LETTER TO THE EDITOR

Development of rapid advice guideline and standard and continuous updating guideline: experiences and practice

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Abstract

We published rapid advice guidelines and updated guidelines for coronavirus disease 2019 (COVID-19) management on February 6, 2020, and September 4, 2020, respectively. These two guidelines vary widely in their developmental background, type of evidence, grade of recommendation and so on. We shared our experience for the development of these two guidelines to help clinical practitioners better understand and implement guidelines and to help guideline developers facilitate communication and discussion for guideline development during the pandemic.

Keywords: COVID-19, SARS-CoV-2, Rapid advice guideline, Clinical practice guideline, Evidence-based medicine

Dear Editor,

Early in 2020, during the novel coronavirus infection outbreak, we published a rapid advice guideline for the diagnosis and treatment of coronavirus disease 2019 (COVID-19) (Guideline 1, https://mmrjournal.biomedcentral.com/articles/10.1186/s40779-020-0233-6 #citeas) [1]. Later, in September 2020, we registered and published an updated guideline named “Chemoprophylaxis, diagnosis, treatments, and discharge management of COVID-19: An evidence-based clinical practice guideline (updated version)” (Guideline 2, https://mmrjournal.biomedcentral.com/articles/10.1186/s40779-020-00270-8) [2, 3]. These two guidelines were both prepared in accordance with the methodology and general rules of World Health Organization (WHO) Guideline Development [4]. The WHO Rapid Advice Guidelines advice was used in the development of Guideline 1, and the guideline was issued within 1 week. We convened multidisciplinary guideline development groups composed of health professionals (experts in respiratory medicine, infectious disease, critical care medicine, cardiology, emergency medicine, pediatrics, oncology, gerontology, laboratory medicine, medical imaging, clinical immunology, and clinical pharmacy) and methodologists for developing both guidelines.

For any newly identified infection, an absolute lack of direct evidence is the greatest challenge for guideline developers. Thus, for Guideline 1, we were totally reliant on indirect evidence, such as that for severe acute respiratory syndrome (SARS), Middle East respiratory syndrome (MERS), and influenza. Although research has reported that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which causes COVID-19, is similar to SARS-CoV (approximately 80% similar), the evidence for the possible benefits of treatment in patients with SARS or MERS disease was considered indirect because the patient populations, viruses, and possibly...
even drug effects were different. Therefore, the rating of
the quality of evidence for all important efficacy out-
comes was downgraded by two levels based on the
Grading of Recommendations Assessment, Development
and Evaluation (GRADE) approach [4]. Indirect evidence
that played an important role in guideline development
during the early stage of the epidemic gradually faded
when direct evidence on COVID-19 appeared.

The COVID-19 pandemic is a rapidly changing situ-
ation. An increasing number of research papers are be-
ing published both in China and internationally,
providing research evidence for managing COVID-19,
which enabled direct evidence from COVID-19 patients
to be used in the development of Guideline 2. Guideline
2 finally included 75 original papers (including 12 ran-
nomized controlled trials) and 33 systematic reviews or
meta-analyses.

During the Guideline 1 development process, 11,500
symptomatic persons were screened, 276 were identi-
cified as suspected victims of infection, and 170 were diag-
nosed (including 33 in critical condition) as having
COVID-19 by the guideline working group’s clinical pro-
essionals. Frontline clinicians have accumulated valu-
able experience in the diagnosis, treatment and nursing
of COVID-19 patients. There was no direct research evi-
dence to inform recommendations at that time, and
these experiences were assessed as “expert evidence” for
our guideline development. Expert evidence was highly
valued in Guideline 1 development. We used a struc-
tured form to collect this information so that it could be
aggregated and presented to the guideline panel in the
summary of findings. Expert evidence can be solicited by
examining case reports, summaries, and reports of
topics. During the consensus process, if the evidence
was agreed upon by more than 70% of frontline clini-
cians, it was considered high-quality evidence. However,
“expert evidence” was used slightly differently in the de-
velopment of Guideline 2. Expert evidence would not
change the direction and strength of recommendations
based on direct evidence, but it could influence ques-
tions that have very limited evidence and may form an
“ungraded consensus-based statement” when more than
70% of working group members in the guideline panel
believed this conclusion to be valid.

In the development of Guidelines 1 and 2, we adhered
to the GRADE approaches and rules to assess the quality
of a body of evidence [5], to develop and report recom-
mandations, and to make some adjustments. First, as-
sessments of the quality of the evidence that were not
for pooled estimates of effect were available as a narra-
tive synthesis of the evidence in the development of
Guideline 1. Second, as COVID-19 spreads worldwide,
there is an increasing number of ongoing trials, resulting
in new research papers being published, possibly every
day. We downgraded the quality of evidence for impreci-
sion based on the threshold that represents the basis for
a management decision rather than considering whether
an optimal information size was reached. Third, rigorous
search techniques were implemented in the development
of Guideline 2; therefore, we thought the possibility of
unidentified studies leading to publication bias was rare.
Fourth, for diagnostic questions, studies measuring the
impact of testing on patient-important or population-
important outcomes were not available; hence, the
guideline panels included only studies with diagnostic
test accuracy outcomes, which were considered a surro-
gate outcome for patient-important benefits and harm.
Last, despite very low evidence or only having expert
evidence suggesting benefit in a life-threatening situ-
ation, strong recommendations may be warranted.
For example, no clinical trials have demonstrated the benefit
of the application of mechanical ventilation or its indica-
tions for use. However, as a common clinical life support
and rescue method, mechanical ventilation is often used
in life-threatening situations.

All guidelines need to be kept up to date and consist-
ent with the best available evidence [6]. This is particu-
larly important but difficult to achieve in the context of
a public health emergency, such as COVID-19, when
new data are constantly emerging and experience is con-
tinually accruing [7]. Although we updated Guideline 2
recently, its recommendations will require continuous
updating in the future to incorporate increasingly high-
quality direct evidence.

Conclusions
Guidelines of all types should always be evidence-based.
It is a common misunderstanding that evidence-based
guidelines can be developed only if well-designed con-
trolled trials exist. Recommendations are derived from a
systematic review of evidence, which is the current best
evidence, and guidelines in a pandemic are no exception.
The guidelines should be updated with continuously
emerging evidence.

Abbreviations
COVID-19: Coronavirus disease 2019; GRADE: Grading of Recommendations
Assessment, Development and Evaluation; MERS: Middle East respiratory
syndrome; SARS: Severe acute respiratory syndrome; SARS-CoV-2: Severe
acute respiratory syndrome coronavirus 2

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