuan, S., Kok, K. H., To, K. K. W., Chu, H., Yang, J., ... & Tsoi, H. W. (2020). A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. The Lancet, 395(10223), 514-523.

Du, Z., Xu, X., Wu, Y., Wang, L., Cowling, B. J., & Meyers, L. A. (2020). The serial interval of COVID-19 from publicly reported confirmed cases. medRxiv.Guan, W. J., Ni, Z. Y., Hu, Y., Liang, W. H., Ou, C. Q., He, J. X., ... & Du, B. (2020). Clinical characteristics of coronavirus disease 2019 in China. New England of Journal Medicine.

Ferretti, L., Wymant, C., Kendall, M., Zhao, L., Nurtay, A., Abeler-Dörner, L., ... & Fraser, C. (2020). Quantifying SARS-CoV-2 transmission suggests epidemic control with digital contact tracing. *Science*.

Ganyani, T., Kremer, C., Chen, D., Torneri, A., Faes, C., Wallinga, J., & Hens, N. (2020). Estimating the generation interval for COVID-19 based on symptom onset data. *medRxiv*.

Guan, W. J., Ni, Z. Y., Hu, Y., Liang, W. H., Ou, C. Q., He, J. X., ... & Du, B. (2020). Clinical characteristics of coronavirus disease 2019 in China. New England Journal of Medicine.

He, X., Lau, E. H., Wu, P., Deng, X., Wang, J., Hao, X., ... & Mo, X. (2020). Temporal dynamics in viral shedding and transmissibility of COVID-19. *medRxiv*.

Hu, Z., Song, C., Xu, C., Jin, G., Chen, Y., Xu, X., ... & Wang, J. (2020). Clinical characteristics of 24 asymptomatic infections with COVID-19 screened among close contacts in Nanjing, China. Science China Life Sciences, 1-6.

Inui, S., Fujikawa, A., Jitsu, M., Kunishima, N., Watanabe, S., Suzuki, Y., Umeda, S., Uwabe, Y. (2020). Chest CT Findings in Cases from the Cruise Ship "Diamond Princess" with Coronavirus Disease 2019 (COVID-19) Radiology: Cardiothoracic Imaging 2(2), e200110. https://dx.doi.org/10.1148/ryct.2020200110

Kim, H., Hong, H., Yoon, S. Y. (2020) Diagnostic Performance of CT and Reverse Transcriptase-Polymerase Chain Reaction for Coronavirus Disease 2019: A Meta-Analysis. Radiology. https://pubs.rsna.org/doi/10.1148/radiol.2020201343

Kimball, A. (2020). Asymptomatic and Presymptomatic SARS-CoV-2 Infections in Residents of a Long-Term Care Skilled Nursing Facility—King County, Washington, March 2020. *MMWR. Morbidity and Mortality Weekly Report*, 69.

Kluytmans- van den Bergh M, Buiting A, Pas S, Bentvelsen R, Van den Bijlaardt W, Van Oudheusden A, Van Rijen M, Verweij J, Koopmans M, Kluytmans J. (2020). SARS-CoV-2 infection in 86 healthcare workers in two Dutch hospitals in March 2020: a cross-sectional study with short-term follow-up. Available at: https://www.medrxiv.org/content/10.1101/2020.03.23.20041913v1

Lei, S., Jiang, F., Su, W., Chen, C., Chen, J., Mei, W., ... & Xia, Z. Y. (2020). Clinical characteristics and outcomes of patients undergoing surgeries during the incubation period of COVID-19 infection. *EClinical Medicine*, 100331.

Chen Yi WA, Yi Bo, Ding Keqin, Wang Haibo, Wang Jianmei, Shi Hongbo, Wang Sijia, Xu Guozhang. The epidemiological characteristics of infection in close contacts of COVID-19 in Ningbo city. Chinese Journal of Epidemiology 2020; 41(0): 0

Li, P., Fu, J. B., Li, K. F., Chen, Y., Wang, H. L., Liu, L. J., ... & Tong, Z. D. (2020). Transmission of COVID-19 in the terminal stage of incubation period: a familial cluster. *International Journal of Infectious Diseases*.

Li, Y. K., Peng, S., Li, L. Q., Wang, Q., Ping, W., Zhang, N., & Fu, X. N. (2020). Clinical and Transmission Characteristics of Covid-19—A Retrospective Study of 25 Cases from a Single Thoracic Surgery Department. *Current Medical Science*, 1.

Li, R., Pei, S., Chen, B., Song, Y., Zhang, T., Yang, W., & Shaman, J. (2020). Substantial undocumented infection facilitates the rapid dissemination of novel coronavirus (SARS-CoV2). Science.Long, C., Xu, H., Shen, Q., Zhang, X., Fan, B., Wang, C., ... & Li, H. (2020). Diagnosis of the Coronavirus disease (COVID-19): rRT-PCR or CT?. *European Journal of Radiology*, 108961. Liu, Y., Yan, L. M., Wan, L., Xiang, T. X., Le, A., Liu, J. M., ... & Zhang, W. (2020). Viral dynamics in mild and severe cases of COVID-19. The Lancet Infectious Diseases.

Luo, L, Liu, D., Liao, X, Wu, X., & Mao, C. (2020), Modes of Contact and Risk of Transmission in COVID-19: A Prospective Cohort Study 4950 Close Contact Persons in Guangzhou of China. Lancet preprint available at

SSRN: https://ssrn.com/abstract=3566149 or http://dx.doi.org/10.2139/ssrn.3566149

Mizumoto, K., Kagaya, K., Zarebski, A., & Chowell, G. (2020). Estimating the asymptomatic proportion of coronavirus disease 2019 (COVID-19) cases on board the Diamond Princess cruise ship, Yokohama, Japan, 2020. *Eurosurveillance*, 25(10).

Moriarty, L., Plucinski, M., Marston, B., Kurbatova, E., Knust, B., Murray,& Richards, J. (2020). Public Health Responses to COVID-19 Outbreaks on Cruise Ships — Worldwide, February–March 2020 MMWR. Morbidity and Mortality Weekly Report 69(12) Available at: https://dx.doi.org/10.15585/mmwr.mm6912e3

COVID working group of the Dutch Radiological Society (2020) COVID-19 CORADS classification. https://www.radiologen.nl/nieuws/handreiking-standaardverslag-ct-thorax-covid-19

Okba, N., Marcel A. Müller, M., Li, W., Wang, C., GeurtsvanKessel, GH., ...& Haagmans B. SARS-CoV-2 specific antibody responses in COVID-19 patients. Preprint unpublished. Available at: https://www.medrxiv.org/content/10.1101/2020.03.18.20038059v1.full.pdf

Oral communications from Italian surgeons, webinar NVvH march 20th and 24th 2020

Qian, G., Yang, N., Ma, A. H. Y., Wang, L., Li, G., Chen, X., & Chen, X. (2020). A COVID-19 Transmission within a family cluster by presymptomatic infectors in China. *Clinical Infectious Diseases*.

Rothe, C., Schunk, M., Sothmann, P., Bretzel, G., Froeschl, G., Wallrauch, C., ... & Seilmaier, M. (2020). Transmission of 2019-nCoV infection from an asymptomatic contact in Germany. New England Journal of Medicine.

To, K., Tsang, O., Leung, W., Tam, A., Wu, T., Lung, D., & Yuen, K. (2020). Temporal profiles of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2: an observational cohort study The Lancet Infectious Diseases. Available at https://dx.doi.org/10.1016/s1473-3099(20)30196-1

Tong, Z. D., Tang, A., Li, K. F., Li, P., Wang, H. L., Yi, J. P., ... & Yan, J. B. (2020). Potential Presymptomatic Transmission of SARS-CoV-2, Zhejiang Province, China, 2020. *Emerging infectious diseases*, 26(5).

Wang, Y., Liu, Y., Liu, L., Wang, X., Luo, N., & Ling, L. (2020). Clinical outcome of 55 asymptomatic cases at the time of hospital admission infected with SARS-Coronavirus-2 in Shenzhen, China. *The Journal of infectious diseases*.

Wei WE, Li Z, Chiew CJ, Yong SE, Toh MP, Lee VJ. Presymptomatic Transmission of SARS-CoV-2 — Singapore, January 23—March 16, 2020. MMWR Morb Mortal Wkly Rep. ePub: 1 April 2020. DOI: http://dx.doi.org/10.15585/mmwr.mm6914e1external icon

Wolfel R et al, Virological assessment of hospitalized cases of coronavirus disease 2019, https://www.medrxiv.org/content/10.1101/2020.03.05.20030502v1.full.pdf

Wu, Z., & McGoogan, J. M. (2020). Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. Jama.

Xia, W., Liao, J., Li, C., Li, Y., Qian, X., Sun, X., ... & Liu, J. (2020). Transmission of corona virus disease 2019 during the incubation period may lead to a quarantine loophole. *medRxiv*.

Xie, X., Zhong, Z., Zhao, W., Zheng, C., Wang, F., & Liu, J. (2020). Chest CT for typical 2019-nCoV pneumonia: relationship to negative RT-PCR testing. Radiology, 200343.

Yang, J., Zheng, Y., Gou, X., Pu, K., Chen, Z., Guo, Q., ... & Zhou, Y. (2020). Prevalence of comorbidities in the novel Wuhan coronavirus (COVID-19) infection: a systematic review and meta-analysis. International Journal of Infectious Diseases.

Ye, F., Xu, S., Rong, Z., Xu, R., Liu, X., Deng, P., ... & Xu, X. (2020). Delivery of infection from asymptomatic carriers of COVID-19 in a familial cluster. *International Journal of Infectious Diseases*.

Zhang, X., Chen, W., Hu, C., Huang, L., Hu, Z., Zeng, Y., ... & Yi, Y. (2020). Characterization of a big family cluster infection associated with SARS-Cov-2 in Nanjing district.

Zhou, F., Yu, T., Du, R., Fan, G., Liu, Y., Liu, Z., ... & Guan, L. (2020). Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. The Lancet.



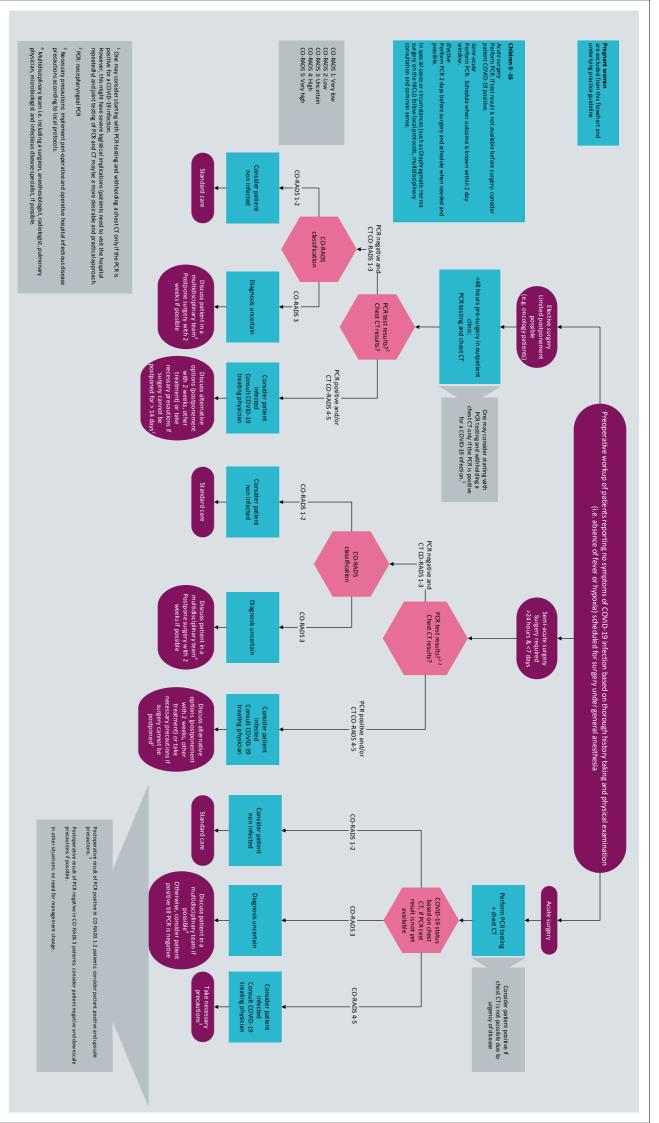
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<u>#17</u>	Search #14 AND #16	<u>233</u>
<u>#16</u>	Search "Asymptomatic Diseases" [Mesh] OR asymptomatic[tiab] OR pre- symptomatic*[tiab] OR presymptomatic[tiab] OR mild*[tiab]	531373
<u>#14</u>	Search ("COVID-19"[Supplementary Concept] OR "severe 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 "severe acute respiratory syndrome cov 2"[tiab] OR "severe acute respiratory syndrome cov*[tiab] OR cov2[tiab]) AND ("2019/12"[Date - Entrez])	

Search	Query	Items found
<u>#23</u>	Search #22 AND #17	<u>166</u>
#22	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 "severe acute respiratory syndrome cov 2"[tiab] OR "severe acute respiratory syndrome cov 2"[tiab] Filters: Publication date from 2019/12/01	<u>1576</u>
#21	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 "severe acute respiratory syndrome cov 2"[tiab] OR "severe acute respiratory syndrome cov2"[tiab]	<u>2552</u>
<u>#20</u>	Search #18 AND #19	<u>326</u>
#19	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]	2690072
<u>#18</u>	Search #1 AND #17	<u>1534</u>
<u>#17</u>	Search #10 OR #12 OR #11 OR #16	1184792
#16	Search "Polymerase Chain Reaction" [Mesh] OR polymerase chain reaction [tiab] OR pcr[tiab]	815485
#12	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 tomograph*[tiab] OR computerised tomograph*[tiab] OR	71470

Search	Query	Items found
	computed x ray tomograph*[tiab] OR computed xray tomograph*[tiab]) AND ("Thorax"[Mesh] OR thorax[tiab] OR thorac*[tiab] OR chest[tiab])	
#11	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])	352018
#10	Search "Radiography, Thoracic"[Mesh] OR "X-thorax"[tiab] OR thoracic radiograph*[tiab]	<u>39381</u>
#1	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 covonavirus[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-cov[tiab] OR sars-associated coronavirus[tiab] OR severe acute respiratory syndrome coronavirus[tiab] OR severe acute respiratory syndrome coronavirus[tiab] OR severe acute respiratory syndrome coronavirus[tiab] OR mers vir* [tiab] OR mers-cov[tiab] OR middle east respiratory syndrome coronavir* [tiab] OR severe acute respiratory infection* [tiab]	13402

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"|

[&]quot;wuhan**coronavirus|cov|ncov|outbreak"|"coronavirus|cov|ncov*wuhan")



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