Radiology

Use of Chest Imaging in the Diagnosis and Management of COVID-19: A WHO Rapid Advice Guide

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The World Health Organization (WHO) undertook the development of a rapid guide on the use of chest imaging in the diagnosis and management of coronavirus disease 2019 (COVID-19). The rapid guide was developed over 2 months by using standard WHO processes, except for the use of "rapid reviews" and online meetings of the panel. The evidence review was supplemented by a survey of stakeholders regarding their views on the acceptability, feasibility, impact on equity, and resource use of the relevant chest imaging modalities (chest radiography, chest CT, and lung US). The guideline development group had broad expertise and country representation. The rapid guide includes three diagnosis recommendations and four management recommendations. The recommendations cover patients with confirmed or who are suspected of having COVID-19 with different levels of disease severity, throughout the care pathway from outpatient facility or hospital entry to home discharge. All recommendations are conditional and are based on low certainty evidence (n = 2), or expert opinion (n = 3). The remarks accompanying the recommendations suggest which patients are likely to benefit from chest imaging and what factors should be considered when choosing the specific imaging modality. The guidance offers considerations about implementation, monitoring, and evaluation, and also identifies research needs.

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Acluster of pneumonia cases in Wuhan, China was first Areported to the World Health Organization (WHO) Country Office in China on December 31, 2019 (1). Soon thereafter, a novel coronavirus was identified as the causative agent (2–4). This virus was named severe acute respiratory syndrome coronavirus 2 and the associated disease was named coronavirus disease 2019 (COVID-19) (5). Since December 2019, COVID-19 has rapidly spread from Wuhan to other parts of China and throughout the world. On January 30, 2020, WHO declared the outbreak a public health emergency of international concern and on March 11, 2020, WHO characterized the outbreak as a pandemic (6,7).

The diagnosis of COVID-19 is currently confirmed with identification of viral RNA in reverse transcriptase polymerase chain reaction. Chest imaging has been considered as part of the diagnostic work-up of symptomatic patients suspected of having COVID-19 in settings where laboratory testing (reverse transcriptase polymerase chain reaction) is not available or results are delayed or are initially negative in the presence of symptoms attributable to COVID-19.

COVID-19 manifests with nonrespiratory symptoms as well as respiratory symptoms that are nonspecific and of variable severity, ranging from mild to life-threatening, which may demand advanced respiratory assistance and artificial ventilation. Imaging has been also considered to complement clinical evaluation and laboratory parameters in the management of patients already diagnosed with COVID-19 (1).

A recent international survey conducted by the International Society of Radiology and the European Society of Radiology found important variations in imaging practices related to COVID-19 (8). Several countries requested advice from WHO on the role of chest imaging in the diagnostic work-up of patients with probable or who are

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Abbreviations

COVID-19 = coronavirus disease 2019, GDG = guideline development group, GRADE = Grading of Recommendations Assessment, Development, and Evaluation, PICO = Population, Intervention, Comparison, and Outcome, WHO = World Health Organization

Summary

The guide includes seven recommendations covering patients with confirmed or who are suspected of having coronavirus disease 2019 with different levels of disease severity, throughout the care pathway from outpatient facility or hospital entry to home discharge.

Key Results

- The rapid guide includes three diagnosis recommendations and four management recommendations covering patients with confirmed or who are suspected of having coronavirus disease 2019 with different levels of disease severity, throughout the care pathway from outpatient facility or hospital entry to home discharge.
- The rapid guide offers considerations about implementation, monitoring, and evaluation, and also identifies research needs.
- The guide will be relevant for clinicians, hospital managers and planners, policymakers, hospital architects, biomedical engineers, medical physicists, logistics staff, infection prevention and control officers, and staff involved in water and sanitation tasks.

suspected of having COVID-19 and in the clinical management of patients with confirmed COVID-19. As a consequence, WHO undertook the development of a rapid guide on the use of chest imaging in the diagnosis and management of COVID-19 (9).

Materials and Methods

The development of this rapid advice guide followed the process outlined in the WHO handbook for guideline development (10), which used the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) methodology (11). Given the nature of the emergency, the process was implemented within a time frame of 2 months. The reporting of this guide followed the Reporting Items for Practice Guidelines in Healthcare checklist (12). The main target audience of the guidance are health professionals involved in the diagnosis and management of COVID-19.

Group Composition

In conformity with the WHO process, the following bodies were established: a core group (coordination role), a steering group (advisory role), a guideline development group (GDG; the expert panel), and an external review group (peer review role). Membership of the GDG and the external review group included experts from 10 high-income countries and 14 low-and middle-income countries. In addition, a systematic review team was contracted to conduct a rapid systematic review for each of the guidance's questions. Appendix E1 (online) provides the details on group composition and roles and list of contributors.

Management of Declaration of Interests

All experts declared their interests prior to participation in the guideline development processes and meetings. All declarations

were managed following WHO regulations on a case-by-case basis and were communicated to the experts at the start of the first GDG meeting. A summary is included in Appendix E2 (online). All authors have completed the ICMJE uniform disclosure form at *http://www.icmje.org/coi_disclosure.pdf* and declare no conflicts.

Identification of the Key Questions

The core group reviewed formal consensus statements from professional bodies and/or national health authorities on the use of chest imaging in COVID-19, with the assistance of the GDG and the International Society of Radiology. Informed by these statements (8,13), the core group formulated the key questions by using the Population, Intervention, Comparison, and Outcome (PICO) format, with the help of the steering group, the GDG, and the systematic review team (see Appendix E3 [online]). The intended populations are those in whom a COVID-19 diagnosis needs to be established and those in whom the diagnosis is already established. The questions addressed three chest imaging modalities (chest radiography, chest CT, and lung US); three questions addressed diagnosis whereas four questions addressed management. These key questions formed the basis of the systematic reviews and of the development of recommendations.

Identification of the Critical Outcomes

The core group drafted a list of outcomes relevant for each PICO question that was circulated to the GDG for importance rating (14). The list included three types of outcomes: diagnostic accuracy, clinical outcomes, and health systems outcomes (see Appendix E3 [online]). The outcomes selected for each question and the scores assessing their importance are included in the evidence-to-decision tables presented in Appendix E4 (online).

Evidence Identification and Retrieval, Quality Assessment, and Synthesis of Evidence

A systematic review team performed a rapid review (initial search on April 15, 2020, with subsequent literature surveillance through April 29, 2020, and update on May 28, 2020). Refer to the full guideline publication for more information on the systematic review (15). The systematic review team produced a GRADE evidence profile for each PICO question (16). According to the GRADE methodology, the certainty of evidence is categorized into "high," "moderate," "low," and "very low," based on study limitations, inconsistency, imprecision, indirectness, and other factors (17,18).

The core group conducted an online cross-sectional survey of stakeholders asking them to rate the importance of the outcomes and also their views on the acceptability, feasibility, impact on equity, and resource use of the relevant chest imaging modalities (chest radiography, CT, and lung US) in the different clinical scenarios.

Formulation of the Recommendations

The GDG formulated the recommendations by using the GRADE framework, with explicit consideration of specific factors that

may affect the direction and strength of each recommendation (benefits and harms, the certainty of the evidence, values and preferences, resource use, equity, acceptability, and feasibility) (11,19). The direction (whether "in favor of" or "against" an intervention) and strength (whether "conditional" or "strong") of the recommendations reflects the GDG's degree of confidence as to whether the desirable effects of the intervention being considered outweigh the undesirable effects.

The methodologist (E.A.A.) developed an evidence-to-decision table for each PICO question (by using GRADEpro software) (17) and used them to guide online discussions (18). The GDG voted on each of the evidence-to-decision factors, then on the direction and strength of the recommendation by using an online voting tool (*https://menti.com*). The voting results served as the starting point for building consensus. None of the GDG members expressed opposition to the final strength or direction of any of the recommendations. The recommendation was termed as "based on expert opinion" when the systematic review identified no relevant evidence.

Peer Review and Quality Assurance

The members of the external review group provided peer review on the draft report of the guidance. The core group considered and addressed all comments with detailed documentation of the responses. The WHO COVID-19 Publications Review Committee provided oversight and approved the final version of the report.

Results

The literature review identified 28 studies that met the eligibility criteria. Of the seven PICO questions, four had no identified evidence (PICO 1, 3, 6, 7), one had low certainty evidence (PICO 2), and two had very low certainty evidence (PICO 4, 5). The summary of the evidence by PICO question is as follows:

PICO 1: The systematic review identified no eligible study evaluating the diagnostic accuracy of imaging in asymptomatic contacts of patients with COVID-19.

PICO 2: The systematic review identified 23 studies that evaluated the diagnostic accuracy of three imaging modalities in symptomatic patients suspected of having COVID-19, against a reference standard, chest radiography (n = 3), chest CT (n = 19), and lung US (n = 1). None of these studies compared two imaging modalities against each other. The systematic review team judged those studies to be at either high risk of bias (n = 17)or moderate risk of bias (n = 6). The studies provided limited information regarding clinical presentation (eg, the severity of symptoms at presentation) and few reported specific criteria for a positive imaging test for COVID-19. Eleven studies did not describe a reference standard to diagnose COVID-19 that included serial reverse transcriptase polymerase chain reaction or clinical follow-up. The median sensitivity and specificity reported by the included studies were 64% and 82% for chest radiography, 92% and 56% for chest CT, and 95% and 83% for lung US. The systematic review team judged the certainty of this evidence to be low for chest radiography, chest CT, and lung US. The corresponding evidence-to-decision table available in Appendix

E4 (online) provides the counts for true-positive, true-negative, false-positive, and false-negative results for four hypothetical prevalence values of COVID-19 infection that were assumed to be 20%, 40%, 60%, and 80% among symptomatic patients suspected of having COVID-19. The update of the review conducted before the publication of the guide identified five new studies that evaluated the diagnostic accuracy of chest radiography, chest CT, and lung US in symptomatic patients suspected of having COVID-19. The synthesized evidence as well as its associated certainty were judged to remain unchanged.

PICO 3: The systematic review identified no eligible study that evaluated any chest imaging modality in patients with confirmed or who are suspected of having COVID-19 not yet hospitalized to support decisions on hospital admission versus home discharge on health outcomes.

PICO 4: The systematic review identified no eligible study that evaluated any chest imaging modality in patients with confirmed or who are suspected of having COVID-19 not yet hospitalized to support decisions on regular admission versus intensive care unit admission on health outcomes. The update of the review conducted before the publication of the guide identified one new study that evaluated the use of chest imaging in patients with confirmed or who are suspected of having COVID-19 not yet hospitalized. The certainty of the evidence was judged as very low.

PICO 5: The systematic review team identified three studies that evaluated chest imaging in patients currently hospitalized with moderate or severe symptoms and with confirmed or who are suspected of having COVID-19, for predicting mortality or admission at the intensive care unit. The certainty of evidence was judged to be very low.

PICO 6: The systematic review team identified no study that evaluated any chest imaging modality to diagnose pulmonary embolism in patients with COVID-19.

PICO 7: The systematic review team identified no study that evaluated any chest imaging modality to support the decision on discharge home.

Refer to the full guideline publication for the citations of studies referred in the summary of evidence (15).

The GDG developed one recommendation for each PICO question with two exceptions: it developed two recommendations for PICO 2 and developed no recommendation for PICO 6 (due to lack of evidence and the rapidly evolving knowledge related to that question). The recommendations for which no evidence meeting inclusion criteria was identified were labeled as based on expert opinion. Table 1 presents a summary of the recommendations. All developed recommendations are conditional, which means that the desirable effects were judged to likely outweigh the undesirable effects under certain conditions. One set of these conditions relates to the characteristics of patients who are likely to benefit from the recommended interventions (listed in Table 1 for each recommendation).

Another set of conditions relates to the factors to consider when choosing a specific imaging modality (included in Table 2 for all recommendations). Appendix E5 (online) provides implementation considerations, monitoring and evaluation considerations, and research priorities for the different

Table 1: Summary of the Recommendations	
Recommendation	Remarks
R1: For asymptomatic contacts of patients with COVID-19, WHO suggests not using chest imaging for the diagnosis of COVID-19. <i>Conditional recommendation, based on expert opinion</i>	RT-PCR should be performed for confirming diagnosis.
R2.1: For symptomatic patients suspected of having COVID-19, WHO suggests not using chest imaging for the diagnostic work-up of COVID-19 when RT-PCR testing is available with timely results. <i>Conditional recommendation based on low certainty evidence</i>	RT-PCR should be performed for confirming diagnosis.
 R2.2: For symptomatic patients suspected of having COVID-19, WHO suggests using chest imaging for the diagnostic work-up of COVID-19 when: (1) RT-PCR testing is not available; (2) RT-PCR testing is available, but results are delayed; and (3) initial RT-PCR testing is negative, but with high clinical suspicion of COVID-19. <i>Conditional recommendation based on low certainty evidence</i> 	 Imaging should be used as one element of the diagnostic work-up that otherwise includes clinical and laboratory data. Patients likely to benefit are those who: (1) have presentations that could represent complications of COVID-19 (eg, pneumonia; pulmonary arterial thrombosis or thromboembolism); (2) need to be admitted irrespective of diagnosis (eg, disease is severe or likely to progress), to help with disposition or triaging (eg, to dedicated COVID-19 ward vs non-COVID-19 ward); (3) need to be transferred to another facility; live with people at high risk if infected with COVID-19 (eg, immunocompromised, persons aged over 60 years); (4) live in small homes, overcrowded households, or densely populated settings where isolation is very difficult to implement; (5) live in communities with people at high risk, such as retirement homes or dormitories.
 R3: For patients with confirmed or who are suspected of having COVID-19, not currently hospitalized and with mild symptoms, WHO suggests using chest imaging in addition to clinical and laboratory assessment to decide on hospital admission versus home discharge. <i>Conditional recommendation, based on expert opinion</i> 	 Imaging should be used as one element of the patient evaluation that otherwise includes clinical, laboratory and epidemiologic data. Patients likely to benefit are those who: (1) have or are at high risk of disease progression; (2) represent an increased risk of dissemination within their community due to their occupational, social, or other circumstances; (3) have associated comorbidities (such as diabetes, hypertension, heart disease, obesity) or other chronic diseases that might decompensate and/or are aged over 60 years; (4) live with individuals at high risk of morbidity and mortality associated with COVID-19 (eg, elderly, immunocompromised), whether at home or retirement home; (5) live in small homes, overcrowded households, or densely populated settings where isolation is very difficult to implement.
R4: For patients with confirmed or who are suspected of having COVID-19, not currently hospitalized and with moderate to severe symptoms, WHO suggests using chest imaging in addi- tion to clinical and laboratory assessment to decide on regular ward admission versus intensive care unit admission. Conditional recommendation, based on very low certainty evidence	 Imaging should be used as one element of the patient evaluation that otherwise includes clinical and laboratory data. Patients likely to benefit are those who: (1) are at higher risk of disease progression (eg, with comorbidities); (2) are not responding to supportive treatment (oxygen supplementation); (3) present acute clinical deterioration not elucidated.
R5: For patients with confirmed or who are suspected of having COVID-19, currently hospitalized and with moderate to severe symptoms, WHO suggests using chest imaging in addition to clinical and laboratory assessment to inform the therapeutic management. Conditional recommendation, based on very low certainty evidence	 Imaging should be used as one element of patient evaluation that otherwise includes clinical and laboratory data. Patients likely to benefit are those who: (1) are at high risk of disease progression; (2) are not responding to treatment (oxygen supplementation); (3) have presentations with clinical suspicion of pulmonary fibrosis, pulmonary artery thrombosis, or thromboembolism.
R6: For hospitalized patients with COVID-19 whose symptoms are resolved, WHO suggests not using chest imaging in addition to clinical and/or laboratory assessment to inform the decision regarding discharge. <i>Conditional recommendation, based on expert opinion</i> Note.—COVID-19 = coronavirus disease 2019, RT-PCR = rever	 When imaging is used, it should be one element of the patient evaluation that otherwise includes clinical and laboratory data. Patients likely to benefit from chest imaging are those who: (1) have had a severe form of COVID-19; (2) have preexisting chronic lung disease. se transcriptase polymerase chain reaction, WHO = World Health Organization.

Table 2: Factors to Consider When Choosing the Specific Imaging Modality (Applies to All Recommendations)

Factors

Compared to chest CT, chest radiography appears to have a lower sensitivity and might have higher specificity. Chest radiography is less resource intensive, is associated with lower radiation doses, is easier to repeat sequentially for monitoring disease progression or disease recovery, and can be performed with portable equipment at the point of care (which minimizes the risk of cross-infection related to patient transport).

Chest CT has the highest sensitivity but relatively lower specificity and can be useful in patients with some preexisting pulmonary diseases. Lung US has very low certainty evidence supporting its diagnostic accuracy, but might be helpful with the appropriate expertise as a supplemental or alternative modality (eg, in pregnant women, children, patients with mechanical ventilation). Lung US can be performed at the point of care but requires closer physical proximity of the operator to the patient for a longer period and needs specific infection prevention and control precautions.

Consider the differential diagnoses and potential complications for each specific case (eg, CT angiography for pulmonary arterial thrombosis or thromboembolism, US for pleural effusions and heart conditions) when choosing imaging modality.

Choice should be made through shared decision making involving the referring physician, the radiologist, and the patient whenever possible. If possible, provide the patient with information regarding the imaging modality and the likelihood of subsequent imaging procedures.

Table 3: Implementation Considerations that Are Common across Recommendations

Considerations

Implement the recommendations based on your equipment availability. Consider the resources needed (budget, health workforce, personal protective equipment, imaging equipment), the need to adapt the clinical workflow, and the need to deprioritize other indications for imaging.

When performing chest radiography, consider using portable equipment, and if feasible, a unit dedicated to patients with COVID-19.

When performing chest radiography and chest CT, minimize radiation dose while maintaining diagnostic image quality (eg, low-dose CT protocols) and use digital imaging rather than film-screen equipment.

Consider the potential harm from exposure to ionizing radiation, in particular for pregnant women and children.

Ensure proper use of personal protective equipment by health care workers and proper disinfection of equipment and devices (see Appendix E6 and Table E1 [online]).

Provide appropriate training of radiologists and technologists on infection prevention and control practices and ensure efficient management of typical imaging findings of COVID-19 through accepted local protocols.

Consider the transfer of images for remote reporting (teleradiology) as needed (eg, settings where radiologists are not available for on-site reporting).

Set policy/pathway for use of imaging related to COVID-19 illustrated with flow charts or diagrams locally developed and accepted.

Whenever is possible, provide information to patients about safety provisions adopted by the facility for infection prevention and control (see Appendix E6 [online]), as well as for radiation protection.

Make provisions to ensure that all patients get the imaging services they need without suffering financial hardship.

Note.—Source.—Reference 32. COVID-19 = coronavirus disease 2019.

recommendations. Table 3 lists only those implementation considerations that are common across all recommendations. The evidence-to-decision tables for the different recommendations are included in Appendix E4 (online).

Discussion

The purpose of the guide is to support World Health Organization (WHO) Member States in their response to the coronavirus disease 2019 (COVID-19) pandemic by providing up-to-date guidance on use of chest imaging in adult patients with confirmed or who are suspected of having COVID-19, including chest radiography, CT, and lung US. It covers the care pathway from outpatient facility or hospital entry to home discharge. The guidance is provided for patients with different levels of disease severity, from asymptomatic individuals to critically ill patients. Additional guidance on infection prevention

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and control in medical imaging procedures for management of COVID-19 is provided in Appendix E6 (online). The infection prevention and control guidance addresses both general measures for all imaging procedures and specific precautions for chest radiography, chest CT, and lung US. The guide also promotes quality and safety of radiation use in health facilities, thus enhancing protection and safety of patients and health care workers (Appendix E6 [online]).

The guide has a number of strengths including its development based on standard methodology (20), the consideration of contextual factors (11), its reporting according the Reporting Items for Practice Guidelines in Healthcare statement, and the consideration of stakeholders views (21). Limitations include that the evidence on which the recommendations are based is either lacking or at best of low certainty, and that scope is relatively narrow (eg, excluded children, did not address the systemic aspects of the disease). However, the latter was necessary to allow the rapid development of recommendations addressing the most pressing questions.

The recommendations address chest imaging in general, but not specific imaging modalities. While there is accumulating evidence about typical findings with each imaging modality (22), evidence about comparative diagnostic and prognostic value of the different modalities is still lacking. The experience indicates that in most cases, chest radiography with portable equipment can provide the information needed at the point of care. In addition to limiting patient transfers, it gives the possibility of adapting procedures to reduce staff exposure and to increase operational efficiencies (eg, portable chest radiography obtained through the glass of an isolation room door) (23). Preliminary studies on lung US seem promising, in particular for use of portable US scanners at the point of care, but further evidence still needs to be generated. A CT scan may be the indicated modality for particular patient groups (eg, those suspected of having thrombotic and/or thromboembolic disease, multisystemic disease). In health facilities, particularly in low- and middleincome countries, where CT scans are not available for those patients, policymakers should consider provisions to facilitate patient transfer to reference hospitals where CT scans can be performed. In the long term, the assessment of clinical, social, economic, organizational, and ethical issues should inform decision making about procurement of imaging technology (24,25). There is wide variability of the contextual factors across settings (eg, availability and cost of each modality and availability of the required expertise). Along with other technical considerations, the guide refers to the choice of a chest imaging modality in the remarks that apply to all recommendations (see Table 2). Indeed, the GDG gave due consideration to resource use, impact on equity, acceptability, and feasibility when drafting the recommendations.

This guide is primarily intended for health professionals working in emergency departments, imaging departments, clinical departments, intensive care units, and other health care settings involved in the diagnosis of COVID-19 and in the treatment of patients with COVID-19. The document can also be useful for hospital managers and planners, policymakers, hospital architects, biomedical engineers, medical physicists, logistics staff, infection prevention and control officers, and staff involved in water and sanitation tasks. Health authorities and radiation regulators can use the guide to develop specific national standards relevant to COVID-19 outbreak preparedness, readiness, and response in different contexts. Finally, it can be useful to funders that wish to donate equipment and devices, as well as funding priority research.

We were able to develop the guideline in about 10 weeks, which fits the 3-month time frame of "rapid" guidelines (26). Two main facilitating factors include the existence of a clear and detailed process in place (as described in the WHO handbook for guideline development) (10) and the use of a rapid review process (27). The latter factor is important considering that conducting the systematic review typically consumes a number of months. In addition, we used a staggered approach when developing the guide: For example, we started training the GDG members even before the findings of the rapid review were available, and we sent out recommendations for peer review (by the external review group) even before all recommendations were developed. Finally, the most critical factor was probably having a dedicated core group that developed and followed a strict timeline and worked on keeping a steady momentum. The core group members met almost daily (including weekends) and maintained intense e-mail communication.

While the guide was developed within a relatively short time frame, we do not believe this has affected the quality of the recommendations. Indeed, we followed standard WHO process, including proper development of PICO questions, determination and prioritization of outcomes of interest, conflicts of interest declaration and management, reliance on systematically collected evidence, use of GRADE methodology, and use of evidence-to-decision tables. Although the rapid review could have missed relevant studies, it is unlikely that any impactful studies have been missed. We did have all members of the GDG verify eligible studies, and we continually monitored the literature over the period of the project. The online format of the GDG meetings, due to the travel restrictions during the pandemic, did not impede proper discussions. On the contrary, GDG discussions were lively constructive and allowed all members the opportunity to contribute.

Moreover, we conducted a survey of stakeholders to capture their views on factors that were important to the development of recommendations, namely resource use, impact on equity, acceptability, and feasibility. The panel paid attention to the resource implications for low resource settings.

As the growing body of literature is confirming the multisystemic nature of COVID-19 (including the nervous, vascular and cardiac systems, kidneys) (28), this raises questions on whether, when, and how imaging other than that of the chest (eg, cardiac US, brain MRI, vascular imaging, abdominal imaging) may contribute to early diagnosis and/or treatment of patients with COVID-19.

Specifically, pulmonary embolism in patients with CO-VID-19 is gaining attention with its relatively high prevalence and the ongoing discussion about its embolic versus intravascular thrombotic mechanism (29,30). When addressing this question, the GDG members felt that both the published literature and the collective clinical experience were not adequate to justify any recommendation. We are aiming to address it in the next update of the guide.

In the future, guidance and policies for procurement of imaging equipment are needed. There is also a need for research on diagnostic accuracy and desirable and undesirable impact of the different modalities on clinical and health systems outcomes. Ideally, the clinical studies should consist of welldesigned clinical trials that are registered (31) and reported according to standard guidelines (22). Finally, there is a need for studies addressing contextual factors, including cost, costeffectiveness, impact on equity, acceptability, and feasibility of the different imaging modalities.

In summary, the guide provides up-to-date guidance on the use of chest imaging in patients with confirmed or who are suspected of having coronavirus disease 2019 for clinicians and other stakeholders. It also provides research recommendations that can hopefully provide a better evidence base for future updates of the guide.

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References

- World Health Organization. Novel Coronavirus China: WHO. https://www.who. int/csr/don/12-january-2020-novel-coronavirus-china/en/. Published 2020. Accessed May 22, 2020.
- Lu R, Zhao X, Li J, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. Lancet 2020;395(10224):565–574.
- Zhou P, Yang XL, Wang XG, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature 2020;579(7798):270–273.
- Zhu N, Zhang D, Wang W, et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. N Engl J Med 2020;382(8):727–733.

- World Health Organization. Novel coronavirus (2019-nCov) Situation Report 22: WHO. https://www.who.int/docs/default-source/coronaviruse/situation-reports/ 20200211-sitrep-22-ncov.pdf?sfvrsn=fb6d49b1_2. Published 2020. Accessed May 22, 2020.
- 6. World Health Organization. Statement on the second meeting of the International Health Regulations (2005) Emergency Committee regarding the outbreak of novel coronavirus (2019-nCoV). https://www.who.int/news-room/detail/30-01-2020-statement-on-the-second-meeting-of-the-international-health-regulations-(2005)-emergency-committee-regarding-the-outbreak-of-novel-coronavirus-(2019-ncov). Published 2020. Accessed May 22, 2020.
- World Health Organization. WHO Director-General's opening remarks at the media briefing on COVID-19 – March 11, 2020. https://www.who.int/dg/speeches/ detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19—11-march-2020. Published 2020. Accessed May 22, 2020.
- Blažić I, Brkljačić B, Frija G. The use of imaging in COVID-19-results of a global survey by the International Society of Radiology. Eur Radiol 2020. 10.1007/s00330-020-07252-3. Published online September 17, 2020.
- World Health Organization. Use of chest imaging in COVID-19: a rapid advice guide. (WHO/2019-nCoV/Clinical/Radiology_imaging/2020.1). Licence: CC BY-NC-SA 3.0 IGO. Geneva, Switzerland: World Health Organization, 2020.
- World Health Organization. WHO handbook for guideline development. https:// www.who.int/publications/guidelines/handbook_2nd_ed.pdf?ua=1. Published 2014. Accessed May 22, 2020.
- Alonso-Coello P, Schünemann HJ, Moberg J, et al. GRADE Evidence to Decision (EtD) frameworks: a systematic and transparent approach to making well informed healthcare choices. 1: Introduction. BMJ 2016;353:i2016.
- Chen Y, Yang K, Marušic A, et al. A Reporting Tool for Practice Guidelines in Health Care: The RIGHT Statement. Ann Intern Med 2017;166(2):128–132.
- Rubin GD, Ryerson CJ, Haramati LB, et al. The Role of Chest Imaging in Patient Management During the COVID-19 Pandemic: A Multinational Consensus Statement From the Fleischner Society. Chest 2020;158(1):106–116.
- Guyatt GH, Oxman AD, Kunz R, et al. GRADE guidelines: 2. Framing the question and deciding on important outcomes. J Clin Epidemiol 2011;64(4):395–400.
- World Health Organization. Rapid advice guide: Use of chest imaging in CO-VID-19: a rapid advice guide. (WHO/2019-nCoV/Clinical/Radiology_imaging/2020.1). Geneva, Switzerland: World Health Organization, 2020.
- Guyatt G, Oxman AD, Akl EA, et al. GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. J Clin Epidemiol 2011;64(4):383–394.
- Guyatt GH, Thorlund K, Oxman AD, et al. GRADE guidelines: 13. Preparing summary of findings tables and evidence profiles-continuous outcomes. J Clin Epidemiol 2013;66(2):173–183 [Published correction appears in J Clin Epidemiol 2015;68(4):475.].
- Andrews J, Guyatt GH, Oxman AD, et al. GRADE guidelines: 14. Going from evidence to recommendations: the significance and presentation of recommendations. J Clin Epidemiol 2013;66(7):719-25.
- Alonso-Coello P, Oxman AD, Moberg J, et al. GRADE Evidence to Decision (EtD) frameworks: a systematic and transparent approach to making well informed healthcare choices. 2: Clinical practice guidelines. BMJ 2016;353:i2089.
- Schünemann HJ, Wiercioch W, Etxeandia I, et al. Guidelines 2.0: systematic development of a comprehensive checklist for a successful guideline enterprise. CMAJ 2014;186(3):E123–E142.
- Petkovic J, Riddle A, Akl EA, et al. Protocol for the development of guidance for stakeholder engagement in health and healthcare guideline development and implementation. Syst Rev 2020;9(1):21.
- Schulz KF, Altman DG, Moher D; CONSORT Group. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. BMJ 2010;340:c332.
- Mossa-Basha M, Medverd J, Linnau K, et al. Policies and Guidelines for COVID-19 Preparedness: Experiences from the University of Washington. Radiology 2020. 10.1148/radiol.2020201326. Published online April 8, 2020.
- World Health Organization. Health technology assessment of medical devices. Geneva, Switzerland: World Health Organization, 2011.
- World Health Organization. WHO compendium of innovative health technologies for low-resource settings, 2016-2017. Geneva, Switzerland: World Health Organization, 2018.
- Thayer KA, Schünemann HJ. Using GRADE to respond to health questions with different levels of urgency. Environ Int 2016;92-93:585–589.
- Tricco AC, Antony J, Zarin W, et al. A scoping review of rapid review methods. BMC Med 2015;13(1):224.
- Zaim S, Chong JH, Sankaranarayanan V, Harky A. COVID-19 and Multiorgan Response. Curr Probl Cardiol 2020;45(8):100618.
- Deshpande C. Thromboembolic Findings in COVID-19 Autopsies: Pulmonary Thrombosis or Embolism? Ann Intern Med 2020;173(5):394–395.
- Lax SF, Skok K, Zechner P, et al. Pulmonary Arterial Thrombosis in COVID-19 With Fatal Outcome : Results From a Prospective, Single-Center, Clinicopathologic Case Series. Ann Intern Med 2020;173(5):350–361.
- Nasrallah AA, Farran SH, Nasrallah ZA, et al. A large number of COVID-19 interventional clinical trials were registered soon after the pandemic onset: a descriptive analysis. J Clin Epidemiol 2020;125:170–178.
- 32. International Atomic Energy Agency. Radiation Protection and Safety in Medical Uses of Ionizing Radiation. IAEA Safety Standards Series No SSG-46. Vienna, Austria: International Atomic Energy Agency, 2018.