Corticosteroids for sore throat

Main editor

Bert Aertgeerts, Romina Brignardello-Petersen, Thomas Agoritsas

Publishing and version history

v2.1 published on 20.09.2017

MAGIC Evidence Ecosystem Foundation

A BMJ-Rapid Recommendation on corticosteroids for sore throat. This is the 5th BMJ-RapidRec, initiated in response to an RCT by Hayward and Colleages, published in JAMA April 18, 2017 (http://jamanetwork.com/journals/jama/article-abstract/2618622). Roles: Panel Chair: Bert Aertgeerts Methods Editors: Romina Brignardello-Petersen Oversight from RapidRecs executive: Thomas Agoritsas Systematic Review Lead: Behnam Sadeghirad

Contact

Sponsors/Funding

This guideline was not funded.

Sections

Summary of recommendations

1 - Corticosteroids for acute sore throat

Weak Recommendation

We suggest using corticosteroids in addition to standard care in patients with sore throat

Steroids are typically given as 10 mg dexamethasone (or 0.6 mg/kg for children, up to a maximum dose of 10mg), taken as a single pill (or as an intramuscular injection). Clinicians could administer the medication in office if possible, or prescribe only one dose per visit, to mitigate the risk of a larger cumulative dose of corticosteroids in case of multiple episodes of sore throat.

2 - BMJ Rapid Recommendations Methods and Process

1 - Corticosteroids for acute sore throat

Weak Recommendation

We suggest using corticosteroids in addition to standard care in patients with sore throat

Steroids are typically given as 10 mg dexamethasone (or 0.6 mg/kg for children, up to a maximum dose of 10mg), taken as a single pill (or as an intramuscular injection). Clinicians could administer the medication in office if possible, or prescribe only one dose per visit, to mitigate the risk of a larger cumulative dose of corticosteroids in case of multiple episodes of sore throat.

Practical Info

- Steroids are typically given as 10 mg dexamethasone (or adapted to weight for children: 0.6 mg/kg, up to a maximum dose of 10mg), typically taken as pill (or intramuscular injection).
- We suggest administering the medication in office if possible, or prescribing only one dose per visit, to mitigate the risk of a larger cumulative dose of corticosteroids in case of multiple episodes of sore throat either through multiple visits, or for patients who would self-medicate after having been prescribed more than one pill in their previous episode.

Who does this recommendation apply to?

The panel is confident the recommendation applies to almost all patients with acute sore throat; children and adults, severe and not severe sore throat, patients who receive immediate antibiotics and those who receive deferred antibiotics, and patients who seek care in the emergency department as well as those who attend to a primary care practice. The systematic review contained adequate representation from such groups and settings and showed consistency (i.e. absence of credible subgroup effects) in the results shown between trials of children and adults, those seen in emergency departments and those in primary care offices.

Since the randomised controlled trials focused on patients who did not have recurrent episodes of sore throat, the panel was less confident of the applicability of the evidence to such patients and the recommendation does not apply to them. Similarly the panel did not consider patients with sore throat following any surgery or intubation, nor immunocompromised patients.

Key Info

Benefits and harms — Small net benefit, or little difference between alternatives

Patients who receive corticosteroids in addition to standard care have, on average, an 18% more chance of achieving complete resolution of pain at 48 hours after treatment. These patients also probably have, on average, a 12% more chance to achieve complete pain resolution at 24 hours after treatment. Corticosteroids probably reduce, on average, the time to onset of pain relief by 5 hours, the time to complete resolution of pain by 11 hours, and the severity of pain by 1.3 points on a 10 point scale.

Corticosteroids may decrease the chance of taking antibiotics in patients given a prescription with instructions to take the antibiotic if unimproved or worse by 10%. They probably have no important effect on the chance that symptoms recur and the days missed fom school or work.

When prescribed at the doses used for treating acute sore throat, corticosteroids probably do not increase the risk of major adverse events .

Certainty of the Evidence — Moderate

We have high certainty in the benefits of corticosteroids in increasing the chance of complete resolution of pain at 48 hours. We have moderate certainy in the benefts of corticosteroids in increasing the chance of complete resolution of pain at 24 hours, reducing the time of onset of pain relief, and reducing the severity of pain. This is due to the confidence intervals of the estimates of these benefits showing that such benefits could be very small and not patient-important in some cases.

We have low certainty in the benefits of corticosteroids in reducing the time to complete resolution of pain due to studies showing inconsistent results. We also have low certainty in the benefits of corticosteroids in decreasing the chance of taking antibiotics in patients given a prescription with instructions to take the antibiotic if unimproved or worse, due to imprecise results that suggest that in some cases, antibiotic presription might increase.

We have moderate certainty in the lack of a patient important benefit of corticosteroids in the chance of symptom recurrence

and days missed from school or work due to imprecise results that suggest that corticosteroids could improve or worsen these outcomes, but that the effect would not be patient-important.

We have modedrate certainty that corticosteroids do not increase the risk of major adverse events when prescribed at the doses used for treating acute sore throat. Certainty is moderate due to concerns about selective reporting of this outcome in the randomized trials.

Preference and values Substantial variability is expected or uncertain

Patients are likely to place a high value on a small but somewhat important reduction of symptoms severity and the time that it takes to achieve such improvement, and an important increase in the chance of complete resolution of pain at 48 hours. The values and preferences, however, are likely to vary greatly across patients, which justifies the strength of the recommendation. For example, achieving complete pain resolution 12 hours earlier may be of little importance for patients who feel less busy in their daily life, have higher tolerance to pain, or whose symptoms are not so severe; whereas it may be important to patients whose abilities to perform at work are compromised, caregivers willing to reduce their childrens' in pain, or patients experiencing their pain as severe.

The panel believes that there is a great variability on how much reduction in pain severity or time to complete pain resolution each patient would consider important. The greater the reduction in hours to achieve complete resolution of pain, the more likely it is that typical patients would place high value on those outcomes. Patients who place a high value in reducing the symptoms by any amount (eg. patients with lower tolerance to pain or those with severe symptoms) are more likely to accept the offer of corticosteroids.

Resources and other considerations Important issues, or potential issues not investigated

Due to the low costs of corticosteroids for treating sore throat, implementation of this recommendation is unlikely to have an important impact on the costs for health funders.

Acceptability of corticosteroids may be a challenge. Some stakeholders may have concerns about treating an usually non-severe and self-limiting disease with a drug that is not considered as standard of care.

In addition, there may be an increase in the risk of a larger cumulative dose of corticosteroids in case of multiple episodes of sore throat, either through multiple visits, or for patients who would self-medicate after having been prescribed more than one pill in their previous episode.

Rationale

We issue a weak recommendation for corticosteroids in addition to standard care because the desirable consequences probably outweight the undesirable consequences. Yet we believe that there is great variability in the value patients would place on the small benefits, despite the very low likelihood of harms. There may be an increase in the risk of a larger cumulative dose of corticosteroids in case of multiple episodes of sore throat, either through multiple visits, or for patients who would self-medicate after having been prescribed more than one pill in their previous episode. To mitigate this issue, we suggest administering the medication in office if possible, or prescribing only one dose per visit.

Acceptability of this intervention may also differ, as it may be perceived as treating a condition that is usually not severe and is self-limiting with a drug that many patients, practitioners, and other stakeholders perceive is most often used for more severe diseases only.

Due to their low cost, resources did not play an important role when formulating this recommendation.

Clinical Question/ PICO

Population: Patients with sore throat
Intervention: Corticosteroids
Comparator: No corticosteroids

Outcome Timeframe	Study results and measurements	Absolute effect estimates No corticosteroids	Corticosteroids	Certainty of the Evidence (Quality of evidence)	Plain text summary
Complete Resolution of Pain at 24 hours	Relative risk 2.24 (CI 95% 1.17 - 4.29) Based on data from 1,049 patients in 5 studies. (Randomized controlled)	100 per 1000	224 per 1000 Difference: **124 more** per 1000 (CI 95% 17 more - 329 more)	**Moderate** Due to inconsistency and imprecision [1]	Corticosteroids probably increase the chance of complete resolution of pain at 24 hours
Complete Resolution of Pain at 48 hours	Relative risk 1.48 (CI 95% 1.26 - 1.75) Based on data from 1,076 patients in 4 studies. (Randomized controlled)	425 per 1000	629 per 1000 Difference: **204 more** per 1000 (CI 95% 111 more - 319 more)	**High** [2]	Corticosteroids increase the chance of complete resolution of pain at 48 hours
Recurrence/ relapse of symptoms	Relative risk 0.52 (CI 95% 0.16 - 1.73) Based on data from 372 patients in 3 studies. (Randomized controlled)	65 per 1000	34 per 1000 Difference: **31 fewer** per 1000 (CI 95% 55 fewer - 47 more)	**Moderate** Due to serious imprecision [3]	Corticosteroids probably have no important effect on the chance that symptoms recur.
Antibiotics prescription during the episode	Relative risk 0.83 (CI 95% 0.61 - 1.13) Based on data from 342 patients in 1 studies. (Randomized controlled) Follow up 28 days	564 per 1000	468 per 1000 Difference: **96 fewer** per 1000 220 fewer - 73 more	**Low** Due to very serious imprecision [4]	Corticosteroids may decrease the chance of taking antibiotics in patients given a prescription with instructions to take the antibiotic if unimproved or worse.
Mean times to onset of pain relief Hours	Based on data from: 907 patients in 8 studies. (Randomized controlled)	12.3 hours (Median)	7.4 hours (Mean) Difference: **MD 4.8 fewer** (CI 95% 7.8 fewer - 1.9 fewer)	**Moderate** Due to inconsistency and imprecision [5]	Corticosteroids probably shorten the time until pain starts to improve.
Mean time to complete resolution of pain hours	Based on data from: 720 patients in 6 studies. (Randomized controlled)	44 hours (Mean)	33 hours (Mean) Difference: **MD 11.1 fewer** (CI 95% 21.8 fewer - 0.4 fewer)	**Low** Due to serious imprecision and inconsistency [6]	Corticosteroids may shorten the duration of pain.

Pain reduction at 24 hours	Measured by: Reduction in VAS Scale: 0-10 High better Based on data from: 1,247 patients in 8 studies. (Randomized controlled)	3.3 points (Mean) — 4.6 points (Mean) Difference: MD 1.3 higher (CI 95% 0.7 higher - 1.9 higher)	**Moderate** Due to inconsistency and imprecision [7]	Corticosteroids probably reduce the severity of pain at 24 hours
Duration of bad/non-tolerable symptoms				There were no studies providing information about this outcome
Days missed from work or school	Based on data from 181 patients in 2 studies.	Two RCTs reported days missed from work/school. In Kinderman et al, 22 out of 40 (55%) patients in the steroids group took time off work and 27 out of 39 (69%) patients in the placebo group took time off work (Relative risk 0.79; 95% confidence interval 0.56 to 1.13). Marvez-Valls et al reported the average time patients in each arm missed from work/school. In the intervention group adult patients missed an average of 0.4 (SD: 1.4) days and in the placebo arm patients missed an average of 0.7 (SD: 1.4) days (mean difference 0.30 days, 95% CI -0.28 to 0.88).	**Moderate** Due to serious imprecision and some concerns of risk of bias [8]	Corticosteroids probably have no important effect on the days missed from work or school.
Adverse events	Based on data from 808 patients in 3 studies.	One study (Hayward et al.) reported 2 serious adverse events (hospitalizations due to pharyngeal or peritonsillar abscess, tonsillitis, and pneumonia) in the corticosteroids group (0.68%) and 3 in the placebo group (1.06%). In another study (Olympia et al), 1 out of the 57 (1.8%) children in the corticosteroids group and 2 out of the 68 (2.9%) children in the control group developed a peritonsillar abscess. In the same study, 3 out of 57 (5.3%) children in the corticosteroid group and 2 out of 68 (2.9%) of children in the placebo group had to be hospitalised due to dehydration. Finally, another study (Wei et al.) reported that 1 patient who received corticosteroids (3%) had hiccups.	**Moderate** Due to serious risk of bias [9]	Corticosteroids probably do not increase the risk of adverse events.

Practical issues	No corticosteroids	Corticosteroids	Both
Medication routine		One (or two) doses of steroids, taken as pill(s) or intramuscular injection(s)	May require concomitant antibiotics, and or over the counter pain relievers

 Tests and visits		May need additional visits if symptoms do not resolve or worsen
 Adverse effects, interactions and antidote	Serious adverse events are unlikely with one-dose steroids. But there may be risks with repeated doses across multiple episodes of sore throat (or through self-medication).	
 Emotional well-being	May cause transient sleep disturbance, and excitability (although infrequently with one-dose steroids)	
 Pregnancy and nursing	Dexamethasone crosses the placenta, and is generally avoided during pregnancy. There is, however, almost no risk of malformation.	
 Costs and access	Inexpensive, available by prescription	
 Food and drinks	May increase appetite (particularly in children)	

1. **Risk of bias: No serious .** All studies are low RoB. ; **Inconsistency: No serious .** The magnitude of statistical heterogeneity was high, with I^2: 68.8 %. However, the clinical inconsistency is not important, as all the studies provide results that have a similar clinical implication. ; **Indirectness: No serious . Imprecision: Serious .** The limits of the confidence interval suggest a very small benefit in one extreme, and a patient important benefit in the other. Because the imprecision is linked to the inconsistency, we decided to rate down the certainty of the evidence only by one level. ; **Publication bias: No serious .** Not statistically tested due to small number of studies. ;
2. **Risk of bias: No serious .** All studies are categorised as low RoB. ; **Inconsistency: No serious .** The magnitude of statistical heterogeneity: I^2 = 3.2%. ; **Indirectness: No serious . Imprecision: No serious .** Low number of patients ; **Publication bias: No serious .** Not statistically tested due to small number of studies. ;
3. **Risk of bias: No serious .** 1 of the 3 RCTs was judged as high risk of bias due to missing participant data. ; **Inconsistency: No serious .** The magnitude of statistical heterogeneity was low, with I^2: 22.8 %. ; **Indirectness: No serious . Imprecision: Serious .** The confidence interval suggests that corticosteroids increase the chance of recurrence of symptoms in now extreme, while it suggests corticosteroids decrease this chance in the other extreme. ; **Publication bias: No serious .** Not statistically tested due to small number of studies. ;
4. **Inconsistency: No serious . Indirectness: No serious . Imprecision: Very Serious .** The confidence interval suggest that corticosteroids could largely reduce the chance of taking antibiotics in one extreme, while it suggest that corticosteroids could

slightly increase this chance in the other extreme. ; **Publication bias: No serious .**

5. **Risk of bias: No serious .** 4 high risk of bias and 4 low risk of bias RCTs. P value for test of interaction: 0.775 ; **Inconsistency: Serious .** There is large unexplained clinical and statistical inconsistency. ; **Indirectness: No serious . Imprecision: No serious .** The confidence interval suggest a very small benefit in one extreme, and a benefit that some patients may consider important in the other extreme. Since this imprecision was a result of the inconsistency, we decided to rate down the certainty of the evidence only by one level. ; **Publication bias: No serious .** Not statistically tested due to small number of studies. ;
6. **Risk of bias: No serious .** 3 high risk of bias and 3 low risk of bias RCTs. However, the high risk of bias trials showed similar results than the low risk of bias trials. ; **Inconsistency: Serious .** Large unexplained clinical and statistical heterogeneity. ; **Indirectness: No serious . Imprecision: Serious .** The confidence interval suggests a trivial benefit in one extreme and a benefit that would be considered patient important by most patients in the other extreme. ; **Publication bias: No serious .** Not statistically tested due to small number of studies. ;
7. **Risk of bias: No serious .** 4 high risk of bias and 4 low risk of bias RCTs. P value for test of interaction: 0.774 ; **Inconsistency: Serious .** High statistical inconsistency. In addition, the trials suggest different magnitudes of effect. ; **Indirectness: No serious . Imprecision: No serious .** The confidence interval suggest a very small benefit in one extreme and a patient-important benefit in the other. Since this imprecision was related to the inconsistency, we decided to rate down only by one level. ; **Publication bias: No serious .** Not statistically tested due to small number of studies. ;
8. **Risk of bias: No serious .** One of the studies was high risk of bias due to concerns with regards to allocate concealment. ; **Inconsistency: No serious . Indirectness: No serious . Imprecision: Serious .** The studies showed that corticosteroids could increase the days missed from school or work in one extreme, while they could decrease them in the other extreme. ; **Publication bias: No serious .**
9. **Risk of bias: Serious .** The high risk of bias studies show similar results than the low risk of bias studies. However, there may be a high risk of selective outcome reporting ; **Inconsistency: No serious . Indirectness: No serious . Imprecision: No serious . Publication bias: No serious .**

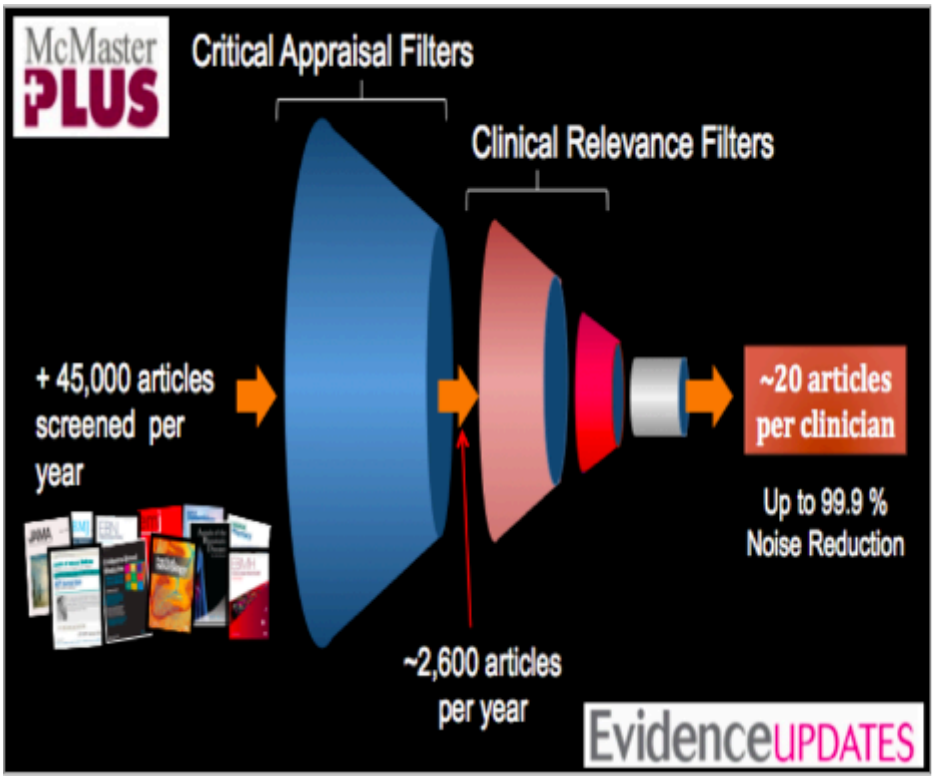
2 - BMJ Rapid Recommendations Methods and Process

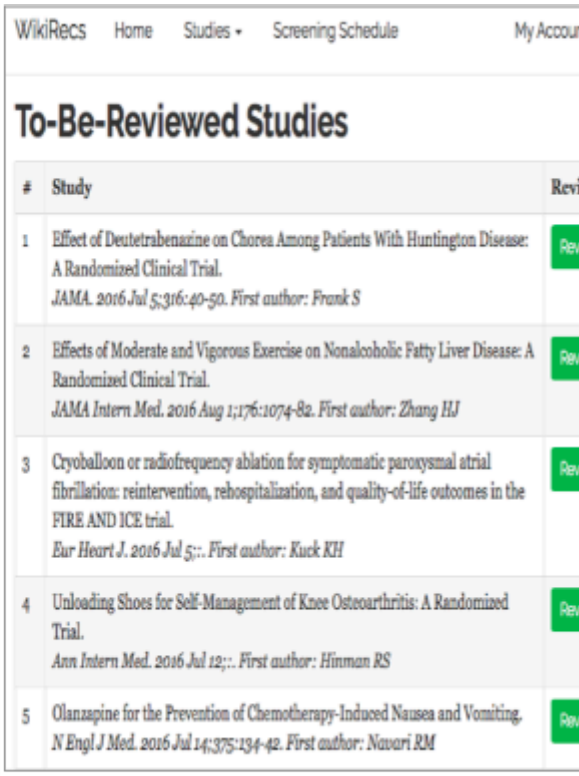
About BMJ Rapid Recommendations

Translating research to clinical practice is challenging. Trustworthy clinical practice recommendations are one useful knowledge translation strategy. Organisations creating systematic reviews and guidelines often struggle to deliver timely and trustworthy recommendations in response to potentially practice-changing evidence. *BMJ* Rapid Recommendations aims to create trustworthy clinical practice recommendations based on the highest quality evidence in record time. The project is supported by an international network of systematic review and guideline methodologists, people with lived experience of the diseases or conditions, clinical specialists, and front-line clinicians. This overview is one of a package that includes recommendations and one or more systematic reviews published by the *BMJ* group and in MAGICapp (http://www.magicapp.org). The goal is to translate evidence into recommendations for clinical practice in a timely and transparent way, minimizing bias and centred around the experience of patients. *BMJ* Rapid Recommendations will consider both new and old evidence that might alter established clinical practice.

Process overview

1. On a daily basis, we monitor the literature for practice-changing evidence:
   - Formal monitoring through McMaster Premium LiteratUre Service (PLUS)
   - Informal monitoring the literature by *BMJ* Rapid Recommendations expert groups, including clinician specialists and patients





2. The *RapidRecs* executive team and editors at *The BMJ* choose which clinical questions to pursue among the identified potentially-practice changing evidence, based on relevance to a wide audience, widespread interest, and likelihood to change practice.
3. We incorporate the evidence into the existing body of evidence and broader context of clinical practice via:
   - A rapid and high-quality systematic review and meta-analysis on the benefits and harms with a focus on the outcomes that matter to patients
   - Parallel rapid recommendations that meet the standards for trustworthy guidelines1 by an international panel of people with relevant lived experience, front-line clinicians, clinical content experts, and methodologists.
   - The systematic review and the recommendation panel will apply standards for trustworthy guidelines.[1,2] They use the GRADE approach, which has developed a transparent process to rate the quality (or certainty) of evidence and grade the strength of recommendations.[3,4]
   - Further research may be conducted including:
     - A systematic review of observational studies to identify baseline risk estimates that most closely represent the population at the heart of the clinical question, a key component when calculating the estimates of absolute effects of the intervention.
     - A systematic review on the preferences and values of patients on the topic.

4. Disseminate the rapid recommendations through:
   - Publication of the research in *BMJ* journals
   - Short summary of recommendations for clinicians published in *The BMJ*
   - Press release and/or marketing to media outlets and relevant parties such as patient groups

- Links to *BMJ* group's *Best Practice* point of care resource
- MAGICapp which provides recommendations and all underlying content in digitally structured multilayered formats for clinicians and others who wish to re-examine or consider national or local adaptation of the recommendations.

Who is involved?

Researchers, systematic review and guideline authors, clinicians, and patients often work in silos. Academic journals may publish work from any one or combinations of these groups of people and findings may also be published in the media. But it is rare that these groups work together to produce a comprehensive package. *BMJ-RapidRecs* circumvents organisational barriers in order to provide clinicians with guidance for potentially practice-changing evidence.

Our collaboration involves:
1. The *RapidRecs* group with a designated Executive team responsible for recruiting and coordinating the network of researchers who perform the systematic reviews and the recommendation panels.. The *RapidRecs* group is part of MAGIC (www.magicproject.org), a non for profit organization that provides MAGICapp (www.magicapp.org) an authoring and publication platform for evidence summaries, guidelines and decision aids, which are disseminated online for all devices.[5]
2. *The BMJ* helps identifiying practice-changing evidence on key clinical questions, coordinates the editorial process and publishes the package of content linking to the MAGICapp that is presented in a user-friendly way.

METHODS FOR THE RAPID RECOMMENDATIONS

The formation of these recommendations adheres to standards for trustworthy guidelines with an emphasis on patient involvement, strict management of conflicts of interests, as well as transparent and systematic processes for assessing the quality of evidence and for moving from evidence to recommendations.[1,2,6]

Guidance on how the panel is picked and how they contribute

Panel members are sought and screened through an informal process. The following panel members are important:
- At least one author of the individual systematic reviews.
- At least one patient representative with lived experience of the disease or condition. This person receives patient-oriented documents to explain the process and is allocated a linked panel member to empower their contribution.
- A full spectrum of practicing clinicians involved in the management of the clinical problem and patients it affects, including front-line clinicians with generalist experience and those with deep content clinical and research expertise in the particular topic.
- Methodological experts in health research methodology and guideline development.

Any potential conflicts of interest are managed with extreme prudence:
- No panel member can have a financial interest – as assessed by the panel chair, the *RapidRecs* executive team or *The BMJ* editors as relevant to the topic.
- No more than two panel members with an intellectual interest on the topic (typically having published statements favouring one of the interventions).

Illustrative example: For the BMJ *Rapid Recommendations on antiretroviral therapy for pregnant women living with HIV, the panel recruitment of content experts and community panel members was challenging. Content experts in this area are infectious diseases experts, many of whom have financial conflicts of interests through interactions with the pharmaceutical industry through advisory boards and participation in industry-funded trials. The group reached out to more than 17 potential panel members who were eventually excluded from participating because of conflicts – notably, all of these persons had not disclosed any relevant conflicts on related and recent publications in the topic area. Many more potential panel members were not recruited because of publicly declared conflicts. The chair and MAGIC team were able, with considerable effort and ingenuity, to recruit several excellent and unconflicted content experts.*

How the panel meets and works

The international panel communicates via teleconferences and e-mail exchange of written documents throughout the process. Minutes from teleconferences are audiorecorded, transcribed, and stored for later documentation (available for peer-reviewers on request).

Teleconferences typically occur at three timepoints, with circulated documents by e-mail in advance:
1. At the initiation of the process to provide feedback on the systematic review protocol (for example, on selection of patient-important outcomes and appropriate prespecified analysis of results) before it is performed.
2. At the evidence summary stage with discussion, feedback and agreement on draft evidence (GRADE evidence profile) prepared by the Chair and the methods editor based on the systematic review.
3. At the recommendation formulation phase with discussion, feedback and agreement on draft recommendations and other content underlying the recommendation (e.g. GRADE SoF-table, key information, rationale, practical advice)

Following the last teleconference the final version of the recommendations is circulated by e-mail specifically requesting feedback from all panel members to document agreement before submission to The BMJ. Additional teleconferences are arranged as needed.

Illustrative example: For the BMJ Rapid Recommendations on antiretroviral therapy for pregnant women living with HIV, two large-group teleconferences were arranged. First, content experts provided crucial input to evidence assessment (e.g. subgroups to identify). For the recommendation formulation phase the panel needed two teleconferences to discuss all elements in detail, followed by more than 100 e-mails with specific issues to be sorted out. Multiple teleconferences were held to allow the scheduling flexibility required so that all could participate.

How we move from research findings to recommendations

What information is considered?
The panel considers best current evidence from available research. Beyond systematic reviews - performed in the context of the BMJ Rapid Recommendations - the panel may also include a number of other research papers to further inform the recommendations.

How is a trustworthy guideline made?
The Institute of Medicine (IOM)'s guidance on out how trustworthy guidelines should be developed and articulated key standards as outlined in the table below.[1] The standards are similar to those developed by the Guideline International Network (G-I-N).[2] These standards have been widely adopted by the international guideline community. Peer reviewers of the recommendation article are asked whether they found the guideline trustworthy (in accordance with IOM standards). The table below lays out how we hope to meet the standards for our rapid recommendations:

1. Establishing transparency **"The processes by which a CPG is developed and funded should be detailed explicitly and publicly accessible."***
• This method is available and published as a supplementary file as well as in MAGICapp where all recommendations and underlying cor is available. • We ask the peer-reviewers to judge whether the guidance is trustworthy and will respond to concerns raised.
2. Managing conflicts of interest **"Prior to selection of the guideline development group, individuals being considered for membership should declare all interests and activitie potentially resulting in COI with development group activity....",**
• Interests of each panel member are declared prior to involvement and published with the rapid recommendations. • No one with any potential financial interests in the past three years, or forthcoming 12 months will participate - as judged by the pane and *The BMJ*. • No more than two panel members have declared an intellectual conflict of interest. Such conflicts include having taken a position on t issue for example by a written an editorial, commentary, or conflicts related to performing a primary research study or written a prior systematic review on the topic. • The Chair must have methods expertise, a clinical background and no financial or intellectual interests. • Funders and pharmaceutical companies have no role in these recommendations.
3. Guideline Development Group Composition **"The guideline development group should be multidisciplinary and balanced, comprising a variety of methodological experts and clinicians, a populations expected to be affected by the CPG."**
• The RapidRecs group will aim to include representation from most or every major geographic region in the world, with specific efforts to achieve gender-balance. • We will facilitate patient and public involvement by including patient experience, via patient-representatives and systematic reviews addressing values and preferences to guide outcome choices and relative weights of each outcome, where available. • Patient-representatives will be given priority during panel meetings and will have an explicit role in vetting the panel's judgements of v and preferences.
4. Clinical Practice Guideline–Systematic Review Intersection **"CPG developers should use systematic reviews that meet standards set by the IOM. Guideline development group and systematic review te should interact regarding the scope, approach, and output of both processes."**
• Each rapid recommendation will be based on one or more high-quality SRs either developed and published in parallel with our *BMJ* Ra Recommendations or produced by other authors and available at the time of making the recommendaiton. • The recommendation panel and SR teams will interact, with up to three members participating in both teams to facilitate communicat

and continuity in the process.

5. Establishing Evidence Foundations for and Rating Strength of Recommendations
"For each recommendation: explain underlying reasoning, including a clear description of potential benefits and harms, a summary of relevar available evidence and description of the quality., explain the part played by values, opinion, theory, and clinical experience in deriving the recommendation, "provide rating of strength of recommendations."

- The GRADE approach will provide the framework for establishing evidence foundations and rating strength of recommendations.[6] For recommendation systematic and transparent assessments are made across the following key factors:
  - Absolute benefit and harms for all patient-important outcomes through structured evidence summaries (e.g. GRADE Summary of Fin tables)[4]
  - Quality of the evidence[7]
  - Values and preferences of patients
  - Resources and other considerations (e.g. feasibility, applicability, equity)

- Each outcome will - if data are available through systematic reviews - include an effect estimate and confidence interval, with a measu certainty in the evidence, as presented in Summary of Findings tables. If such data are not available narrative summaries will be provided.
- A summary of the underlying reasoning and all additional information (e.g. key factors, practical advice, references) will be available on an interactive format at www.magicapp.org. This summary will include descriptions of how theory (e.g. pathophysiology) and clinical expe played into the evidence assessment and recommendation development.
- Recommendations will be rated either weak or strong, as defined by GRADE.[8]
- If the panel members disagree regarding evidence assessment or strength of recommendations, we will follow a structured consensus process customized to the GRADE system and report any final differences in opinion, with their rationale, in the online supplement and o at www.magicapp.org.

6. Articulation of recommendations
"Recommendations should be articulated in a standardized form detailing precisely what the recommended action is, and under what circumstances it should be performed, and so that compliance with the recommendation(s) can be evaluated."

- Each recommendation will appear at the top of the guideline infographic, published in *The BMJ*, and will be available in standardised fo in MAGICapp, articulated to be actionable based on best current evidence on presentation formats of guidelines.[9]
- There will be a statement included in each summary article in *The BMJ* and in the MAGICapp that these are recommendations to provi clinicians with guidance. They do not form a mandate of action and should be contextualised in the healthcare system a clinician's works i or with an individual patient.

7. External review
"External reviewers should comprise a full spectrum of relevant stakeholders....., authorship should be kept confidential....., all reviewer comm should be considered....a rationale for modifying or not should be recorded in writing.... a draft of the recommendation should be made availa general public for comment..."

- At least two external peer-reviewers and one patient reviewer will review the article for *The BMJ* and provide open peer review. Each have access to all the information in the package. They will be asked for general feedback as well as to make an overall judgement on whe they view the guidelines as trustworthy.
- A *BMJ* series adviser with methodological and/or statistical expertise will review the *BMJ* Rapid Recommendations publication and the systematic reviews.
- The *RapidRecs* panel will be asked to read and respond to the peer review comments and make amendments where they judge reasona
- *The BMJ* and *RapidRecs* executive team may, on a case-by-case basis, choose to invite key organizations, agencies, or patient/public representatives to provide and submit public peer-review.
- There will be post-publication public review process through which people can provide comments and feedback through MAGICapp (o through *The BMJ*). The Chair will, on behalf of panel authors, aim to respond to each publicly-available peer-review within 30 days, for a p of six months after publication.

8. Updating
"The date for publication, systematic review and proposed date for future review should be documented, the literature should be monitored regularly and the recommendation should be updated when warranted by new evidence."

- The *RapidRecs* panel will, through monitoring of new research evidence for published *BMJ* Rapid Recommendations, aim to provide up of the recommendations in situations in which the evidence suggests a change in practice. These updates will be initially performed in MAGICapp and submitted to *The BMJ* for consideration of publication of a new Rapid Recommendation.

References

1. Laine C, Taichman DB, Mulrow C. Trustworthy clinical guidelines. Annals of internal medicine. 2011;154(11):774-775.
2. Qaseem A, Forland F, Macbeth F, et al. Guidelines International Network: toward international standards for clinical practice guidelines. Annals of internal medicine. 2012;156(7):525-531.
3. Guyatt GH, Oxman AD, Kunz R, et al. Going from evidence to recommendations. Bmj. 2008;336(7652):1049-1051.
4. Guyatt G, Oxman AD, Akl EA, et al. GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. Journal of clinical epidemiology. 2011;64(4):383-394.
5. Vandvik PO, Brandt L, Alonso-Coello P, et al. Creating clinical practice guidelines we can trust, use, and share: a new era is imminent. Chest. 2013;144(2):381-389.
6. Guyatt GH, Oxman AD, Vist GE, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. Bmj. 2008;336(7650):924-926.
7. Balshem H, Helfand M, Schunemann HJ, et al. GRADE guidelines: 3. Rating the quality of evidence. Journal of clinical epidemiology. 2011;64(4):401-406.
8. Andrews JC, Schunemann HJ, Oxman AD, et al. GRADE guidelines: 15. Going from evidence to recommendation-determinants of a recommendation's direction and strength. Journal of clinical epidemiology. 2013;66(7):726-735.
9. Kristiansen A, Brandt L, Alonso-Coello P, et al. Development of a novel, multilayered presentation format for clinical practice guidelines. Chest. 2015;147(3):754-763.

References