Supplement 1: Living Phase Methods

Background

The methods for living reviews and living guideline recommendations were informed by the following sources:

- https://community.cochrane.org/sites/default/files/uploads/inline-files/Transform/201912_LSR_Revised_Guidance.pdf
- Schünemann HJ, et al. Ventilation Techniques and Risk for Transmission of Coronavirus Disease, Including COVID-19: A Living Systematic Review of Multiple Streams of Evidence. Ann Intern Med. 2020 Aug 4;173(3):204-216. doi: 10.7326/M20-2306
- Sieminiuk RA, et al. Drug treatments for covid-19: living systematic review and network meta-analysis. BMJ. 2020 Jul 30;370:m2980. doi: 10.1136/bmj.m2980

Living Systematic reviews

Objectives:

- Identify new evidence for baseline risk, effects of anticoagulation, as well as other Evidence-to-Decision (EtD) criteria
- Update systematic reviews (SR) and meta-analyses
- Inform the guideline panel of changes in the evidence, according to pre-defined criteria
- Publish the living SR's

Methods

- Monthly updated searches
- Same processes and criteria for screening and data abstraction as initial phase
    - Update search results, screening results, and data abstraction will be saved with date
- BLR review:
    - Use of machine learning to prioritize title & abstract screening of high probability citations
    - Include studies on prognostic factors for venous thromboembolism (VTE), major bleeding
- Potential methodology changes during living phase:
    - Baseline risk: additional screening criteria for sample size, for outcomes with multiple studies
    - Anticoagulation effects: focus inclusion on moderate/high certainty evidence only, based on observational studies with low risk of bias and/or randomized controlled trials
- Analyses: pooled analyses will be updated on monthly basis

Informing the guideline panel:

- Monthly reports to panel, regardless of results of updated SR's
- Changes in methodology compared with initial phase will be described
- No new evidence: simple statement for panel
- New evidence, report:
    - Describe new evidence and put it into context of previous findings
    - Report updated overall evidence in Evidence Profile (EP)
    - Describe how addition of new evidence changed the certainty, direction, and/or magnitude of effects

Publication of living SR results:

- To be determined with Blood Advances
- Considerations:
    - Use same ASH declaration of interest management policy, online publication contains most up-to-date version
    - No new evidence: simple statement in online publication
    - Minor updates: update analyses and manuscript, state that there were no important changes in findings
    - Major updates: update all documents, highlight changes in main findings
    - Authorship:
        - Guideline recommendations: SR/Methods team members, as well as panel members, who contributed to the update will be invited to co-author guideline recommendation updates. If Blood Advances editors are not interested in the SR paper (updates), the living SR paper will be published elsewhere
        - Methods paper(s): SR/Methods team members, as well as panel members, who contributed to the methods development will be invited to co-author one or more Methods papers. If Blood Advances editors are not interested in the Methods paper(s), they will be published elsewhere

Retiring living SR:

SR's will be retired at the end of one year, according to agreement with ASH unless this agreement is revised.

Living Guideline Recommendations

Objectives:

The objectives of the ASH living recommendations on VTE management in patient with COVID-19 related illness are to:

- Update EP's and EtD's with new evidence based on living systematic reviews
- Review and revise EtD judgments and recommendations
- Publish updated EP's, EtD's and recommendations

Process and methods:

In general, the panel will have to decide if there is a potential change in the direction or strength of a recommendation.

1. The CHAIRS will review the monthly SR TEAM report which will focus on new studies included compared to the base SR and the last version of the SR
2. CHAIRS consult with the METHODS TEAM if the new evidence may warrant engaging the panel to determine if an update to a recommendation may be required (USING SPECIFIC CRITERIA below)
3. If the chairs decide to move forward, the panel will be asked whether or not the new evidence will warrant discussion of a revised EP and EtD based on the following criteria:
   3.1. Information on a critical outcome that previously had no included studies
   3.2. Magnitude of the absolute effect changed importantly for at least one critical outcome
      3.2.1. The panel will be asked to make judgments of the magnitude of effects for individual outcomes going forward and subsequently if this magnitude of effect may change (including the direction of change), e.g. from moderate to large for a critical outcome
   3.3. Certainty of the evidence for absolute effect increased for at least one critical outcome
      3.3.1. Suggestion: increase from Very low or Low to Moderate or High
   3.4. Potential change in the judgments regarding any other criteria that had an important bearing in the recommendation (costs, feasibility, acceptability, equity)
4. The panel will be asked to vote whether or not to move forward with an updated recommendation using a simple majority vote (>50% for an update of voting panel members, in case of a 50% split, the panel chair's vote will have a weight >1).
   If the panel decides to move forward with a full discussion of the EtD, we will use a process similar to the formulation of the base recommendation to formulate an updated recommendation (which may or may not be similar to the prior one depending on the discussion) in a teleconference and through SurveyMonkey and PANELVOICE - a new versions of the EtDs created in GRADEpro (duplication – allowing for full EtD process)
5. If panel decides to reassess the EtD and recommendation changes in judgments and recommendations will be tracked in date stamped documents. The new EtD will include a rationale for the change.

End of the living phase

6. The chairs may propose a vote to end the living phase. This vote will be triggered by the following considerations:
   6.1. Formulation of a strong recommendation based on high quality evidence or moderate quality evidence in which the balance of desirable and undesirable consequences is clear and unlikely to change.
   6.2. ASH decides to end the living recommendation phase

Expert evidence

7. We will consider to use expert evidence from panel members to supplement the systematic review findings when are no published studies for the effect of anticoagulation intensity on specific critical outcomes, or when there is insufficient evidence for other EtD domains (cost, acceptability, others) relating to COVID-19specifically

Publication of living recommendations:

ASH staff and the Methods Team will also explore with Blood Advances editors how to communicate to journal audiences when the guideline panel re-assesses but does not change a recommendation, for example when some judgments of the EtD change but the recommendation does not. Options may include a short commentary, or an "Update" that uses the "Erratum" or "Corrigendum" tools in order to keep the update linked to the original publication.

Considerations:

- A report describing the recommendations and summarizing the supporting evidence will be submitted for publication within *Blood Advances*, the official home journal for published ASH guidelines
- A living publication presents updated recommendations within the original guideline publication in a way that preserves the impact of the original publication, provides publication credit to the living guideline panel, and meets the needs of guideline users
- Use same DOI, online publication contains most up-to-date version
- No re-assessment: simple summary of changes in evidence, statement that EtD's and recommendations were not re-assessed with reasons
- Re-assessment: update all documents, highlight (lack of) changes in evidence, EtD judgments and recommendations
- Authorship: all guideline panel members and SR/Methods team members will be invited to author updated recommendations in accordance with ASH guideline authorship policy
- ASH guidelines app: determine if recommendations will be published within the mobile and web versions of the ASH guidelines app in advance or after publication of the recommendations (IDSA publication was 'website first')