

Supplementary material

Mejza F, Lesniak W, Jaeschke R. Quality and methodology of clinical practice guidelines on antiviral pharmacotherapy for COVID-19 during the early phase of the pandemic. Pol Arch Intern Med. 2021; 131: 356-360. doi:10.20452/pamw.15875

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1. Search strategies

The search strategies included the following terms or combinations of terms:

MEDLINE/PubMed

1. "COVID-19"
2. "SARS-COV-2"
3. "Wuhan coronavirus"
4. "2019-nCov"
5. #1 OR #2 OR #3 OR #4
6. antivirals {MESH} (antiviral*)
7. remdesivir OR ""lopinavir/ritonavir"" OR ""lopinavir-ritonavir"" OR lopinavir OR ritonavir OR Kaletra OR hydroxychloroquine OR Plaquenil OR chloroquine OR Aralen OR oseltamivir OR Tamiflu OR favipiravir OR Avigan OR umifenovir OR Arbidol OR alpha-interferon OR interferon OR interferon-alpha OR ribavirin OR Copegus OR Rebetol OR Virazole
8. #6 OR #7
9. guideline*
10. statement
11. consensus

12. guidance
13. position
14. "position statement"
15. recommend*
16. #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15
17. #5 AND #8
18. #5 AND #16
19. #5 AND #8 AND #16

Embase

("COVID-19" OR "SARS-COV-2" OR "Wuhan coronavirus" OR "2019-nCov") AND (antiviral\$ OR remdesivir OR "lopinavir/ritonavir" OR "lopinavir-ritonavir" OR lopinavir OR ritonavir OR Kaletra OR hydroxychloroquine OR Plaquenil OR chloroquine OR Aralen OR oseltamivir OR Tamiflu OR favipiravir OR Avigan OR umifenovir OR Arbidol OR Alpha-interferon OR interferon OR interferon-alpha OR ribavirin OR Copegus OR Rebetol OR Virazole) AND (guideline\$ OR statement OR consensus OR guidance OR position OR recommend\$)

Google Search (www.google.com)

(COVID-19 OR SARS-COV-2) AND (antiviral OR remdesivir OR lopinavir OR ritonavir OR hydroxychloroquine OR chloroquine OR oseltamivir OR favipiravir OR umifenovir OR interferon OR ribavirin) AND (guideline OR statement OR consensus OR guidance OR position OR recommendation)

2. Document selection flowchart

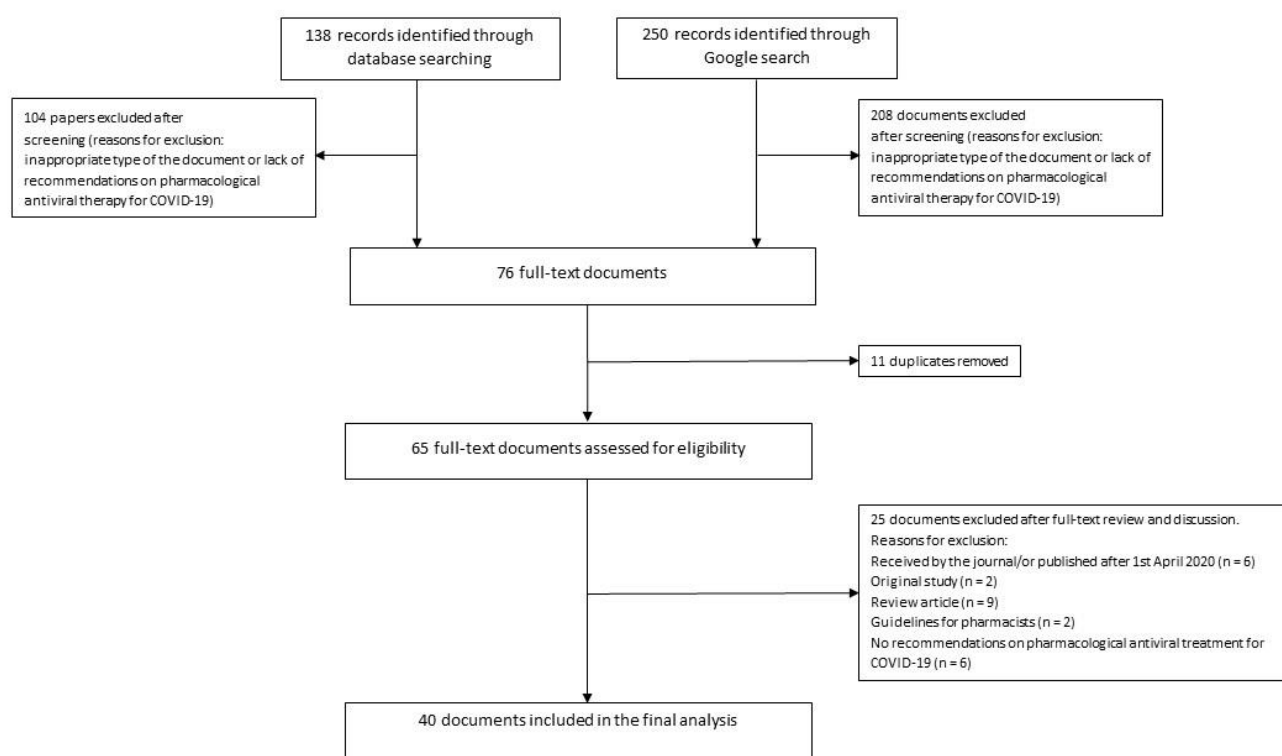


Figure S1. Document selection flowchart

3. Data extracted

The following data were extracted:

1. publication details (date of the first publication, authors, citation)
2. mode of publication (peer-reviewed journal article, a document published on the website)

3. an issuing institution, classified as follows: international organizations (eg, World Health Organization [WHO]), international medical societies (eg, International Society of Infectious Diseases, European Respiratory Society), national government organizations (eg, National Health Service, Center for Disease Control and Prevention), national medical societies, international groups of experts, national or local groups of experts, and single institutions, hospitals, or healthcare providers
4. type of the document (CPGs, guidance, position statement)
5. recommendations related to antiviral therapy (a relevant excerpt from the guideline document)
6. strength of a recommendation (classified according to the guideline document; if no classification was provided, the recommendation was classified as “strong” when the words such as “recommend” or “it should be done” or “it should not/must not be done” were used and as “conditional or weak” when the words such as “suggest” or “propose” or “it should/may be considered” were used)
7. presentation of evidence (including the search strategy), classified as follows: a) full presentation of available evidence along with references based on the described search strategy; b) selective presentation of available evidence along with references based on the described search strategy; c) references based on the described search strategy; d) only references; and e) no references
8. quality of evidence, if assessed (with the classification of evidence quality)
9. decision process (ie, how the balance between benefits and risks was assessed)
10. external reviewing
11. financial disclosures, classified as follows: a) no relationship to pharmaceutical industry (no sponsorship, authors’ COIs available and irrelevant); b) a potential relationship to pharmaceutical industry (no sponsorship, authors’ COIs available and COIs identified); c) a

clear relationship to pharmaceutical industry (sponsorship, authors' COIs available and multiple important COIs identified); d) no information on COIs; and e) no COIs declared.

4. List of included documents

1. Flisiak R, Horban A, Jaroszewicz J, et al. Management of SARS-CoV-2 infection: recommendations of the Polish Association of Epidemiologists and Infectiologists as of March 31, 2020. *Pol Arch Intern Med.* 2020; 130: 352-357
2. Lombardy Section Italian Society Infectious And Tropical Diseases Vademecum for the treatment of people with COVID-19. Edition 2.0, 13 March 2020. *Infect Med.* 2020; 28: 143-152.
3. Jin YH, Cai L, Cheng ZS, et al., for the Zhongnan Hospital of Wuhan University Novel Coronavirus Management and Research Team, Evidence-Based Medicine Chapter of China International Exchange and Promotive Association for Medical and Health Care (CPAM). A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia (standard version). *Mil Med Res.* 2020; 7: 4
4. Kevin C. Wilson, Sanjay H. Chotirmall, Chunxue Bai, Jordi Rello on behalf of the International Task Force on COVID-19 COVID-19: Interim Guidance on Management Pending Empirical Evidence. From an American Thoracic Society-led International Task Force <https://www.thoracic.org/covid/covid-19-guidance.pdf>. Date of access May 16, 2020
5. British Pediatric Respiratory Society. Guidance for the clinical management of children admitted to hospital with suspected COVID-19. https://www.rcpch.ac.uk/sites/default/files/2020-03/bprs_management_of_children_admitted_to_hospital_with_covid19_-_20200319.pdf. Date of access May 16, 2020
6. Alhazzani W, Møller MH, Arabi YM, et al. Surviving Sepsis Campaign: guidelines on the management of critically ill adults with Coronavirus Disease 2019 (COVID-19). *Intensive Care Med.* 2020; 46: 854-887

7. The Australian and New Zealand Intensive Care Society (ANZICS) COVID-19 Guidelines Version 1. <https://www.anzics.com.au/wp-content/uploads/2020/03/ANZICS-COVID-19-Guidelines-Version-1.pdf>. Date of access May 16, 2020
8. World Health Organization. (2020). Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected: interim guidance, 13 March 2020. World Health Organization. <https://apps.who.int/iris/handle/10665/331446>. Assessed March 15, 2020
9. University of Michigan. Inpatient guidance for treatment of COVID-19 in adults and children. https://www.med.umich.edu/asp/pdf/adult_guidelines/COVID-19-treatment.pdf. Date of access May 16, 2020
10. HUNTINGTON HOSPITAL INPATIENT GUIDANCE FOR TREATMENT OF COVID-19/SARS-CoV-2 INFECTION IN ADULTS 03/23/2020. <https://www.huntingtonhospital.org/our-services/emergency-trauma/hospital-preparedness-covid-19-information/#resources>. Date of access May 16, 2020
11. Faculty in Infectious Diseases, Emergency Medicine, Pulmonary/Critical Care, Hospital/General Medicine, & Radiology: Clinical Recommendations for Treatment of COVID-19 Adult Patients <https://www.vumc.org/coronavirus/sites/default/files/COVID%20Documents/Weekly%20COVID-19%20Clinical%20Guidelines%20Update%20Summary%20-%203.22.2020-%20FINAL.pdf> Date of access May 16, 2020
12. Clinical management of patients with moderate to severe COVID-19 - Interim guidance. <https://www.canada.ca/en/public-health/services/diseases/2019-novel-coronavirus-infection/clinical-management-covid-19.html>. Date of access May 16, 2020
13. Specific Antiviral Therapy in the Clinical Management of Acute Respiratory Infection with SARS-CoV-2 (COVID-19). <https://www.hse.ie/eng/about/who/acute-hospitals->

division/drugs-management-programme/guidelines/specific-antiviral-therapy-in-the-clinical-management-of-acute-respiratory-infection-with-sars-cov-2-covid-19.pdf. Date of access May 16, 2020

14. Tinku J. (edit). INTERNATIONAL PULMONOLOGIST'S CONSENSUS ON COVID-19 JHMI Clinical Guidance for Available Pharmacologic Therapies for COVID-19. https://www.saudedafamilia.org/coronavirus/artigos/international_pulmonologists_consensus.pdf. Date of access May 16, 2020
15. JHMI Clinical Guidance for Available Pharmacologic Therapies for COVID-19. https://www.hopkinsguides.com/hopkins/ub?cmd=repview&type=479-1124&name=4_538747_PDF. Date of access May 16, 2020
16. Inpatient Pharmacotherapy Guidelines for COVID-19 in Adult Patients/ <https://mainehealth.org/-/media/mainehealth/pdfs/clinical-guidelines-and-resources/emergency-medicine/covid/mainehealth-inpatient-pharmacotherapy-guidelines-for-covid-v1-3192020.pdf?la=en>. Date of access May 16, 2020
17. Indian Council of Medical Research: Recommendation for empiric use of hydroxy-chloroquine for prophylaxis of SARS-CoV-2 infection. <https://www.mohfw.gov.in/pdf/AdvisoryontheuseofHydroxychloroquinasprophylaxisforSARSCoV2infection.pdf>. Date of access May 16, 2020
18. Government of India, Ministry of Health & Family Welfare, Directorate General of Health Services (EMR Division).:Revised Guidelines on Clinical Management of COVID – 19. <https://www.mohfw.gov.in/pdf/RevisedNationalClinicalManagementGuidelineforCOVID1931032020.pdf>. Date of access May 16, 2020
19. National centre for Infectious Diseases Singapore: Interim Treatment Guidelines for COVID-19. <https://www.ncid.sg/Health-Professionals/Diseases-and->

- Conditions/Documents/Treatment%20Guidelines%20for%20COVID-19%20%282%20Apr%202020%29%20-final.pdf. Date of access May 16, 2020
20. Nebraska Medicine: COVID-19 Antiviral and Pharmacotherapy Recommendations.
<https://www.nebraskamed.com/sites/default/files/documents/covid-19/antiviral-and-pharmacotherapy-information.pdf?date=03242020>. Date of access May 16, 2020
21. New South Wales Health Interim Guidance on use of antiviral therapy in COVID-19.
<https://www.health.nsw.gov.au/Infectious/covid-19/Pages/antiviral-therapy.aspx>. Date of access May 16, 2020
22. Interim guidelines for covid-19 management in hematopoietic cell transplant and cellular therapy patients Version 1.2. March 18, 2020.
https://higherlogicdownload.s3.amazonaws.com/ASBMT/a1e2ac9a-36d2-4e23-945c-45118b667268/UploadedImages/COVID-19_Interim_Patient_Guidelines_3_18_20.pdf
Date of access May 16, 2020
23. Vetter P., Lan Vu D., Agoritsas T. New coronavirus : SARS-CoV-2 Specific antiviral treatment. <https://www.hug.ch/en/> . Date of access May 16, 2020
24. Trinity Health: COVID-19 Pharmacotherapy Treatment Guidance.
<https://www.samc.com/assets/documents/covid19/nursing/covid-19-treatment-gidance.pdf>
Date of access May 16, 2020
25. Shen K, Yang Y, Wang T, et al. Diagnosis, treatment, and prevention of 2019 novel coronavirus infection in children: experts' consensus statement World J Pediatr. 2020; 1-9. [published online ahead of print, 2020 Feb 7]. Date of access May 16, 2020
26. Li T. Diagnosis and clinical management of severe acute respiratory syndrome Coronavirus 2 (SARS-CoV-2) infection: an operational recommendation of Peking Union Medical College Hospital (V2.0). *Emerg Microbes Infect.* 2020; 9: 582-585.

27. Tucson Medical Center Interim Adult Treatment Guidelines for SARS-CoV-2 Infection COVID-19. <https://www.tmcaz.com/mednews/clinical-algorithms-protocols/3-20-tmc-interim-adult-treatment-guidelines-for-sars-cov-2-infection-covid-19>. Date of access May 16, 2020
28. Michigan Department of Health and Human Services COVID-19 Practice Management Guide. https://www.michigan.gov/documents/coronavirus/COVID19_Practice_Management_Guide_Final_685523_7.pdf. Date of access May 16, 2020
29. Clinical Presentation and Management of COVID-19. <https://www.sccgov.org/sites/phd-p/Diseases/novel-coronavirus/Documents/Clinical-Management-Handout-20200318.pdf>. Date of access May 16, 2020
30. Greater Toronto Area (GTA) Clinical Practice Guidelines for Antimicrobial and Immunomodulatory Therapy in Patients with COVID-19 (Last updated April 2, 2020). <https://www.google.com/url?sa=t&rct=j&q=&esrc=s&source=web&cd=&ved=2ahUKEwjE49qCwerpAhWxw8QBHX8IDx4QFjAAegQIBBAC&url=https%3A%2F%2Fwww.criticalcare.utoronto.ca%2Ffile%2F207%2Fdownload%3Ftoken%3DgynCDgX7&usg=AOvVaw3tPUipx-tykxSfkwhf0WqD>. Date of access May 16, 2020
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34. Australasian Society for Infectious Diseases Limited (ASID): Interim guidelines for the clinical management of COVID-19 in adults. <https://www.asid.net.au/documents/item/1873>. Date of access May 16, 2020
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40. Chen D, Yang H, Cao Y, et al. Expert consensus for managing pregnant women and neonates born to mothers with suspected or confirmed novel coronavirus (COVID-19) infection. *Int J Gynaecol Obstet.* 2020; 149: 130-136

5. AGREE II GRS Scores of included documents

Table S1. AGREE II GRS Scores of included documents

Ref. N°	Issuing Organization	AGREE II GRS Scores*						
		Process of development	Presentation style	Completeness of reporting	Clinical validity	Overall quality assessment	Evaluator would recommend guideline for use in practice	Evaluator would make use of a guideline of this quality in professional decisions
1	Polish Association of Epidemiologists and Infectiologists	1.5	4	2.5	2	2	2.5	2.5
2	Lombardy Section Italian Society Infectious And Tropical Diseases	1.5	3	2	1	1.5	1.5	1.5
3	China International Exchange and Promotive Association for Medical and Health Care	5.5	5.5	5	3.5	3.5	4	4
4	American Thoracic Society-led International Task Force	5.5	6	5.5	5	4.5	5.5	5.5
5	British Pediatric Respiratory Society	2.5	3.5	3.5	4	3	3.5	3.5
6	Surviving Sepsis Campaign	7	7	7	7	7	7	7
7	The Australian and New Zealand Intensive Care Society	2.5	4	2.5	4	2.5	3	3
8	World Health Organization	2.5	5	2.5	5.5	3.5	4.5	4.5
9	University of Michigan	1.5	3	1.5	3.5	2	2	2
10	Huntington Hospital	1	3	1	3.5	2.5	2	2
11	Vanderbilt University Medical Center	1	2	1	1.5	1	1	1
12	Government of Canada; COVID-19 Clinical Care Guidance Working Group	2	4.5	2	3.5	2.5	2.5	2.5
13	Feidhmeannacht na Seirbhíse Sláinte Health Service Executive	1.5	3	1.5	2.5	2.5	2	2
14	International Pulmonologist's Group (ed. Tinku J.)	1.5	2.5	1.5	2.5	2	2	2
15	John Hopkins University/John Hopkins Hospital	3	3	2.5	3.5	2.5	3	3
16	Maine Health	1	2.5	1	1.5	1	1	1
17	Indian Council of Medical Research	1	1.5	1	1	1	1	1
18	Government of India, Ministry of Health & Family Welfare	1	2.5	1.5	1.5	1.5	1.5	1.5
19	National centre for Infectious Diseases Singapore	2.5	4	2.5	2.5	3	3	3
20	Nebraska Medicine	1.5	3.5	1.5	2	2	1.5	1.5
21	New South Wales Government	1.5	2.5	1	1.5	1.5	1.5	1.5
22	American Society of Transplantation and Cellular Therapy Infectious Diseases Special Interest Group	1.5	2.5	2	2	2	2	2
23	Hospitaux Universitaires Geneva	2	2.5	1.5	1.5	1.5	2	2
24	Trinity Health	1.5	2.5	2	2	2	2	2

25	Shen K et al. (Group of experts)	2	3	2	2	2	2	2
26	Peking Union Medical College Hospital	1.5	3.5	2.5	2.5	2	2	2
27	Tucson Medical Center	1.5	2.5	1	1	1	1	1
28	Michigan Department of Health and Human Services	2	2.5	1.5	2.5	2	2.5	2.5
29	Santa Clara County	1	2.5	1	2	1.5	1	1
30	Greater Toronto Area Antimicrobial Stewardship Program	4.5	4.5	4	5	4.5	4	4
31	International Pharmaceutical Federation	1.5	2	1.5	2	2	1.5	1.5
32	European Society for Blood and Marrow Transplantation	1	1.5	1	2	2	2	2
33	Ministry of Health & Family Welfare; Government of the People's Republic of Bangladesh	1.5	2.5	1.5	2	2	2	2
34	Australasian Society for Infectious Diseases	1	2	1.5	2	1.5	1.5	1.5
35	Alberici F. at al (Group of experts)	1	1.5	1	1	1	1	1
36	Ceribelli A. at al (Group of experts)	1	2	1.5	1.5	1.5	1	1
37	National Health Commission & National Administration of Traditional Chinese Medicine	1	1.5	1.5	1.5	1.5	1	1
38	Wang Y. at al (Group of experts)	1.5	1	1	1	1	1	1
39	American Association for the Study of Liver Diseases Expert Panel	1.5	2	1.5	1.5	1.5	1.5	1.5
40	Chen D. et al (Group of experts)	1.5	2.5	2	2	2	1	1

*mean from the scores of 2 evaluators; (from 1 - lowest to 7 - highest)

6. Detailed quality characteristics of included documents

Table S2. Basic quality characteristics of included documents and claims for pharmacological antiviral therapy

Ref. N°	Issuing Organization/First Author*	Item										AGREE II GRS Overall Quality Assessment Score**	Recommendations for pharmacological antiviral therapy**	
		Formation of the working group described	Searching for evidence described	Existing methodology of guidelines development used	Strength of recommendations provided	Quality of evidence rated	Existing methodology of rating the quality and sources of evidence used	References to recommendations provided	Document updated after new evidence available	External reviewers	COI information provided			
1	Polish Association of Epidemiologists and Infectiologists	-	-	-	-	-	-	-	-	-	-	+	2	weak
2	Lombardy Section Italian Society Infectious And Tropical Diseases	-	-	-	-	-	-	+	-	-	-	+	1.5	strong
3	China International Exchange and Promotive Association for Medical and Health Care	+	+	+	+	+	+	+	-	-	-	+	3.5	weak
4	American Thoracic Society-led International Task Force	+	-	+	-	-	-	+	-	-	-	-	4.5	weak
5	British Pediatric Respiratory Society	-	+	-	-	-	-	-	-	-	-	-	3	no
6	Surviving Sepsis Campaign	+	+	+	+	+	+	+	-	-	-	+	7	no
7	The Australian and New Zealand Intensive Care Society	-	-	-	-	-	-	-	-	-	-	-	2.5	no
8	World Health Organization	-	-	-	+	-	-	+	-	+	-	-	3.5	no
9	University of Michigan	-	-	-	-	-	-	-	+	-	-	-	2	no
10	Huntington Hospital	-	-	-	-	-	-	+	-	-	-	-	2.5	no
11	Vanderbilt University Medical Center	-	-	-	-	-	-	-	+	-	-	-	1	weak
12	Government of Canada; COVID-19 Clinical Care Guidance Working Group	-	-	-	-	-	-	+	-	+	-	-	2.5	no
13	Feidhmeannacht na Seirbhíse Sláinte Health Service Executive	-	-	-	-	-	-	+	-	-	-	-	2.5	weak
14	International Pulmonologist's Group (ed. Tinku J.)	-	-	-	-	-	-	+	-	-	-	-	2	no
15	John Hopkins University/John Hopkins Hospital	+	-	-	-	-	-	-	-	-	-	-	2.5	weak
16	Maine Health	-	-	-	-	-	-	-	-	-	-	-	1	weak
17	Indian Council of Medical Research	-	-	-	-	-	-	-	+	-	-	-	1	weak
18	Government of India, Ministry of Health & Family Welfare	-	-	-	-	-	-	-	+	-	-	-	1.5	weak

19	National Centre for Infectious Diseases Singapore	-	-	-	+	+	+	+	-	-	+	3	weak
20	Nebraska Medicine	-	-	-	-	-	-	+	-	-	-	2	weak
21	New South Wales Government	-	-	-	-	-	-	-	+	-	-	1.5	weak
22	American Society of Transplantation and Cellular Therapy Infectious Diseases Special Interest Group	-	-	-	-	-	-	-	+	-	-	2	weak
23	Hospitaux Universitaires Geneva	-	-	-	-	+	-	+	+	-	-	1.5	weak
24	Trinity Health	-	-	-	-	-	-	-	+	-	-	2	weak
25	Shen K et al. (Group of experts)	-	-	-	-	-	-	-	-	-	+	2	strong
26	Peking Union Medical College Hospital	-	-	-	-	-	-	-	-	-	+	2	weak
27	Tucson Medical Center	-	-	-	-	-	-	-	-	-	-	1	strong
28	Michigan Department of Health and Human Services	-	-	-	-	-	-	+	-	-	-	2	no
29	Santa Clara County	-	-	-	-	-	-	-	+	-	-	1.5	no
30	Greater Toronto Area Antimicrobial Stewardship Program	+	-	-	-	-	-	+	+	-	+	4.5	no
31	International Pharmaceutical Federation	-	-	-	-	-	-	-	-	-	-	2	weak
32	European Society for Blood and Marrow Transplantation	-	-	-	-	-	-	-	-	-	-	2	no
33	Ministry of Health & Family Welfare; Government of the People's Republic of Bangladesh	-	-	-	-	-	-	-	-	-	-	2	no
34	Australasian Society for Infectious Diseases	-	-	-	-	-	-	-	-	-	-	1.5	no
35	Alberici F. at al (Group of experts)	-	+	-	-	-	-	-	-	-	+	1	no
36	Ceribelli A. at al (Group of experts)	-	-	-	-	-	-	-	-	-	-	1.5	weak
37	National Health Commission & National Administration of Traditional Chinese Medicine	-	-	-	-	-	-	-	-	-	-	1.5	strong
38	Wang Y. at al (Group of experts)	-	-	-	-	-	-	-	-	-	+	1	strong
39	American Association for the Study of Liver Diseases Expert Panel	-	-	-	-	-	-	+	-	-	-	1.5	no
40	Chen D. et al (Group of experts)	-	-	-	-	+	-	-	-	-	+	2	weak

* in case of *ad hoc* formulated groups; ** the mean value for two evaluators, from 1 – lowest to 7 – highest (full AGREE II GRS Rating provided in Supplementary Materials); *** Strong – strong or explicit recommendation for use; Weak – recommendation for use, suggestion for use; No – recommendation not to use outside trials or statement that evidence is lacking