health

Department:
Health
REPUBLIC OF SOUTH AFRICA

National Essential Medicines List Therapeutic Guidelines Subcommittee on Covid-19 Terms Of Reference

26 NOVEMBER 2020 VERSION 4.0

Contents

Abbreviations 2
Introduction 2
Purpose and Scope 2
Authority to act 3
Membership 3
Code of conduct 3
Rapid review process 4
Communication 6
Roles and Responsibilities 7

Abbreviations

Coronavirus Disease-2019	-	Covid-19
HTA	-	Health Technology Assessment
MAC	-	Ministerial Advisory Committee
NDoH	-	National Department of Health
NEMLC	-	National Essential Medicines List Committee
WHO	-	World Health Organization

Introduction

Outbreaks of emerging and re-emerging infectious diseases confer a direct threat to human health, the integrity of our health system, and the national and global economy. Like the influenza pandemics of 1918 and 2009, and epidemics of Ebola Virus Disease (2014), SARS (2002), and MERS (2012), the novel coronavirus SARS-CoV-2 now causing a pandemic of Coronavirus Disease-2019 (Covid-19) focuses our attention on the inter-sectoral, multidisciplinary response required to respond to Covid-19 and the lessons that can be learnt for a future pandemic.

Purpose and Scope

The National Essential Medicines List Therapeutic Guidelines Subcommittee is an advisory Subcommittee of the ministerially appointed National Essential Medicines List Committee (NEMLC) (refer to the Terms of Reference of the NEMLC, version 6, April 2019). The Subcommittee is tasked with providing specific patient-focused evidence-based recommendations to support therapeutic and preventative therapies for Covid-19, as well as, supportive agents for the management of comorbid diseases, for inclusion in the *Clinical Management of Suspected or Confirmed Covid-19 Disease Guideline*. This guideline applies to situations where guidance is lacking from standard management of similar clinical conditions (e.g. pneumonia, severe acute respiratory distress) already recommended in the current NEMLC-approved Standard Treatment Guidelines (STGs) and Essential Medicines List (EML). Recommendations will be provided in a rapid medicine review format, based on the principles of evidence-based medicine and the approach used by NEMLC.

The Subcommittee may also, in consultation with the chairperson of the Clinical Guideline Writing Committee on Covid-19 and the Lead of the Clinical Care work stream of the Incident Management Team (IMT) of the National Department of Health (NDoH), provide input regarding:

- Therapeutic agents to be prioritised for rapid review to inform the clinical management guidelines;
- Information and issues which require intervention by the South African Health Products Regulatory Authority;
- Recommendations to clinicians about therapeutic interventions under investigation in clinical trials; and
- Recommendations on other issues that emerge during the Covid-19 epidemic.

Authority to act

The NEMLC Therapeutic Guidelines Subcommittee is an advisory committee to the Clinical Guideline Writing Committee on Covid-19 and does not have any delegated powers to act on behalf of, or to commit, the Government to any actions. The Clinical Guideline Writing Committee engages with the Ministerial Advisory Committee (MAC) on Covid-19.

The Chairperson and the Vice-chairperson of the Subcommittee will either be the current standing Chairperson and Vice-chairperson of NEMLC or be appointed by the Subcommittee. The Chairperson will appoint a lead and co-lead, who will contribute to the development and updating of the *Clinical Management of Suspected or Confirmed Covid-19 Disease Guideline.* The lead and co-lead will also liaise with, and share rapid evidence reviews with the Clinical Guideline Writing Committee on Covid-19. The NEMLC Therapeutics Guidelines Subcommittee will be dissolved, once the Clinical Guideline Writing Committee on Covid-19 is dissolved.

Membership

The NEMLC Therapeutic Guidelines Subcommittee, is comprised of members of the ministerially- appointed NEMLC, members of the ministerially-appointed Expert Review Committees and members who are not appointed to the NEMLC (including stakeholders with expertise in evidence-based medicine and representation from the national health products regulatory authority). Non-members may be invited to attend meetings and provide presentations as required. Attendance must be approved by the Chairperson of the Subcommittee prior to the meeting. The process for the management of conflict of interest and confidentiality will follow the standard NEMLC process.

Members of the Subcommittee are participants in their individual capacity and do not represent any constituency, organisation or sector except the NEMLC. The recommendations of the NEMLC Therapeutic Guidelines Subcommittee would be considered representative of the views of the current NEMLC, whose Term of Office ends on 30th June 2020. Members have a duty to act honestly and in good faith and to exercise skill, care and diligence in carrying out their duties and not make improper use of information. Members are subject to all of the applicable provisions and procedures surrounding conflict of interest and confidentiality, as per the standard NEMLC process.

Members **may not** nominate representatives to attend meetings in their absence. Members may not allow non-members to listen to or attend the meetings unless approved by the Chairperson.

Code of conduct

Members are expected to:

- avail themselves for meetings, punctually and for the whole of the scheduled meeting time;

- indicate their failure to attend any meeting in writing to the secretariat, in good time with the reason as to why they were unable to attend;
- act with the highest professional and ethical standards at all times;
- contribute to debate in an informed and rational way and take decisions solely in the interest of the public;
- regard the views expressed by individual members of the Subcommittee and recommendations as strictly confidential;
- respect and value each member's perspective and contribution;
- make decisions together and take joint responsibility for decisions taken; and
- be informed and prepared for the meeting by reading the agenda and papers.

Under no circumstances may an individual member, other than the Chairperson, officially represent the views and decisions of the Subcommittee, unless the Chairperson has authorised thus.

Rapid review process

Rapid review is a focused synthesis of the available evidence and is an appropriate tool during a pandemic (such as the Covid-19 pandemic) where time-sensitive questions of healthcare decision-makers need to be answered as fast as possible. At the same time, sound scientific rigor and methodology should be applied at all times.

Process

New questions may arise from:

- Clinical Guideline Writing Committee on Covid-19
- Feedback from MAC
- Feedback from Provincial Pharmaceutical Therapeutics Committees as a result of input from clinicians and patients.
- Feedback from NDoH.

Question prioritisation

The Subcommittee may apply criteria to prioritise questions for a rapid review. Questions should meet the following criteria:

- Question is high priority to clinicians and patients
- There is limited evidence and therefore uncertainty about the benefit or harm of the intervention
- There is research evidence emerging on the topic that may inform a recommendation

Conducting rapid reviews

- A standard protocol including an outline of the Population, Intervention/s, Control, and Outcomes (PICO) and related methods will guide the conduct of rapid reviews.
- The PICO for each review is approved by the Subcommittee in collaboration with the Clinical Guideline Committee, as required (Appendix 1: Generic PICO template).
- Rapid review reports should be submitted to the Subcommittee within one week from the time of PICO approval in the standard reporting template (Appendix 2).
- Rapid reviews evaluating the effectiveness of an intervention aim to summarise available reviews, but where these are not available, randomised trials may be presented in the narrative format. In their absence observational studies may be reported.
- Review teams: A lead reviewer from the Subcommittee, or delegated lead, oversees the process, drafts the PICO for approval and leads drafting of the background, key findings and recommendations. Two independent reviewers with experience of conducting evidence syntheses can be co-opted to support the review process. All co-opted members need to sign the conflict of interest and confidentiality forms.
- Once the Subcommittee has approved a rapid review report, the Secretariat finalises the report for public dissemination.
- All finalised reviews will be shared with the Clinical Guideline Writing Committee and MAC by the co-leads or NDoH Secretariat.
- Where recommendations differ from those in place in the current version of the COVID-19 National Guidelines, discussion and collaboration should take place to understand value aspects of decision-making between the Subcommittee and the Clinical Guideline Writing Committee. Such liaison may be led by members of the Subcommittee designated by the chairperson of the Subcommittee.
- All reviews will be placed in an open access repository: http://www.health.gov.za/index.php/national-essential-medicine-list-committee-nemlc/category/633-covid-19-rapid-reviews
- Where relevant, rapid reviews will be adapted for information and use by different stakeholders including the public, and may be disseminated via relevant platforms including social media (e.g. development of a simple one page summary – see Appendix 3).

Topics to be researched are determined in collaboration with the Clinical Guideline Writing Committee and prioritised accordingly, using consensus criteria (or an appropriate decision-making tool). A topic is assigned to a minimum of two reviewers and the PICO is proposed. (A generic template specific to the pandemic and developed by the Subcommittee will be used). The specific PICO is reviewed by the Subcommittee in collaboration with Guideline Committee, where required.

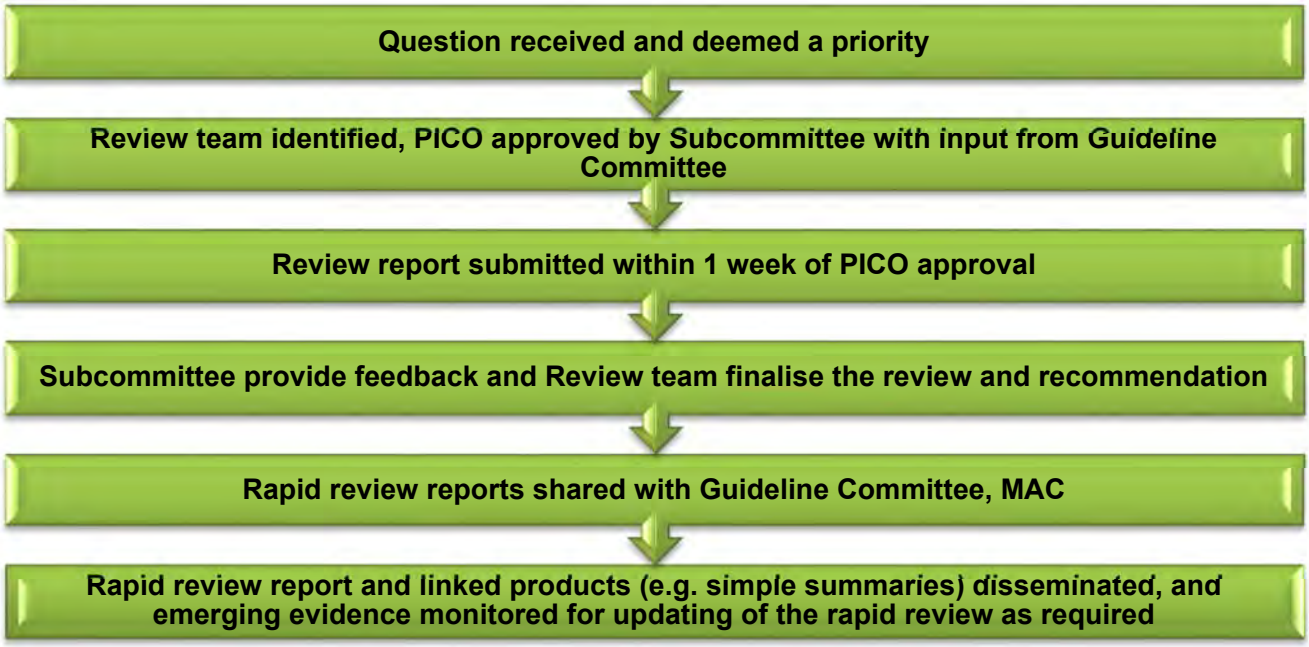
The initial draft review (guided by a generic rapid review report template) is peer-reviewed by the Subcommittee and a recommendation is prepared. If the Clinical Guideline Writing Committee has a contrary view, consultation should take place to understand other value aspects of decision-making.

The final approved rapid review is published on the NDoH website and the URL link added to the updated version of the *Clinical Management of Suspected or Confirmed Covid-19 Disease Guideline*. A one-page summary is developed, as required for publication on the NDoH website or in a peer-reviewed journal, as required.

Updating reviews

As evidence is continuously emerging, the rapid reviews will be updated if and when more evidence becomes available. However, to minimise duplication of efforts and facilitate efficient use of resources, completed systematic reviews and Health Technology Assessments (HTAs) identified in the literature may be reported in a rapid review with appropriate appraisal. Living systematic reviews will also be reviewed, and if used, acknowledged accordingly. Framework for updating rapid reviews is described in Appendix 4.

Figure 1: Steps in conducting a rapid review:

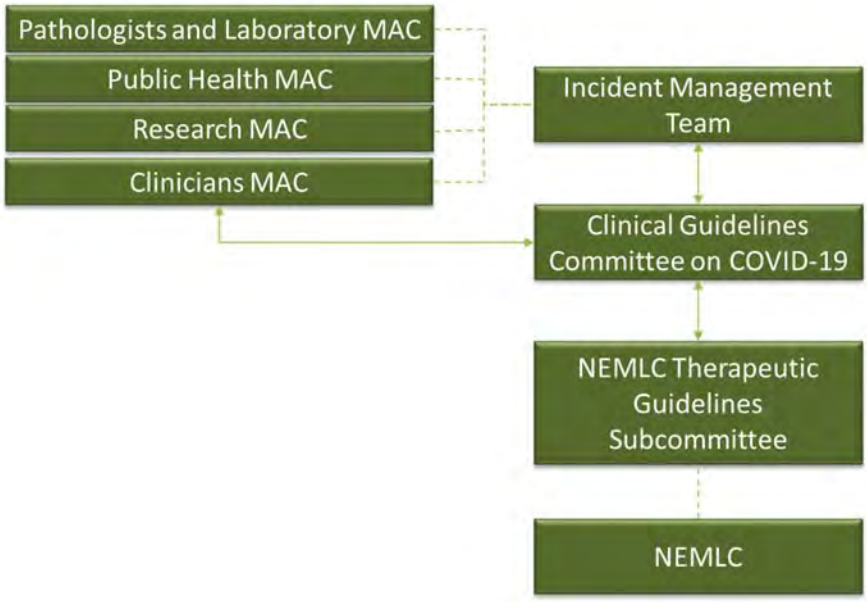


Communication

The Chairperson of the NEMLC Therapeutic Guidelines Subcommittee, or nominated lead and co-lead will communicate the recommendations of the Subcommittee to the Chairperson of the Clinical Guideline Writing Committee and the Lead of the Clinical Care work stream of the IMT, either directly or through the Secretariat supporting the Subcommittee. The lead or co-lead may be invited as an observer, on request of the Chairperson of the Clinical Guideline Writing Committee or Chairperson of the MAC on COVID-19, to participate in meetings of the

Ministerial Advisory Committees (MAC) on COVID-19 as depicted below in Figure 1. This should be done in consultation with the lead of the Clinical Care work stream of the IMT.

Figure 2: Communication between the Committees on Covid-19



Roles and Responsibilities

Stakeholder	Role and Responsibility
Clinical Guideline Writing Committee	• Review and updating of the Clinical Management Guideline for Covid-19. • Addressing of queries from stakeholders on the guideline.
Chairperson of the Clinical Guideline Committee	• Co-ordination of the development and updating of the guideline • Responds to queries from stakeholders on the guideline on behalf of the Committee • Communication of recommendations to the Clinical Care Lead of the IMT
Lead or Co-Lead of the Therapeutic Guidelines Subcommittee	• Nominated by the Chairperson to communicate the Therapeutic Guidelines Subcommittee recommendations to the Clinical Guideline Writing Committee on appropriate therapeutic management and/or share the recommendations of the Subcommittee with the MAC on Covid-19, either directly or through the Secretariat supporting the Subcommittee.
Secretariat of the NEMLC Therapeutic Guidelines Subcommittee	• Develop and maintain a dynamic list of therapeutic agents to be prioritised for rapid review, as per Subcommittee recommendations.

Stakeholder	Role and Responsibility
	• Convene meetings and make all the necessary logistic arrangements; or maintain electronic discussion within the Subcommittee. • Facilitate the proper functioning of the Subcommittee in accordance with the principles of good governance. • Compile minutes of meetings and finalise the draft in consultation with the Chairperson/ Vice-chairperson of the Subcommittee. • Support the Subcommittee pertaining to any research that is required and contribute to the development of rapid reviews as required. • Support with editing, formatting and publication of the final rapid reviews (on the required platform). • In consultation with the Chairperson/ Vice-chairperson of the Subcommittee, source reviewers from NEMLC, Expert Review Committees or other organisations. • Maintain a list of relevant randomised controlled trials that have been completed and advise the Subcommittee accordingly.
Director-General	• Approval of guideline.
Clinical Care Work stream of the IMT	• Clinical editing of guideline. • Formatting of guideline. • Dissemination of guideline to the Communications Department of NDoH. • Receipt and coordination of queries from stakeholders on the guideline and communication thereof to the Chairperson of the Clinical Guideline Writing Committee.
Lead of the Clinical Care Work stream of the IMT	• Addressing queries from stakeholders on the guideline.
Communications Department	• Dissemination of the guideline to all internal and external stakeholders.

Version	Date	Revisions
1.1	11 May 2020	N/A; Initial version
2.0	4 June 2020	Appendix 1 – Population 1 amended from “pre-hospital” to “ambulatory” Appendix 2 – Evidence to decision framework added to rapid review report
3.0	25 July 2020	Appendix 2 – Summary of findings table added; Evidence to decision framework updated
4.0	26 November 2020	Appendix 1 – Included clinical improvement on an ordinal scale that may be considered as an outcome. Appendix 4 – Framework for updating rapid reviews Appendix 2 – updated to include rationale for updating a review

APPENDIX 1: Generic PICO for COVID-19 rapid reviews

Process – preliminary overview of the agent to determine if it is being used in multiple severity stages or only one. If the latter, only use PICO for that stage; if the former either do separate reviews per stage, or if a single review is planned (likely until evidence base much larger) then ensure that subgroup analyses focus on endpoints appropriate for each level of severity being considered.

Population 1 – ambulatory Ambulant patients with confirmed COVID-19, no restriction to age but disease sufficiently mild that management outside hospital is feasible.
Intervention Medicine under review either alone or in combination with other medicines. No restriction on dose, frequency, or timing with respect to onset of symptoms/severity of disease.
Comparators Any (standard of care/placebo or active comparator).
Outcomes Mortality; progression to hospitalisation; proportion with negative SARS-CoV-2 PCR on nasopharyngeal swab at chosen time point(s) post-diagnosis; time to negative SARS-CoV2 PCR on nasopharyngeal swab; adverse reactions and adverse events.

Population 2 – hospitalised Patients with confirmed COVID-19, no restriction to age but disease severity such that hospitalisation required.
Intervention Medicine under review either alone or in combination with other medicines. No restriction on dose, frequency, or timing with respect to onset of symptoms/severity of disease.
Comparators Any (standard of care/placebo or active comparator).
Outcomes Mortality; duration of hospitalisation; proportion with negative SARS-CoV-2 PCR on nasopharyngeal swab at chosen time point(s) post-diagnosis; time to negative SARS-CoV2 PCR on nasopharyngeal swab; progression to ICU admission; progression to mechanical ventilation; duration of ICU stay; duration of mechanical ventilation; adverse reactions and adverse events.

Population 3a – requiring oxygen Patients with confirmed COVID-19, no restriction to age but severe disease requiring oxygen or ventilatory assistance.
Intervention Medicine under review either alone or in combination with other medicines. No restriction on dose, frequency, or timing with respect to onset of symptoms/severity of disease.
Comparators Any (standard of care/placebo or active comparator).
Outcomes Mortality; progression to mechanical ventilation; duration of ventilatory support; duration of mechanical ventilation; duration of ICU stay; adverse reactions and adverse events.

Population 3b – requiring ventilatory support (non-invasive/invasive) Patients with confirmed COVID-19, no restriction to age but severe disease requiring oxygen or ventilatory assistance.
Intervention Medicine under review either alone or in combination with other medicines. No restriction on dose, frequency, or timing with respect to onset of symptoms/severity of disease.
Comparators Any (standard of care/placebo or active comparator).
Outcomes Mortality; duration of ventilatory support; duration of mechanical ventilation; duration of ICU stay; adverse reactions and adverse events.

Population 4 – prophylaxis Patients at risk of COVID-19 but currently asymptomatic, no restriction to age or comorbidities
Intervention Medicine under review either alone or in combination with other medicines. No restriction on dose or frequency.
Comparators Any (standard of care/placebo or active comparator).
Outcomes Development of COVID-19 with positive SARS-CoV-2 PCR; duration of symptoms; proportion requiring hospitalisation; adverse reactions and adverse events.

Various scales are used to measure outcomes in COVID-19 clinical trials and the World Health Organisation R&D Blueprint expert group has proposed the following:

ORDINAL SCALE FOR CLINICAL IMPROVEMENT SCORE		
Patient state	**Descriptor**	**Score**
Uninfected	No clinical or virological evidence of infection	0
Ambulatory	No limitation of activities	1
	Limitation of activities	2
Hospitalised: mild disease	Hospitalised, no oxygen therapy	3
	Oxygen by mask or nasal prongs	4
Hospitalised: severe disease	Non-invasive ventilation or high-flow oxygen	5
	Intubation and mechanical ventilation	6
	Ventilation + additional organ support – pressors, RRT, ECMO	7
Dead	Death	8

Reference: World Health Organisation R&D Blueprint for the novel Coronavirus, Covid-19 therapeutic trial synopsis, February 18, 2020. https://www.who.int/teams/blueprint/covid-19

Note: Clinical improvement on an ordinal scale at chosen time points may be considered as an outcome.

APPENDIX 2

South African National Department of Health
Brief Report of Rapid Review
Component: COVID-19

TITLE:

Date:

Key findings

- *x*
- *x*
- *x*

NEMLC THERAPEUTIC GUIDELINES SUB-COMMITTEE RECOMMENDATION:					
Type of recommendation	We recommend against the option and for the alternative (strong)	We suggest not to use the option or to use the alternative (conditional)	We suggest using either the option or the alternative (conditional)	We suggest using the option (conditional)	We recommend the option (strong)
				X	
Rationale: **Level of Evidence:**					

(Refer to appendix 2 for the evidence to decision framework)

APPENDIX 2

BACKGROUND

RESEARCH QUESTION: Should *therapeutic agent* be used for managing COVID-19?

METHODS

Eligibility criteria for review

Population:

Intervention:

Comparators:

Outcomes:

Study designs:

RESULTS

CONCLUSION

Reviewers:

Declaration of interests:

REFERENCES

APPENDIX 2

Table 1. Characteristics of included studies

Citation	Study design	Population (n)	Treatment	Main findings

Table 2. Characteristics of planned and ongoing studies

Citation	Study design	Population (n)	Treatment

Table 3: Summary of findings

Outcomes	Anticipated absolute effects* (95% CI)			Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with Placebo	Risk with *Intervention*	Risk difference with *Intervention*			
	x per 1.000	**y per 1.000** (95% CI)	z fewer/more per 1.000 (95% CI)	**RR (95% CI)**		

Appendix 1: Search strategy

Database A *Search strategy* *Output*
Database B *Search strategy* *Output*

Appendix 2: Evidence to decision framework

	JUDGEMENT	EVIDENCE & ADDITIONAL CONSIDERATIONS
QUALITY OF EVIDENCE OF BENEFIT	**What is the certainty/quality of evidence?** High ☐ Moderate x Low ☐ Very low ☐ *High quality:* confident in the evidence *Moderate quality:* mostly confident, but further research may change the effect *Low quality:* some confidence, further research likely to change the effect *Very low quality:* findings indicate uncertain effect	*The quality of the evidence of benefit across all outcomes is critical to the strength of the recommendation. The higher the quality, the greater the likelihood of a strong recommendation.*
EVIDENCE OF BENEFIT	**What is the size of the effect for beneficial outcomes?** Large ☐ Moderate ☐ Small ☐ None ☐	*e.g. Report direction of benefit*
QUALITY OF EVIDENCE OF HARM	**What is the certainty/quality of evidence?** High ☐ Moderate x Low ☐ Very low ☐ *High quality:* confident in the evidence *Moderate quality:* mostly confident, but further research may change the effect *Low quality:* some confidence, further research likely to change the effect *Very low quality:* findings indicate uncertain effect	*The quality of the evidence of harm across all outcomes is critical to the strength of the recommendation. The higher the quality, the greater the likelihood of a strong recommendation.*
EVIDENCE OF HARMS	**What is the size of the effect for harmful outcomes?** Large ☐ Moderate ☐ Small ☐ None ☐	*e.g. Report any harms*
BENEFITS & HARMS	**Do the desirable effects outweigh the undesirable harms?** Favours intervention x ☐ Favours control ☐ Intervention = Control *or* Uncertain ☐	*An evaluation of the absolute effects of both benefits and harms of the intervention and their importance. The greater the net benefit or net harm associated with an intervention, the greater the likelihood of a strong recommendation in favour or against the intervention.*
FEASABILITY	**Is implementation of this recommendation feasible?** Yes ☐ No ☐ Uncertain ☐	*The greater the feasibility of an option from the standpoint of all or most stakeholders, the greater the likelihood of a strong recommendation. Feasibility overlaps with values and preferences, resource considerations, existing infrastructures, equity, etc.* *e.g. Provide information on: SAHPRA registration, Medicine availability; Training requirements; Other interventions required to deliver this intervention.*
RESOURCE USE	**How large are the resource requirements?** More intensive ☐ Less intensive ☐ Uncertain ☐	*Pertains to how resource-intense an intervention is, whether it is cost-effective and whether it offers any incremental benefit. The more advantageous or clearly disadvantageous the resource implications are, the greater the likelihood of a strong recommendation either for or against the intervention.* Cost of medicines/ month: **Medicine** | **Cost (ZAR)** | | | | **Additional resources:**

APPENDIX 2

VALUES, PREFERENCES, ACCEPTABILITY	**Is there important uncertainty or variability about how much people value the options?** Minor ☐ Major ☐ Uncertain ☐ **Is the option acceptable to key stakeholders?** Yes ☐ No ☐ Uncertain ☐	*Values and preferences: Describes the relative importance assigned to health outcomes by those affected by them; how such importance varies within and across populations; and whether this importance or variability is surrounded by uncertainty. The less uncertainty or variability, the greater the likelihood of a strong recommendation.* *Recommendation: The greater the acceptability of an option to all or most stakeholders, the greater the likelihood of a strong recommendation.*
EQUITY	**Would there be an impact on health inequity?** Yes ☐ No ☐ Uncertain ☐	*The greater the likelihood that the intervention will reduce inequities, improve equity or contribute to the realization of one or several human rights as defined under the international legal framework, the greater the likelihood of a strong recommendation.*

Appendix 3: Updating of a rapid report

Date	Signal	Rationale

Version control:

Version	Date	Reviewer(s)	Recommendation and Rationale

APPENDIX 3: SUMMARY TEMPLATE

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

Rapid Review for COVID-19

Simplified question reviewed

e.g. "Should chloroquine be used to treat COVID-19?"

one sentence in bold

Introduction to the medicine in question, including what it is currently used for and background to the review

3-5 sentences

Summary of evidence reviewed, including number of trials, number of participants, publication dates and key findings

3-5 sentences

Summary of conclusion, including strength of evidence and the evidence for and against the question to be answered

3-5 sentences

Final answer to the question

e.g. "Chloroquine is not recommended to treat chloroquine outside of a clinical trial setting."

one sentence in bold

Date of publication and link to the date-stamped rapid review

e.g. "Date of Publication: 5 May 2020. See the full medicine review at http://www.health.gov.za/index.php/national-essential-medicine-list-committee-nemlc/category/633-covid-19-rapid-reviews"

Note: As evidence is continuously emerging, the rapid review will be updated if and when more relevant evidence becomes available.

APPENDIX 4: FRAMEWORK FOR UPDATING A REVIEW

Initially, the need for revision of rapid reviews was decided on an *ad hoc* basis. As the body of evidence expands, an explicit framework informing update decisions for rapid reviews is required. Existing reviews contain an explicit evidence to decision framework and recommendation. Sensible stewardship of reviewers' time requires screening of new information to gauge the probability that it will lead to a change in a recommendation. This necessarily happens before a full GRADE-level review of the new evidence; once that has happened, the resources/time has already been expended. This framework aims to guide recommendations for review updating and provide a governance record of these decisions.

Considerations favouring the updating of a review:

1. Emerging evidence of efficacy that appears likely to impact the recommendation.
2. A new signal of harm likely to impact a recommendation.
3. Important change in cost-effectiveness estimates, either from new prices or a change in the health service delivery environment.
4. Generally, where the recommendation is weak or in equipoise, have a lower threshold to consider new evidence.

Factors unlikely to prompt an update:

1. New high-quality efficacy evidence pointing in the same direction as previous evidence where an existing recommendation is already strong, unless providing new clinically useful details of value to guideline development.
2. New evidence of efficacy that appears of lower quality than that already reviewed.
3. New evidence of harm when the review already contains a strong recommendation against use.
4. Cost-effectiveness analyses where a review has failed to find clinically meaningful evidence of efficacy.

Signals not to be used on their own for updating a review:

1. Press releases
2. Approval by Regulatory Authorities for emergency use authorisations (EUA)

When to retire a review:

1. High certainty data
2. Existing strong recommendation
3. Evidence that 'zone of futility' has been reached (where there is high probability that further evidence accrual is unlikely to change a meta-analytic conclusion.)

Process:

1. When a new signal is detected, the secretariat to inform both the authors of the original review and the sub-committee.
2. The authors to indicate whether they think the new information warrants a review update based on the guiding principles listed above.
3. A decision to be made through email correspondence amongst committee members, with the framework-based reason for the proposed decision explicitly stated.
4. If the decision is unanimous then it is date-stamped and recorded as such, with the signal and the reason for the decision placed as an addendum to the review (see the rapid review report template, Appendix II: of the Terms of Reference).
5. If there is not unanimity or rapid resolution by email or verbal communication, then the updating decision is to be brought to the next NEMLC sub-committee meeting for discussion and resolution.

Algorithm to guide decision-making