ESOT manual for clinical practice guidelines and other guidance documents

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1. Introduction and purpose

The European Society for Organ Transplantation (ESOT) actively engages in the publication of high-quality, evidence-based guidance documents to support best practice in solid organ transplantation.

Clinical Practice Guidelines (CPGs) are statements that include recommendations intended to optimise patient care, lead to better clinical outcomes, and improve cost-effectiveness. Furthermore, they provide the opportunity to identify areas requiring further research and serve an educational scope. CPGs are informed by a systematic review of evidence and an assessment of the benefits of alternative care options.

This handbook formalises the processes associated with the preparation of ESOT CPGs, including the selection of topics for new guidelines, writing and reviewing, approval, dissemination, and updating. Moreover, it defines the governance of the process.

1.1 Types of guidance documents

ESOT supports the development and maintenance of CPGs and other guidance documents in the field of solid organ transplantation. This document focuses on CPGs, but the same principles and processes apply to other types of ESOT guidance documents, with any differences arising only from the methodology of development.

- **Clinical practice guidelines:** These documents provide the official position of ESOT on major topics in the field of transplantation, regenerative medicine and end-stage-organ disease. Based on a comprehensive literature review, grading of evidence, and expert discussion and consensus, an independent panel will develop statements that include recommendations intended to optimise medical practice. Clinical practice guidelines are produced following a robust methodology including searching, selecting and appraising the evidence; they offer an assessment of the likely benefits and harms of a particular treatment, medical procedures as well as procedures involving donors or concerning organ quality. When appropriate, the process will highlight unmet needs to be addressed in future research.

- **Guidelines produced in response to an emergency or urgent need:** ESOT will produce these documents only to provide guidance in response to public health emergencies or other circumstances that preclude the development of standard guidelines. Such guidelines may need to be produced within a short time, in which case the methodology used will vary according to the imposed time frame.

- **Consensus documents** Guidance documents for areas not covered in sufficient detail by guidelines, in which a body of scientific evidence may be available, but controversy still exists. A consensus statement differs from a CPG in that it is usually focused on a narrow and specific topic, it synthesises the latest information, often from current and ongoing medical research, it reports clinical options, and summarises expert opinions after reaching an agreement. These documents may provide standard definitions of clinical conditions to guide clinical practice or future research (e.g. definition of surrogate endpoints in kidney

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transplantation; definition of primary graft dysfunction in liver transplantation). They may provide suggestions or recommendations for specific clinical actions, but with the knowledge that statements are mostly based on experience rather than robust scientific evidence.

- **Positions papers:** ESOT position papers present an evidence-based opinion on a specific topic or a course of action. They focus on providing a detailed explanation of an issue, reviewing treatment options and suggesting a specific form of patient care. Not being based on rigorous methods of literature search and synthesis, their value as a guidance document is inferior to that of a CPG or a consensus document.

- **White papers:** documents containing proposals or opinions by an authoritative group in a specific area or on a complex issue that convey ESOT position mainly on non-medical issues, such as education, science advocacy and public health.

1.2 General instruments for guidelines development

The development of ESOT guidelines must be based on a rigorous development process and on a through evaluation of evidence and recommendations. ESOT adopts ~~the~~ the "Grading of Recommendations Assessment, Development and Evaluation (GRADE)" approach and the "Appraisal of Guidelines Research and Evaluation Collaboration (AGREE II)" tool. The "Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)" may be used for reporting in systematic reviews and meta-analyses.

1.3 Governance

The development of all ESOT guideline documents is under the supervision of the *ESOT Guidelines Taskforce* established by the ESOT Executive Committee. The primary responsibility of the Guidelines Taskforce is the identification of areas where guidelines are needed and the promotion of initiatives aimed at the development of guidelines. In addition, the Guidelines Taskforce promotes education around the methodology of guideline development and a culture of scientific rigour in preparing guideline documents. The Guidelines Taskforce is led by a chair, who is a member of the Executive Committee, and comprises additional members with expertise in a particular topic and ~~in~~ guideline development, publication and dissemination.

2. Proposal, selection and evaluation of topics

The Guidelines Taskforce continuously monitors the need for the development of new guidelines or the update of existing guidelines. They may initiate the process leading to the development of guidelines on a specific topic, but favour a bottom-up approach to collect proposals for guideline topics by issuing calls; unsolicited proposals from Sections and Committees are accepted, particularly in case of urgent need or collaboration with other scientific societies.

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2.1 Call for proposals

Upon consultation with the ESOT Executive Committee, the Guidelines Taskforce may decide to open a call to receive proposals for new guidelines. The call is addressed to ESOT Sections and Committees; in addition, ESOT will inform all members of the call and invite them to contact the relevant Section and Committee to suggest topics. The Guidelines Taskforce defines the terms and the timelines of the call, in collaboration with the ESOT office.

When a call for proposals is launched, Sections and Committees must invite their members to suggest topics within a specified time frame. Topics are received and discussed by individual Sections and Committees boards, who finally select topics to endorse by completing the standard application form and submitting it to the Guidelines Taskforce. The ESOT office supports Sections and Committees by reaching out to members.

ESOT may liaise with other scientific societies to develop joint scientific documents and may as well endorse documents produced by other societies. The partnerships for these activities need to be formalised in specific MoUs.

2.2 Selection of topics

The Guidelines Taskforce reviews and prioritises submitted proposals considering novelty and suitability as well as available resources, as agreed with the Executive Committee. In particular, proposals are evaluated for:

- their completeness;
- the availability of new, clinically-significant evidence that could support recommendations;
- the importance of the topic as expressed by the burden of disease of the addressed topic;
- the potential of the proposed guidelines to have an impact on healthcare;
- the importance of the topic for European practitioners and for ESOT members;
- the lack of similar guidelines/consensus documents.

The Guidelines Taskforce may suggest modifications to the submitted proposals, or consider additional topics. Selected proposals are recommended by the chair of the Guidelines Taskforce to the Executive Committee, which decides on financial support.

3. Development of the guidelines

3.1 The Steering Committee

The Guidelines Taskforce nominates a Steering Committee, its chair and co-chair, in charge of developing the scientific document. The members of the Steering Committee are

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chosen to liaise with the topic proposer or the Section/Committee related to the topic of the guidelines to develop or select independently experts in the field. In principle, the members of the Steering Committee should be independent from the topic proposer. Based on topic and circumstances, some of the members may be selected via an open call within the ESOT community.

Besides the renowned expertise on the topic, the selection of Steering Committee members must consider:

- gender balance;
- broad representation of European countries;
- representation of different professional backgrounds/disciplines/expertise;
- involvement of allied healthcare professionals whenever appropriate;
- involvement of members of ESOT Young Professionals;
- patient representation may be considered for specific topics.

If guidelines are developed jointly with another organisation, representatives of that organisation will also be members of the Steering Committee. In this case, the co-chair is selected by the partner organisation.

The role of the Steering Committee is:

- to define the scope of the guidelines document and the key questions in PICO format, when appropriate (PICO = Population, Intervention, Comparator and Outcome);
- to oversee evidence retrieval, and its subsequent assessment and synthesis;
- to draft recommendations based on the available evidence;
- to draft the final document;
- to submit the Guidelines to *Transplant International (TI)* upon formal approval by the Guidelines taskforce, and to manage the publication process;
- to assist the ESOT office with the dissemination of the published Guidelines.

Members of the Steering Committee participate on a voluntary basis and are not paid for their contribution. Travel and accommodation costs for meetings are, however, reimbursed according to the ESOT travel and meetings policy. Once the guidelines are approved and published, the Steering Committee will be dissolved.

3.2 Systematic review and weighing evidence team

ESOT may ask an external entity to assist the Steering Committee in developing the key questions in the PICO format, conducting detailed literature searches to identify the relevant evidence, providing the Steering Committee with overviews, and grading of the evidence.

The Steering committee will:

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- choose and rank priority outcomes that will guide the evidence reviews;
- examine the GRADE evidence profiles used to inform the recommendations and provide input;
- interpret the evidence, with explicit consideration of the overall balance of benefits and harms;
- formulate recommendations considering benefits, harms, values and preferences, feasibility, equity, acceptability, resource requirements and other factors, as appropriate;
- review and approve the final guideline document before submission to peer review.

3.3 Conflicts of interest

ESOT is aware that conflicts of interest can bias recommendations and affect the credibility and reliability of guidance documents. In the interest of transparency, ESOT requests from the members of the Guidelines Taskforce and from all experts invited to join the Steering Committee to complete a Declaration of Interests (DOI). In addition, Steering Committee members are requested to inform the Guidelines Taskforce of any situation occurring during the Guidelines development process leading to a potential conflict of interests, including agreements that will enter into effect within 6 months after the planned publication of the Guidelines.

All DOIs will be reviewed and assessed by the Guidelines Taskforce before final invitations to participate in the Steering Committee are issued. A summary of DOIs for all experts involved in guideline development will be published on the ESOT website as well as in the final guideline document, if requested by the journal.

Interest is defined as any direct or indirect financial or nonfinancial interest besides the development of the CGPs itself, i.e. for the purposes of the guidance document development, it represents a secondary interest. A conflict of interest arises when there is a risk that the professional judgement of an author regarding the specific guidance document will be influenced by a secondary interest. In general, any funding by interested parties – whatever or whoever they are – should be disclosed. Non-financial interests might not always be considered problematic (sometimes they are even considered an added value). On the other hand, they can induce bias, and therefore need to be disclosed. Examples include publishing or being involved in research that may be used in the guidance document, being considered an expert or opinion leader on an intervention or treatment that will be considered in the guidance document. Conflicts of interests of first-degree relatives and close personal relationships (e.g. partner) need also be disclosed. All DOIs are to be included into the dedicated ESOT form, suitable for all ESOT-related activities.

3.4 Confidentiality

ESOT strives towards absolute transparency in the guideline development process, and aims at publishing information on topics and drafts as soon as available. In cases where

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confidentiality is requested, the Guidelines Taskforce will decide whether to delay or not the publication of some information.

4. Review process

As other ESOT scientific documents, the ESOT guidelines will undergo standard peer review. This process is agreed between the Guidelines Taskforce and *TI* board; here some options:

4.1 By a dedicated TI reviewer group

Peer review of the draft guidelines is conducted by a selected group of *TI* Reviewers trained in guidelines review and not involved in the production of the guidance document to review. This group is established by the *TI* board, which informs publicly about its composition. The Guidelines Taskforce may propose additional members for selected guidelines based on expertise in the field and training in guidelines methodology. The *TI* Board leads the review process.

6.4 Following the usual peer review process of TI

Review is carried out by *TI* independently from the Guidelines Taskforce. *TI* Editorial Office keeps the Guideline Taskforce informed of progress. Once the review process is completed, the Editor in Chief of *TI* analyses and streamlines comments and prepares a message to the Steering Committee with a clear indication of how they should reshape the draft document. All comments are considered and formal responses made to those in the 'major revision' category. A new version of the draft document is prepared and resubmitted to the *TI*.

4.2 By ad hoc reviewers appointed by the Guidelines Taskforce

The Guideline Taskforce, in agreement with the Editor in Chief of *TI*, appoints a panel of external reviewers, fully independent from the development of the guidance document, who will be responsible for carrying out a thorough peer review of the draft guidelines. The external review group should be balanced in terms of geography and gender. The Steering Committee addresses the concerns raised by the reviewers until reviewers are fully satisfied. The reviewed draft is submitted for publication to *TI*.

4.3 Public consultation with registered stakeholders

The Guidelines Taskforce may consider an additional step of consultation before submission to *TI*. This consultation is intended to reach out to registered stakeholders interested in the subject of the guidelines, healthcare professional units, scientific societies, advocacy groups, patients' associations or groups of individuals that will be affected by the recommendations (e.g. patients' families). Methods for registering stakeholders vary: the Guidelines Taskforce may rely on existing ESOT partnerships or issue an open call for interested persons and organisations.

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4.4. Reviewers' declarations of interests

When reviewers are appointed by the Guidelines Taskforce, Declarations of interest should be collected for Steering Committee members.

5. Publication and dissemination

5.1 Publication

ESOT guidelines will be published as open-access documents in *TI* following one of the review processes described above. In the case of joint Guidelines developed in association with another society, simultaneous publication in *TI* and another selected journal is possible, previous approval by the *TI* Editor-in-Chief. In addition, ESOT will publish guidelines on its website. The Steering Committee, in agreement with the Guidelines Taskforce, manages the review process.

5.2 Authorship

The order of the authors will be based on their contribution and decided by the Steering Committee in agreement with the standard of the journal publishing the guidelines.

5.3 Dissemination

ESOT will use a range of different methods to raise awareness of the guidelines. A press release accompanies the publication of the guidelines together with an announcement via ESOT newsletter and social media channels.

- Translations. ESOT guidelines are developed, written, and published in English only. If any stakeholder would like to undertake the translation of ESOT guidelines, they must obtain written approval from ESOT. Requests to translate ESOT guidance documents are submitted to the ESOT Executive Committee which consults with the Guidelines Taskforce. The translation must include the reference to the original English language version published by ESOT.

- Derivative products. Based on the full-text version of the guideline document, the Guidelines Taskforce may decide to develop derivative products. These may take the shape of pocket guidelines in printed or electronic formats, slide sets, summary cards for non-specialists, questions for continuing medical education, frequently asked questions, and take-home messages. All of these must be derived from, and be consistent with, the scientific content of the published guidelines. Additional material may be produced for educational purposes. For the development of derivative products, the Guidelines Taskforce may establish dedicated working groups and accept external funding. ESOT retains copyright for all derivative products, unless a specific agreement with a third-party society has been signed in the context of joint guidelines.

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6. Ongoing surveillance and updating

All ESOT guidelines should be kept up to date and reflect current evidence and clinical practice. At any time, ESOT members, Sections and Committees can provide the Guidelines Taskforce with information on new evidence, and propose updating the guidelines. The Guidelines Taskforce decide whether to undertake a focused update; if so, a new Steering Committee is established. There is no barrier to previous members from being selected again.

7. Funding

The ESOT Executive Committee decides on financial resources to allocate to the development of guidelines; they approve or disapprove proposals for new guidelines addressed by the Guidelines Taskforce taking into account financial needs including personnel costs.

ESOT actively raises funds to support the activities of the Guidelines Taskforce and the development of guidelines whose financial support has previously been approved by the ESOT Executive Committee.

Private funders (including industry and public/private foundations) willing to support the dissemination of guidelines are invited to do so via unrestricted grants. In addition, private funders are strongly encouraged to support the production of derivative products, as specified in section 5.3.

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