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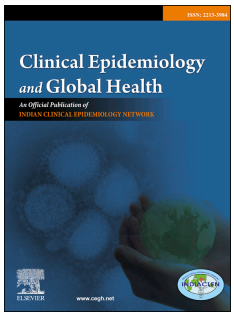

The COVID guidelines India project: A rapid living evidence synthesis during a pandemic in a LMIC setting

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PII: S2213-3984(24)00044-7

DOI: https://doi.org/10.1016/j.cegh.2024.101548

Reference: CEGH 101548

To appear in: *Clinical Epidemiology and Global Health*

Received Date: 4 November 2023

Revised Date: 23 January 2024

Accepted Date: 6 February 2024

Please cite this article as: Singh B, Alexander H, Tharyan P, Mathew JL, Covid management guidelines India group, Rupali P, Peter JV, Abraham OC, Christopher DJ, Jasmine S, Gopalakrishnan R, Soman R, Gupta N, Karthik R, Saha B, Sunavala A, Garner P, Rupali P, Core Committee, Garner P, Tharyan P, Mathew JL, Jasmine S, Ryan H, Singh B, Thomas K, Kadhiravan T, Kirubakaran R, Priscilla Rupali , Tharyan P, Garner P, Ryan H, Singh B, Alexander H, Mathew JL, Steering committee, Tom Fletcher , Solomon T, Vivekanandan M, Kumar PS, Ramesh M, Alangadan G, Wijesinghe PR, Sharma A, Thwaites G, Alejandria M, John L, Paul P, Paul T, Guha SK, Bhargava B, Oomen J, Philip G, Pulimood T, Methodology committe, Rajeev Soman , Gopalakrishnan R, Abraham OC, Rupali P, Singh B, Sunavala AJ, Ashley E, Rose W, Singh A, Mahajan A, Patel A, Pujari S, CS P, Lenin A, Suri V, R A, Saravu K, Karthik R, External Advisory Panel, Abraham OC, Subramanian R, Christopher DJ, Madan S, Tayade A, Sathyendra S, Danda D, Nagvekar V, Pichamuthu KK, Jasmine S, Patel A, Jiwanmall P, Mathew P, Mishra N, Malladi S, Arjun R, Expert Working Group – Antiviral, John Mammen J, Swaminanthan S, Narreddy S, Manesh A, Kang G, Varghese GK, Singhal T, Gangakhedkar R, Sabnis K, S D, Sundaramoorthy V, Deswal V, R A, Expert Working Group – Anti-inflammatory, Balamugesh T,

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Drafting the manuscript: B Singh , H Alexander , P Rupali

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Title: The COVID Guidelines India Project: A rapid living evidence synthesis during a pandemic in a LMIC setting

Short Title: The COVID Guidelines India Project

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Word count:
Abstract: 250 words
Full Text: 2524 words
Total number of references: 4
Number of figures: 3
Number of tables:1

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Funding

This work was partly supported by a grant given to CMC by the Research, Evidence and Development Initiative (READ-It project number 300342-104) for salaries of administrative staff. All the expert working group members are funded by the institutions by which they are employed and none were paid by the project.

Conflicts of interest: Standardised mandatory disclosure forms were scrutinised by the Steering Committee to assess for potential conflicts of interest from other sources of funding.

Acknowledgements

The institutions/organisations involved in the project included the Clinical Infectious Diseases Society (CIDS) based in India; Research, Evidence and Development Initiative (READ-It) Foundation; Cochrane Infectious Diseases Group (CIDG); Christian Medical College (CMC), Vellore; Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh; Apollo Hospitals, Chennai and Hyderabad; P. D. Hinduja Hospital and Medical Research Center, Mumbai; Gleneagles Global Hospitals, Chennai; Emmanuel Hospital Association; Kasturba Medical College, Manipal; Jupiter Hospital, Pune; Kingsway Hospital, Nagpur; Manipal Hospitals, Bengaluru; MGM Hospital, Vashi; KIMS Health Trivandrum and Believers Church Medical College hospital, Tiruvalla. Technical partners of the initiative were identified from CIDS, READ-It, Professor BV Moses Center and Clinical Epidemiology Unit, CMC Vellore and CIDG.

READ-It is funded by UK aid from the UK government; however, the views expressed in this manuscript do not necessarily reflect the UK government's official policies.

The COVID Guidelines India Project: A rapid living evidence synthesis during a pandemic in a LMIC setting

Abstract

Background: COVID-19 has had an unprecedented impact worldwide. Evidence for management interventions emerged rapidly but was difficult for clinicians and others to assess and decide how to use. Our team in India set up a national and international collaboration preparing guidance in real time to help guide clinical practice in the country during a pandemic setting. We describe our methods and the product in this paper.

Methods: Specialized groups comprising core, steering, methodology, evidence synthesis, dissemination and intervention expert working groups were formed. A Cochrane Rapid Review approach was used for prioritised questions in areas of clinical equipoise in management of COVID-19. GRADE methodology was incorporated into this process and expert working groups tailored guidelines for India using the WHO Evidence to Decision framework. This was then disseminated on a widely accessible platform: indiacovidguidelines.org. A questionnaire was then used to obtain end-user feedback on the guidelines.

Results: Since May 2021, a total of 20 guidelines have been developed spanning pharmacological, respiratory and other supportive interventions for management of COVID-19, with over 83,600 unique page views up to December 2023. Results from a pilot survey suggest usefulness of the guidelines, but also highlighted areas for improvement. A key output was adoption of our anticoagulation recommendation in state level COVID-19 guidelines (Kerala, India). National and institutional capacity for evidence synthesis and guidelines was strengthened.

Conclusions: The COVID Guidelines India project successfully developed contextually relevant, nationally applicable, evidence-based guidelines in a timely manner, and disseminated these freely through a dedicated website while successfully building capacity amongst Indian clinicians for evidence-based guideline development. Throughout the ongoing COVID Guidelines India project, the team has maintained a 'living' approach, continuously updating and refining recommendations in response to emerging evidence during the ever-evolving pandemic landscape.

Key words: Guideline development; Evidence-based; GRADE methodology; India; COVID-19

Background

The COVID-19 pandemic caused mortality, morbidity and societal impact on an unprecedented scale. Uncertainties with regard to transmission, diagnosis and treatment led to widespread panic and confusion.(1) Early on in the pandemic, various publications appeared in scientific literature claiming efficacy of a wide variety of medications.(2) Preprints rather than robust peer-reviewed literature dictated management across the world.(3) Observational studies, small trials with a high risk of bias and expert opinion led to rampant use of drugs such as hydroxychloroquine and ivermectin.(4) Drug regulatory bodies like the US Food and Drug Administration (FDA) and the Drug Controller General of India (DCGI) were also quick to provide drugs with emergency use authorization if drug activity was shown in *in vitro* or animal studies without evidence of benefit or exploration of potential harm in clinical studies. (5)

While new data on treatments and management strategies emerged rapidly, evidence could not be synthesized systematically in a timely manner to inform decision making for policy and practice.(6) Urgency of the situation meant that most country and institution guidelines were formulated based on consensus from experts or available literature on other similar illnesses. After several months, guidelines from highly-regarded bodies like the World Health Organization (WHO), National Institutes of Health (NIH) and US Centers for Disease Control and Prevention (CDC) using systematic evidence synthesis and GRADE approaches gradually appeared.(7–9) However these were often not relevant to situations encountered in some low- and middle-income countries e.g. due to cost or availability of interventions. In addition, shortages and delay in procurement of essential drugs used for COVID-19 further compounded the desperation and chaos.

Due to the paucity of reliable evidence and concerns about applicability of the aforementioned guidelines to the Indian scenario, we set up the Covid Management Guidelines India Group. This was a collection of senior expert clinicians, academics and methodologists in reputed institutions nationally, led by Christian Medical College (CMC) Vellore in partnership with the Clinical Infectious Diseases Society of India (CIDS). The initiative was supported by expert methodologists at the Prof BV Moses Centre for Evidence-Informed Healthcare and the Cochrane Infectious Diseases Group. The major aim was to address unanswered priority questions relating to COVID-19 management, using rapid systematic reviews and evidence summaries, incorporating the GRADE approach to assess certainty in the available evidence and strength of recommendations. As the guidelines were primarily developed for clinicians managing patients presenting to secondary and tertiary care hospitals in India, we used the WHO 'evidence to decision' framework to ensure relevance to this setting. (10)

Methods

Table 1 provides an overview of the structure of the group. The members of the various Committees are listed on the website (indiacovidguidelines.org). A Core Committee and Scientific Steering Committee were formed, who confirmed the remit of the guidelines, and decided on specific areas of highest priority, focusing on the degree of importance to patient care, and equipoise. The Core Committee took overall responsibility for decision making, including arbitration where needed, as well as for operational delivery of work. An External Advisory Panel comprising experts in infection, respiratory disease, public health and guidelines from throughout the world was also formed. Six Expert Working Groups were created; each group developed a long-list of priority COVID-19 management questions in the "Population, Intervention, Comparator, Outcome" (PICO) format. PICO questions were circulated to the wider group, discussed and prioritized, with further refinement into a short-list in order of priority by the Steering Committee and Methodology Committee. The methodology committee was a collection of methodologists with decades of experience in evidence synthesis, Cochrane systematic reviews and guideline development for WHO and national bodies. These questions were then presented to the External Advisory Panel and a consensus was arrived at to enable the Evidence Synthesis Team to work on the questions, starting with those of greatest importance.

The Expert Working Groups included experts from the fields of infectious diseases, internal medicine, pulmonary medicine, microbiology, virology, rheumatology, haematology, immunology, physiotherapy and rehabilitation. The specific interventions examined included antivirals, anti-inflammatories, anticoagulants, antibody therapies, respiratory support interventions and other supportive therapies.

Figure 1 summarises the overall process employed in development of the guidelines. Evidence synthesis for each intervention used Cochrane rapid systematic review methodology with data extraction, evaluation of trials included for risk of bias using the Cochrane Risk of Bias-2 (RoB2) tool (11) , followed by the application of GRADE(12) to assess the level of certainty in the evidence by the Evidence Synthesis Teams. This was reviewed by the Methodology Committee, some of whom had not been involved in the evidence synthesis process, to ensure the results were appropriately framed to the Expert Working Group. Where existing guidelines were available, these were considered to see whether they could be adopted or adapted. While none of the guidelines were found to be relevant to the needs of the recommendations being made, these were summarised to provide context to the expert working groups. Existing systematic reviews were considered, and if relevant to the PICO and of moderate or high quality, the search was updated and new results added to the previous review's results to ensure efficiency of the process.

Due to logistical challenges during the pandemic, all interactions among the Expert Working Groups took place via online platforms. The Expert Working Groups appraised the evidence and applied the WHO Evidence to Decision (EtD) framework to develop contextually relevant guidelines guided by the methodology and core committee for the Indian healthcare setting.(10) In the absence of adequate direct evidence a good practice statement was formulated. The Core Committee with final input from the Dissemination Committee and External Advisory Panel, finalised and uploaded the recommendations to the website.

A bespoke template was made to present every recommendation or good practice statement and all supporting information for each intervention on a dedicated webpage on the guideline website, included the following sections: Recommendation/Good Practice Statement; Justification; Evidence summary (comprising the following sub-sections: Summary of findings; Background; Methods; Results; Summary of characteristics of included trials; Forest plots; Evidence to decision; Implementation considerations; Subgroup considerations; Monitoring & evaluation; Research priorities; References and Citation.

As soon as each recommendation was ready, it was made available on the specially designed, dedicated website indiacovidguidelines.org in a modular format, enabling immediate use by clinicians. The guidelines were also circulated informally through social media and healthcare worker circles. For each intervention, periodic updates of the literature search and brief review of new studies informed decisions about when to update the recommendation. The decision on update frequency is contingent on intervention relevance, although an annual update is the anticipated schedule, aligning with current plans.

The project adopted a 'living' approach to evidence synthesis for interventions.(13) This involved setting a timeframe for updating the search and extracting new data from the literature. However, every time the steering group met, any new trials and recommendations in other guidelines that members were aware of were discussed in terms of their likelihood of influencing a change in our recommendations, to allow for earlier updates driven by potentially practice-changing new evidence.

In order to investigate the helpfulness of our guidelines, we sought feedback from end users, which is becoming recognised as best practice in ensuring responsive useful guidelines that are more likely to be adhered to, and has now been attempted by several guidelines groups using simple surveys (14). We developed and piloted a structured questionnaire with questions that focused on capturing feedback from clinicians managing patients with COVID-19 during the pandemic, including their awareness of the guidelines, and judgements regarding the practicality, feasibility and relevance of the guidelines for implementation for patient care. We performed a pilot survey using social media and informal networks to access as many clinicians as possible.

Results

Outputs of the project

Since May 2021, a total of 20 recommendations have been developed for management interventions, including seven antiviral drugs; seven anti-inflammatory agents; dosing of anticoagulants; two antibody-based treatments; two respiratory therapy interventions; and the supportive management intervention prone positioning. These provide comprehensive summaries of the evidence as well as supporting information for clinicians, policymakers and the public on these interventions. Several recommendations have been updated since the original judgement. **Figure 2** provides an overview of the interventions, and recommendations about their use, along with strength of and the level of certainty in the evidence informing the guideline.

Up to December 2023, the website has been accessed by around 27,000 unique users, with a total of over 83,600 views of recommendations. Over 18,000 of the users and 60,000 of the page views were in 2021.

A key output of this process was a coordinated national effort to produce real-time evidence-informed guidelines using systematic transparent GRADE and Evidence to Decision approaches. Over 100 clinicians from over 20 hospitals from across India contributed to this effort, most of whom had no prior experience in systematic review or GRADE-informed guidelines. Thus building individual and organisational capacity for evidence synthesis and guidelines for clinical practice in India has been a major output of the project. This led to the creation of a critical mass of evidence-informed practice experts who could then go on to use this knowledge for making guidelines in their respective fields in the future.

The rapidity of the guidelines also ensured that evidence was current and could be easily applied in a clinical setting. For example, our first intervention was ivermectin. The median time from the initial search of the literature to finalising the first recommendation for an intervention was 61 days (interquartile range 46-89 days), with the quickest being 30 days. (**Figure 3**).

Members of the Group subsequently went on to be involved in various Cochrane review teams synthesising evidence for the use of interventions for COVID-19, namely: hydroxychloroquine/chloroquine; inhaled corticosteroids; prone positioning; molnupiravir; and favipiravir. The former three have comprehensive reviews that have informed guidelines and practice internationally, whereas the latter two have protocols and reviews are due to be published soon. Our Group members are lead authors of three of these reviews.

Several institutions (such as Christian Medical College (CMC) Vellore and Apollo Hospitals) and state governments (such as Kerala Directorate of Health Services) adopted or adapted parts of the guidelines into their own institutional guidelines. For example, the Kerala state guidelines cited our recommendation for use of therapeutic anticoagulation in moderately-to critically-ill patients with COVID-19, thus encouraging state-wide implementation of our recommendation.(15) It is noteworthy that therapeutic anticoagulation for treatment of moderate to severe COVID-19 was controversial at that time with varying expert opinions for and against. Several members of our group were members of other guideline development groups, such as WHO, and various national guidelines, including the Indian Council of Medical Research. Cross-pollination of ideas and mutual benefit in terms of informing each other's guidelines is likely to have occurred, though this impact would be difficult to measure.

The guidelines were also widely disseminated on social media platforms such as Twitter and WhatsApp, which anecdotally was reported to be of help to many institutions, hospitals and healthcare facilities at the local, regional and national levels. We had members in our Expert Working Groups from community, secondary and tertiary care levels, who ensured the recommendations equipped clinicians to tailor their practice based on the resources available.

End-user survey

We received 89 responses from clinicians in 14 states in India (and one each from the USA and the UK). The majority (69%) of participants were aged 31-50 years; 60% identified as male; and 87% were senior physicians. Most were specialists in internal medicine (24%) or infectious diseases (45%), and practised in non-government settings (83%). The majority (69%) said the COVID Guidelines India website was one of the main sources they use to inform their practice for COVID-19 care. Almost 83% had been recommended the website by a colleague or friend or through social media and search engines.

The proportion of participants agreeing with the following statements about the guidelines (including "strongly agree", "agree" and "somewhat agree" on a Likert scale) ranged from 83% to 89%: "The recommendations are easy to understand"; "I find it easy to implement the recommendations in my practice"; "The recommendations are relevant for my setting of practice"; "The recommendations have influenced my practice"; "The level of detail in the rationale and the evidence summary for the recommendations was appropriate"; and "The website was easy to navigate and use".

Thirteen (15%) reported experiencing barriers to implementation of the guidelines, including availability and cost of the medications, perceptions regarding toxicity of treatments and difficulty convincing patients that certain treatments were not indicated. A few said that the guidelines are not well known among their medical fraternity and another expressed disagreement with the remdesivir guidelines.

Regarding suggestions for improvement, participants provided diverse feedback - some appreciated the website's informativeness and detailed content for managing COVID patients, and wanted the user interface to be enhanced and user-friendly with additional information regarding vaccines and management of drug related complications. Respondents provided valuable suggestions to improve the COVID management website, including adding time stamps to ensure up-to-date information and increasing its visibility through publicity.

It is worth noting that these pilot data reflect the perceptions and experiences of a limited number of healthcare professionals who actively engaged with the website. While the positive feedback highlights the usefulness and impact of the guidelines, further research and feedback from a larger and more diverse sample would provide a more comprehensive understanding of the website's effectiveness in guiding COVID-19 management practices in India. This is being planned for rollout later this year.

Discussion

Key learning points from the project

Academic and government bodies have strong incentives towards developing guidelines to influence local, regional and national policies. The need was amplified during the COVID-19 pandemic. However, producing guidelines which are evidence-informed needs expertise which is often lacking in a low- or middle-income country setting. Though WHO and NIH did eventually develop evidence-based guidelines relatively quickly, the resources employed were considerable, and it is difficult for recommendations to apply to every country. Considerations such as equitable distribution of required resources, cost and acceptability of various interventions can vary greatly between countries, especially in a middle-income country with a resource-limited health system like India.

The COVID Guidelines India project was one of a few notable initiatives in low middle-income countries aiming to address the need for evidence-based guidelines during the pandemic, similar to groups in South Africa and the Philippines (16,17) providing locally relevant recommendations. They all emphasized rapid evidence synthesis, using a living-guideline approach for evolving evidence, while employing GRADE methodology and providing detailed evidence summaries. The Evidence to decision approach by the Expert Working Group took into account common challenges of medication availability and barriers to guideline implementation. On comparison, distinct differences emerge in the scope and specific interventions that were covered. While COVID Guidelines India and the Philippines guidelines included a range of interventions spanning pharmacological, respiratory, and supportive measures, the reviews in South Africa were more focused on drug treatments. The Philippines guidelines are very broad, including vaccines, screening and diagnostic testing. However, this in itself exemplifies the need to ensure the scope of guidelines is defined according to individual countries' context and needs. Moreover, the

outreach strategies, feedback mechanisms, and integration of guidelines into local healthcare structures might have varied, reflecting the unique healthcare landscapes of each country.

Rapid dissemination of evidence-based guidelines is always challenging and to do so during a pandemic with ambitious timelines even more so. However, with our group of motivated clinicians and methodologists we were able to achieve this with a modular workflow. This enabled dissemination of individual recommendations as soon as they were ready to inform local practice.

This dynamic, 'living' approach to evidence synthesis for interventions, emphasized real-time responsiveness to emerging evidence, with continual updates and refinements to the recommendations. Scrutiny of the evidence from various perspectives embedded within the process enabled a swift and pragmatic response to emerging findings while maintaining methodological rigour and relevance to the evolving needs of clinicians managing COVID-19 across India.

The project had some limitations. Despite inclusion of some patients and non-medical practitioners (including physiotherapists, respiratory therapists and pharmacists) in the guidelines Group, a large majority of members were medical doctors and/or clinical academics. This is a challenge faced by many guidelines groups, for which approaches are being developed actively.(18) Additionally, the initial reviews and recommendations were produced at a time when there was a global focus and urgency on the disease for which the guidelines were made, so sustainability of this approach will need to be determined, potentially with adaptations to the process.

Future plans

In addition to ongoing periodic updates of the guidelines on the website, the network of institutions and individuals involved in the project have expressed the desire to gain further experience in evidence synthesis and GRADE-informed guidelines. To capitalize on the capacity built during the COVID Guidelines India project, the Centre for Guideline Development has been set up at Christian Medical College (CMC) Vellore, in collaboration with partners at the Postgraduate Institute for Medical Education & Research (PGI), Chandigarh (India), and the READ-It initiative (UK/South Africa). Inaugurated in July 2023, the first project of the CGD is Indian national guidelines for diagnosis and management of brain infections, in collaboration with the Clinical Infectious Diseases Society (CIDS), Indian Academy of Neurology (IAN) and the Indian Academy of Paediatrics (IAP).

Conclusion

The COVID Guidelines India project developed contextually relevant, nationally applicable, evidence-based guidelines in a timely manner, and disseminated these freely through a dedicated website, building capacity and expertise making it a model pilot project, to use

a phrase coined by one of our Group members “of the people, by the people, and for the people”.

Ethical approval statement

"Ethical clearance was not sought for the India COVID Guidelines Initiative, as it primarily focused on appraising the evidence and interpreting it to develop guidelines for the management of COVID-19. It did not involve enrolling patients. The institution's administrative committee approved the same (min number-16-q/2/21 dated 04.02.2021) and a letter of support were obtained. Additionally, participating experts provided conflict of interest statements before the commencement of the initiative"

Funding

This work was partly supported by a grant given to CMC by the Research, Evidence and Development Initiative (READ-It project number 300342-104) for salaries of administrative staff. All the expert working group members are funded by the institutions by which they are employed and none were paid by the project.

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Acquisition of data: B Singh , H Alexander , P Tharyan , JL Mathew ;P Rupali

Analysis and/or interpretation of data: B Singh, H Ale, xander, P T,haryan, P Garner, JL Mathew ;P Rupali

Drafting the manuscript: B Singh , H Alexander , P Rupali

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Acknowledgements

The institutions/organisations involved in the project included the Clinical Infectious Diseases Society (CIDS) based in India; Research, Evidence and Development Initiative (READ-It) Foundation; Cochrane Infectious Diseases Group (CIDG); Christian Medical College (CMC), Vellore; Postgraduate Institute of Medical Education and Research

(PGIMER), Chandigarh; Apollo Hospitals, Chennai and Hyderabad; P. D. Hinduja Hospital and Medical Research Center, Mumbai; Gleneagles Global Hospitals, Chennai; Emmanuel Hospital Association; Kasturba Medical College, Manipal; Jupiter Hospital, Pune; Kingsway Hospital, Nagpur; Manipal Hospitals, Bengaluru; MGM Hospital, Vashi; KIMS Health Trivandrum and Believers Church Medical College hospital, Tiruvalla. Technical partners of the initiative were identified from CIDS, READ-It, Professor BV Moses Center and Clinical Epidemiology Unit, CMC Vellore and CIDG.

READ-It is funded by UK aid from the UK government; however, the views expressed in this manuscript do not necessarily reflect the UK government's official policies.

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Table 1: Structure of the COVID Guidelines India Group

Group	Composition[1]	Role
Cross-cutting groups		
Core committee	Included the chair of the guidelines group, and chairs of the Methodology Committee and Evidence Synthesis Team	Overall administrative and coordination responsibilities, including workflow, operational delivery and financial aspects.
Steering committee	Included the chairs of each working group and committee	Decided on the scientific scope of the guidelines; determined and re-evaluated prioritisation of the various interventions.
Methodology committee	Methodologists specialising in evidence synthesis and guidelines	Ensured appropriate methods were followed for evidence summaries and development of recommendations & good practice statements; helped Expert Working Groups interpret results and apply the Evidence to Decision framework.
External advisory panel	Experts in infections, public health, respiratory medicine, evidence synthesis and guidelines from various countries	External impartial scrutiny of the interpretation of evidence and relevance & applicability to the Indian setting; provided scientific challenge.
Evidence synthesis team	Clinicians and academics with experience in (or keen to learn) evidence synthesis	Producing evidence summaries from synthesis of data from the available literature; presentation of these to expert working groups after input from the methodology committee.
Dissemination committee	Experts in dissemination of guidelines and other health-related information from a variety of disciplines	Oversight of the website and text/presentation of recommendations/statements for individual interventions; guidance on dissemination to end users and liaison with external bodies.
Expert working groups		
Antiviral	Experts in clinical and academic aspects of each intervention	Provide interpretation of the evidence; judgements on various aspects of how the evidence relates to potential use of each intervention; decisions on overall recommendation or good practice statement; drafting of wording for these and for supporting statements.
Anti-inflammatories		
Anticoagulation		
Antibodies		
Respiratory support treatments		
Other supportive management		

[1]Members of each group/committee are listed on the website: XYXYXYXYXYX

Figure 1. Overview of the Guideline Development Process

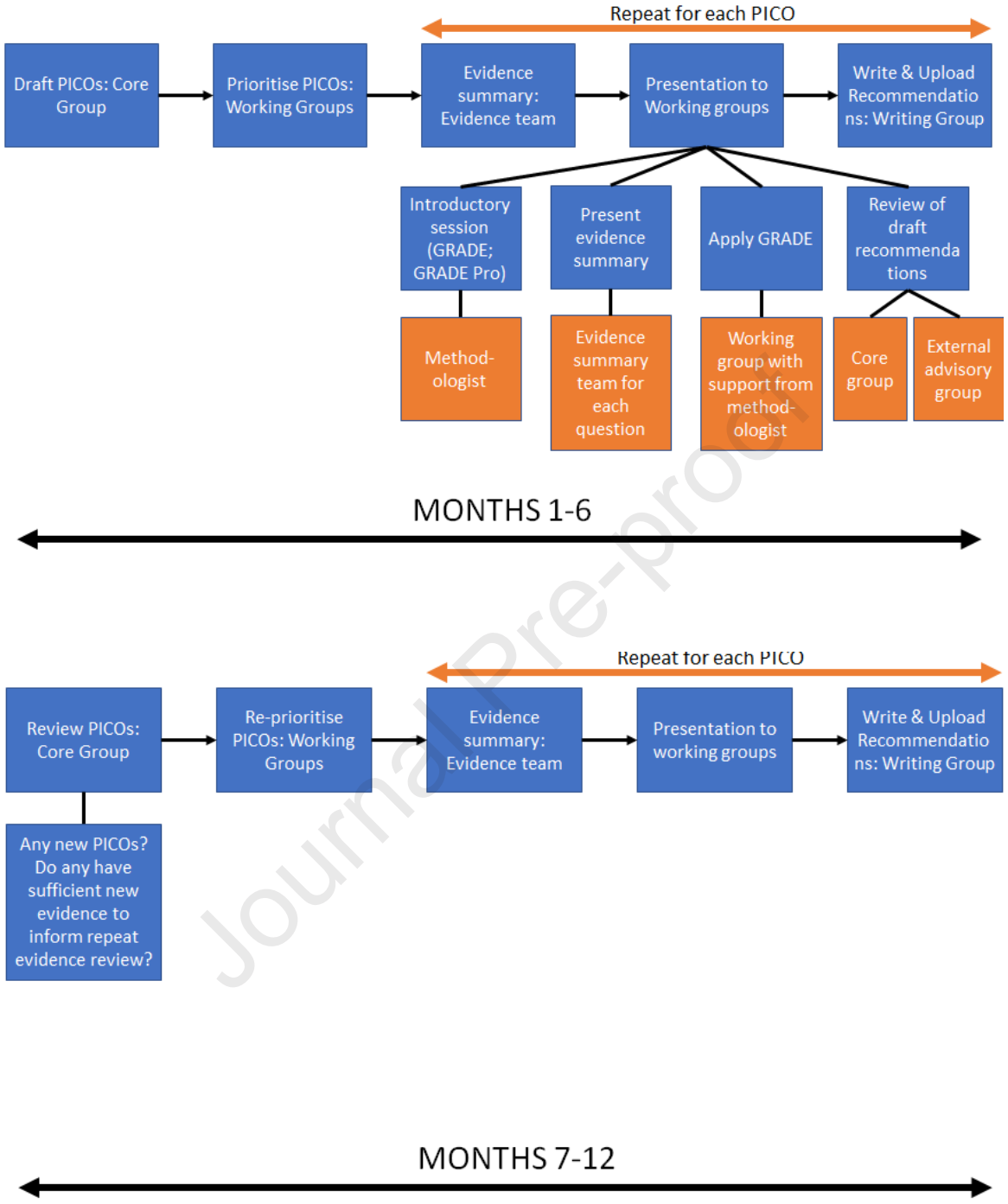


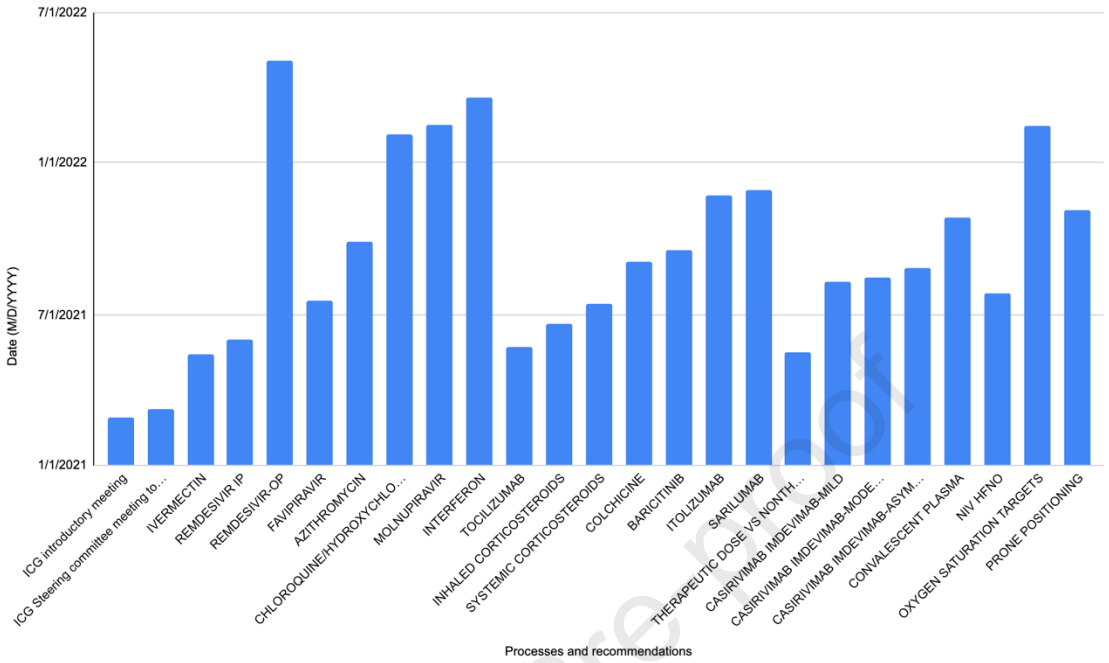
Figure 2. Summary of recommendations (as of 23rd September 2023)

Intervention		Mild	Moderate	Severe	Critical	Certainty of evidence	Date of Recommendatio
		• Symptomatic (any acute COVID-19 related symptoms) • AND respiratory rate • WITHOUT pneumonia or hypoxia	*• Pneumonia (clinical or radiological) OR hypoxia (SpO2 • AND respiratory rate ≤30/min • AND SpO2 ≥90% on room air*	*Pneumonia with ANY ONE of the following: • RR >30/min • severe respiratory distress • SpO2 • NO invasive or non-invasive respiratory support needed*	*• Requirement for high-level respiratory support: NIV or HFNO or IMV • OR ARDS (PaO2/FiO2 ratio of • OR sepsis • OR shock*		
Antiviral	Azithromycin	Not recommended	Not recommended	Not recommended	Not recommended	⊕⊕⊕⊕ HIGH	27/09/2021
	Ivermectin	Not recommended	Not recommended	Not recommended	Not recommended	⊕⊕⊕⊕ HIGH	15/05//2021
	Hydroxychloroquine / Chloroquine	Not recommended	Not recommended	Not recommended	Not recommended	⊕⊕⊕◯ MODERATE	04//02/2022
	Favipiravir	Not recommended	Not recommended	Not recommended	Not recommended	⊕◯◯◯ VERY LOW	19/07/2021
	Remdesivir	Not recommended	Recommended %	Recommended %	Recommended %	⊕⊕⊕◯ MODERATE	16/06/2022
	Interferons	Not recommended	Not recommended	Not recommended	Not recommended	⊕⊕⊕◯ MODERATE	27/10/2021
	Molnupiravir	Recommended *	Recommended *	Not recommended	Not recommended	⊕◯◯◯ VERY LOW	16/02/2022
Anti- inflammatories	Tocilizumab / Sarilumab	Not recommended	Not recommended	Recommended #	Recommended #	⊕⊕⊕◯ MODERATE	24/05/2021
	Baricitinib	Not recommended	Recommended π	Recommended π	Recommended π	⊕⊕⊕◯ MODERATE	17/09/2021
	Inhaled corticosteroids	Recommended $	Not recommended	Not recommended	Not recommended	⊕⊕◯◯ LOW	21/06/2021
	Systemic corticosteroids	Not recommended	Not recommended	Recommended @	Recommended @	⊕◯◯◯ VERY LOW	15/07/2021
	Colchicine	Not recommended	Not recommended	Not recommended	Not recommended	⊕⊕◯◯ LOW	03/09/2021
	Itolizumab	Not recommended	Not recommended	Not recommended	Not recommended	⊕◯◯◯ VERY LOW	22/11/2021
Thromboprophylaxis	Therapeutic dose Vs Nontherapeutic dose of thromboprophylaxis	Recommended α	Recommended β	Recommended β	Recommended α	⊕⊕⊕◯ MODERATE	08/08//2022
Antibody	Convalescent Plasma	Not recommended	Not recommended	Not recommended	Not recommended	⊕⊕⊕⊕ HIGH	27/10/2021
	Casirivimab-Imdevimab	Recommended £	Recommended £	Not recommended	Not recommended	⊕⊕⊕⊕ HIGH	11/08/2021
Respiratory Therapies	NIV Vs HFNO	Recommended	Recommended	Recommended	Recommended	⊕◯◯◯ VERY LOW	27/07/2021
	Oxygen Saturation Targets	Recommended Ω	Recommended Ω	Recommended Ω	Recommended Ω	⊕◯◯◯ VERY LOW	12/02/2022
Other Supportive Management	Prone Positioning	Not recommended	Recommended	Recommended	Recommended	⊕◯◯◯ VERY LOW	05/11/2021

* :- Only in patients with mild to moderate covid-19 with risk factors for developing severe disease.
# :- Tocilizumab 8mg/kg, maximum 800mg as a single dose
$:- for symptomatic relief.
@ :- 6 mg of Dexamethasone or equivalent per day IV or Oral till normalization of Oxygen saturation or max 10 days.
% :- Remdesivir 200 mg IV OD on the first day followed by 100 mg IV OD from Day 2-5, to be given with in 5 days of symptom onset
α :-Enoxaparin 40 mg SC OD
β :- Enoxaparin 40 mg OD to 1 mg/Kg BD SC
π :- 4 mg once daily for 14 days or until discharge
£ :- Only for patients with non-omicron variant with a risk factor for severe illness, and no detectable covid-19 antibodies present in their body. Casirivimab 600 mg + Imdevimab 600 mg as a single infusion within 10 days of symptom onset.
Ω :- Target SPO2 at 94-98%.

Strong against recommendation
Conditional against recommendation
Conditional for recommendation
Strong for recommendation

Figure 3. Timelines of processes and recommendations, from 1st January 2021 onwards



Declaration of interests

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐ The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: