The ESMO guideline strategy: an identity statement and reflections on improvement


Guidelines should provide recommendations on the optimal management of a patient in specific clinical circumstances based on the scientific evidence. ESMO, as Europe’s leading society in medical oncology produces a range of guideline products in order to assist the cancer specialist towards implementation of quality cancer care, as well as in order to provide information to patients establishing standards for up-to-date optimal management. The ESMO ‘guideline products’ include the Clinical Practice Guidelines, the complementing Consensus Conferences on focused clinical scenarios, as well as memory tools such as print and e-Pocket Guidelines and Patient Guides. In this manuscript, methodology, design and characteristics of the ESMO guideline products are explained and discussed by their strengths and weaknesses, opportunities and threats in order to stimulate reflections on room for improvement and future strategy.

Key words: cancer, guidelines, consensus, oncology, ESMO

introduction

In order to make decisions in their clinical practice, clinicians have to deploy a huge amount of rapidly growing knowledge available in their areas of specialisation. Clinical practice guidelines (CPGs) are defined as ‘systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances’ [1]. In oncology, CPGs should clearly set out the scientific evidence and should appraise the likely benefits and harms behind clinical recommendations. Their goal should be to assist the physician to implement quality cancer care, improve the health outcomes of the patient, as well as to establish and communicate standards for optimal management [2].

As Europe’s leading cancer care society, ESMO is highly committed to these tasks since 1999. Guideline development is regarded as an important service to ESMO members and a pivotal factor for setting pan-European standards of appropriate, optimised patient care [3]. Each ESMO CPG provides all-inclusive recommendations pertaining to diagnosis, staging, treatment and follow-up of a tumour entity or a field of oncology practice that transcends tumour types (e.g. palliative and supportive care etc.).

Since 2007, ESMO has complemented the CPGs with a further instrument, ESMO Consensus Conferences (ESMO CCs) which are a group decision-making process that seeks the consensus by a panel of experts in order to address focused questions on specific clinical, pathological or molecular circumstances [4]. All of the ESMO Guideline products and their scope are summarised in Table 1.

In this manuscript, we set out to clearly describe the philosophy, methodology/production and characteristics of the ESMO Guideline products. Moreover, we seek to emphasise the perceived strengths and key distinguishing features, and to reflect on room for improvement. This ‘Identity Statement’, providing a detailed profiling of the ESMO Guideline project, aims to generate a critical discussion and suggestions for optimisation.

ESMO guideline family products

**ESMO Clinical Practice Guidelines and related activities**

**scope.** The scope of ESMO Clinical Practice Guidelines (ESMO CPGs) is to serve as evidence-based, peer-produced, multi-disciplinary guidelines that can convert the wealth and complexity of scientific research into recommendations that are easy to use in everyday practice on a pan-European scale. They are intended to improve the quality of patient care and health care outcomes and to make clinical decisions more transparent. As they address a heterogeneous mixture of health care systems, financial realities and cultures, they are not intended to become systematic-reviewed voluminous reference repositories for health technology assessments, resource allocation strategies or health policy decision making. However, the contribution of the ESMO CPGs in the establishment of accepted European standards of quality cancer care should help each member-state in devising the best adapted strategies for accomplishing this goal. ESMO is committed to the multi-disciplinary nature of the CPGs, evident in authorship and in the review process on either an expert basis or on a professional society basis, as this is regarded a sine qua non feature of quality cancer care.

**methodology.** The ESMO Guidelines Committee (GC) consists of an Editorial Board overseeing its activities and 18 Subject Editors and deputy Subject Editors, each of whom coordinates
the production, revision and update of CPGs of allocated tumour entities or fields of cancer care. The production process for each CPG is a dynamic and repeatable interaction between four basic constituents: the author tasks (literature search and CPG writing up), the reviewer tasks (at least five ESMO Faculty experts from various disciplines review the CPG drafts), the Subject Editor tasks (appoint authors, reviewers and review/edit all CPG drafts) and the GC Editorial Board and Staff review/approval tasks. The process has been standardised by the formulation of Standard Operating Procedures (SOPs), can be re-iterated as many times as necessary and ensures that all involved parties accept the final end-product as scientifically accurate and relevant. The ESMO CPG production process is shown in Figure 1, while the detailed SOPs can be found in supplementary File S1, available at Annals of Oncology online.

**Table 1. ESMO guideline products**

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<tr>
<th>Guidelines product</th>
<th>Scope</th>
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<tr>
<td>ESMO Clinical Practice Guidelines</td>
<td>To assist the cancer health professional in optimal cancer patient management.</td>
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<tr>
<td>ESMO Pocket Guidelines</td>
<td>To assist the practising oncologist with a 'hands-on' memory tool providing bullet-point recommendations, tables and flow charts.</td>
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<tr>
<td>ESMO Consensus Conferences</td>
<td>To supplement ESMO CPGs by addressing focused questions in specific tumour contexts by the 'consensus' opinion synthesis of expert panels.</td>
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<tr>
<td>ESMO Patient Guides</td>
<td>To provide the cancer patient and family with accurate, understandable information.</td>
</tr>
<tr>
<td>Smartphone Apps</td>
<td>To provide key information from ESMO Pocket Guidelines in mobile electronic formats.</td>
</tr>
<tr>
<td>Potential future Guidelines products</td>
<td>Scope</td>
</tr>
<tr>
<td>E-Updates of ESMO CPGs</td>
<td>To enable rapid communication of management breakthroughs and their electronic incorporation in the e-ESMO CPGs.</td>
</tr>
<tr>
<td>E-Newsletters</td>
<td>To communicate newly produced ESMO CPGs or the release of E-Updates to ESMO members.</td>
</tr>
<tr>
<td>Smartphone Apps for algorithm-based Risk and Management suggestions</td>
<td>To provide risk estimation or management suggestions based on user input of key patient and tumour features.</td>
</tr>
<tr>
<td>‘ESMO-brand’ flow charts and algorithms</td>
<td>To produce a standardised, easily recognisable and user-friendly flow chart/algorithm of stage- or risk-tailored management strategies.</td>
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Although a weighted emphasis on medical oncology practice is seen in several of the CPGs. The authors generally include medical oncologists, surgeons, radiation oncologists and other medical specialties or health experts as deemed necessary and usually a total of five to seven professionals. The multi-disciplinarity concept also holds true with the composition of experts who critically review each CPG during its development [5]. Whenever a mutual agreement on scope, methodology and concept could be reached, ESMO produced CPGs jointly with other professional societies (ESSO, ESTRO, ESGO, ESO and MASCC among others). In those instances, each society appointed authors as well as reviewers and shared publication rights.

The ESMO CPGs are intended to be conveniently used in the clinic, either as an up-to-date, easy to study, concise reference document or as an abbreviated, hands-on ‘memory tool’. The former is better served by the CPGs, which are usually 10–20 pages long and follow a standardised section format:

- Incidence and Epidemiology,
- Diagnosis and Pathology /Molecular Biology,
- Staging and Risk assessment,
- Multi-disciplinary Tumour Specific Treatment Plan (generally stage adopted)
- Response evaluation,
- Aspects of ‘Personalised Medicine’
- Supportive Care
- Follow-up and Long-term Implications.

The ‘memory tool’ function is better served by the ESMO Pocket Guidelines which are shorter, and generally include a ‘bullet point’ list of key recommendations on:

- Diagnosis,
- Staging,
- Risk assessment,
- Treatment,
- Response evaluation,
- Aspects of ‘Personalised Medicine’,
- Supportive Care,
- Follow-up

supplemented by tables, flow charts and management algorithms.

**Figure 1.** ESMO CPG task allocation process. CPG, clinical practice guidelines; GC, Guidelines Committee; SE, Subject Editor.
Each recommendation is followed by a designated Level of Evidence (LOE) score, which reflects the quality and quantity of clinical research that supports it, as well as by a Grade of Recommendation (GOR). The latter is a more complex metric that incorporates not only the quality of evidence but also the magnitude of the clinical benefit associated with the recommendation. ESMO uses an adapted form of the Infectious Diseases Society of America–United States Public Health Service Grading System [6]. The designation of each recommendation with LOE and GOR scores assists the physician to prioritise clinical decisions, the patient to be appropriately informed on benefits and risks of any intervention, and the policymakers to apply weighted information in their strategic planning.

ESMO CPGs adopt the concise format of a guideline produced by cancer health professionals who are experts in a specific field for use by cancer health professionals with a broader emphasis on ‘all day practical management’. Most importantly, ESMO acknowledges the rapid pace at which clinical advances occur in oncology and is committed to updating each ESMO CPG at least every second or third year (or sooner, if necessary). The update process is similar to the production methodology of ESMO CPGs and is fully guaranteed with the safeguard of dynamic feedback between Subject Editors, Authors, Reviewers and the ESMO GC and Staff.

It has to be kept in mind that the ESMO guiding purpose is dominated by the goal for improvement in patient outcomes. For this, we need to place cancer patients next to us, as partners in the same struggle and endow them with an informed, proactive role in treatment planning. ESMO took a step in this direction by producing the ESMO Patient Guides. These are documents adapted from the ESMO CPGs, supervised by the guideline coordinating author and the Subject Editor, reviewed by patient representatives and produced by ESMO and the non-profit charity Anticancer Fund. They are freely available (http://www.esmo.org/Patients/Patient-Guides, http://www.anticancerfund.org/guides/cancertype) to provide evidence-based, responsible information for the cancer patient and family. The ESMO Patient Guides have so far been translated in fourteen languages, an indication of their wide uptake.

ESMO Consensus Conferences

Since 2007, a novel format was developed in addition to ESMO CPGs, reflecting the need for discussions in complex fields of oncology care. ESMO CCs reflect a group decision-making process by experts and the fulfilment of key objectives. Development of guidelines through CCs was considered a more enriched and integrative approach to producing evidence-based, focused recommendations for specific clinical contexts [4].

The model of participatory CCs was based on the expert CC model, upon which CC SOPs were established and adhered to (supplementary File S2, available at Annals of Oncology online). In short, the CC chairs, who include the Subject Editor and one chair nominated by the GC, select acclaimed experts with pan-European and multi-disciplinary distribution. The CC chairs also identify topics within a specific tumour type to be studied by working groups (WGs). Each WG undertakes the task of studying relevant evidence and providing critical questions and answers pertaining to the topic assigned, followed by formulation of recommendations. The ‘question and answer’ format was chosen, since it is considered the most relevant and communicable form to the practicing oncologist. After this important preparatory work has been accomplished via electronic communication, all the WGs meet at a 2-day CC, present and discuss their findings until a consensus recommendation is reached. The writing up of the Consensus document is delegated to the WGs before being finalised by the CC chairs and approved by all CC participants and the ESMO GC (Figure 2). Alongside this strategy, there are some special situations, with particular collaborations, where a different process can be taken but all following high-quality standards, as in the cases of the ESO-ESMO Advanced Breast Cancer and the MASCC-ESMO Consensus Conferences (CCs).

The ESMO CCs are intended to serve as a separate tool, supplementing ESMO CPGs. While CPGs focus on daily-practice recommendations on staging, risk assessment, management and follow-up etc., the CCs provide focused information and deeper insights into controversial fields of oncology standards, resulting in recommendations that address questions arising in well-defined clinical, pathological or molecular tumour contexts. Since 2007, ESMO holds up to four CCs annually, the tumour clinical scenarios to be addressed being chosen by the ESMO GC.

implementation, uptake and evaluation of ESMO guideline products

A guideline on its own will not result in improvement of health outcomes if not adequately disseminated and thoroughly implemented [7]. ESMO is systematically working on dissemination and adoption of ESMO CPG/CCs by practising oncologists via a range of policies. These include:

- Availability of CPGs and CC manuscripts for download from ESMO and Annals of Oncology websites (http://www.esmo.org/Guidelines, http://annonc.oxfordjournals.org/content/)
- Print publication of new CPGs and CC manuscripts in Annals of Oncology
- Promotion and free use of printed ESMO Pocket Guidelines, Patient Guides and availability of key CPG recommendations in mobile electronic apps
- Occurrence of ESMO Guideline Interactive Sessions in each ESMO or joint annual congress, in which clinical cases are presented, discussed and reviewed by presenting junior and senior oncologists and the attending audience, based on the ESMO CPGs and available evidence. These sessions are usually among the blockbusters of every ESMO Congress, a fact emphasising their acceptance by the oncologic community.

The evaluation of dissemination and implementation of ESMO CPGs/CCs by the global oncology community is based on metrics such as citations in medical literature, downloads from ESMO/Annals of Oncology websites and attendance of the Guideline Interactive Sessions. The number of ESMO CPG page views on the ESMO website and the number of CPG downloads from Annals of Oncology exhibit a steadily increasing trend over the last five years. Since 2012, more than 100 000 pdf downloads take place annually, while the CPG page views increased from 100 000 in 2012 to more than 700 000 in 2014 (Figures 3 and 4).
Despite their European orientation, ESMO CPGs have been universally accepted as updated, easy to use, peer-produced guidelines: in fact, the United States, Central and Latin America and Asia feature high in the list of areas from where CPG page views and downloads originate (Figure 5). In view of this, ESMO is actively pursuing presentation, dissemination and adaptation of...
its CPGs in the world and is inviting non-European distinguished physicians to participate in CPG authorship and in the CCs in order to contribute with their expertise and ‘local’ views.

The number of citations of ESMO CPG manuscripts exhibits an increasing trend and is summarised in detail in supplementary File S3, available at Annals of Oncology online.

does not affect the result

a critical appraisal and further developments

ESMO is a lively network of active researchers and cancer health professionals who interact and exchange ideas on ways forward towards the implementation of precision medicine that benefits the patient. As such, an intensive and productive discussion is taking place within the context of the ESMO Committees, congresses and fora on ways to enhance the perceived strengths and remedy the weaknesses of the ESMO Guidelines. The SWOT (Strengths, Weaknesses, Opportunities, Threats, Table 2) analysis we provide as a brainstorming experiment represents the considerations of the ESMO Guidelines Committee [8].

strengths

The ESMO guidelines are produced by multi-disciplinary expert panels of health professionals for their peers, they are clear, easy to use and free to use. They were perceived in their design so as to be sufficiently extensive to convey a detailed, articulate scientific message, but concise enough in order to be easily consulted, studied and updated when necessary. Bearing the ESMO brand and expertise, they are recognisable and pan-European, both scientifically and geographically. The designation of each recommendation with LOE and GOR supplies all interested stakeholders with coded data on the quality of supporting evidence and magnitude of clinical benefit. Moreover, the CC guidelines complement the CPGs in specific clinical scenarios by adding

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<tr>
<th>Strengths</th>
<th>Weaknesses</th>
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<tr>
<td>Clarity</td>
<td>No formal opinion synthesis procedures for CCs</td>
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<tr>
<td>Ease of use</td>
<td>No systematic patient involvement in GL development</td>
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<tr>
<td>Free access</td>
<td>No systematic evidence review</td>
</tr>
<tr>
<td>Peer-produced</td>
<td>No independent audit on GL quality, implementation and impact</td>
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<td>Multi-disciplinary authorship and review</td>
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<td>Up-to-date</td>
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<td>Pan-European perspective</td>
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<td>Recommendation rating for quality of evidence and magnitude of clinical benefit</td>
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<td>Expert opinion</td>
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<td>Information for patients</td>
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<td>Print and electronic memory tools</td>
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opportunities |

Develop a flexible tool for ‘targeted’ systematic review of evidence |
To incorporate the ESMO Magnitude of Clinical Benefit scale in recommendations on new drugs |
To cooperate with professional societies in multi-disciplinary CPGs |
To design ‘ESMO-Brand’ flow charts on tumour risk assessment and tailored management |
To issue e-updates on breakthroughs and new drug approvals |
To incorporate the guidelines in post-graduate training, CME, oncology certification examinations |

threats |

Transformation to bulky reference tools for health technology assessments |
Poor production, update, dissemination |
Patient alienation |
Cooperation strategies without clear memoranda of understanding/rules/common scope |
Dependence on industry or government |
To become ‘irrelevant’ for European authorities in quality cancer care schemes |

Figure 4. Number of ESMO Clinical Practice Guidelines pdf downloads from the Annals of Oncology website over time.

Figure 5. Top 20 countries: traffic based on unique ESMO Clinical Practice Guidelines web page views during first quarter of 2015.
the expert opinion on top of the standard, evidence-based ESMO Guideline methodology. ESMO Pocket Guidelines, patient guides and e-applications complete a product range that aims to empower physicians and patients to practice scientific, informed and tailored medical decision making. All guideline products are funded by ESMO, are independent from the pharmaceutical industry and do not have promotional intention for any of the therapeutic compounds analysed. Moreover, they are not a standalone project but instead are fully incorporated and functionally linked with other ESMO activities: education, E-learning, congress presentations, ESMO Examination certification, National Representative Committee tasks and quality of cancer care audits.

weaknesses and opportunities
Weaknesses are an accepted term in SWOT analyses [8]; however, in the case of ESMO Guidelines, we consider them not as inherent deficits in development aspects but rather as opportunities for improvement.

There are no formal audit/review mechanisms for the selection of contributing participants in CPG or CC activities (authors, experts, reviewers) [9]. Instead, the Guideline Committee relies on the expertise, networking, credibility and objectivity of involved committee members, subject editors and coordinating authors. The dedicated work of those contributors made it possible to embark on such a project with successful results. Moreover, the formal operating procedures/tools for opinion expression and synthesis in CGs can be elaborated and developed in more detail, so as to guarantee the recording of minority opinions, encourage ‘silent’ contributors and strengthen the consensus process [10].

Patient representatives are not systematically involved in the development and production of ESMO CPGs and do not always participate in CCs (although they were successfully involved in some GLs and CCs). As guidelines seek to distil best medical care in specific clinical circumstances for appropriately informed patients, the contribution of the latter in some stages of guideline development is morally justified and methodologically logical [11]. The involvement of patient representatives, possibly via the ESMO Patient Advocacy Group, in the review and signing off of the CPGs and CCs, may be the way forward.

In order to conserve their design, orientation and upgradability, ESMO CPG production is based on a narrative review of the evidence, i.e. one that is not carried out by systematician task forces performing exhaustive literature searches with stringent criteria and search algorithms [12, 13]. Despite setting up several safeguards against bias (expert authorship, reiterated cycles of peer review), further efforts could be made to minimise bias when collecting and studying evidence. The development of a flexible system for systematic evidence review that avoids burdening authors and minimises the mining of outdated, irrelevant or redundant data is indeed a challenge.

The ESMO guideline development methodology and design can be further enhanced: standardised, user-friendly ‘ESMO-Branded’ algorithms/flow charts for risk or stage-tailored management are expected to increase the recognition and acceptance of the CPGs. Electronic updates on breakthroughs/new drug approvals to be circulated via e-newsletters and incorporated in the electronic web versions of the guidelines could further optimise the up-to-date nature of ESMO CPGs. The development of electronic applications for smartphones and computers that use smart algorithms in order to provide risk assessment and management suggestions after user input of patient and tumour characteristics would also enhance practicability.

The ESMO Magnitude of Clinical Benefit Scale (http://www.esmo.org/Policy/Magnitude-of-Clinical-Benefit-Scale), a bold initiative that uses an integrated clinical, systematician and statistical approach so as to emphasise therapeutic compounds with a substantial clinical benefit in oncology, could be incorporated in the ESMO CPGs in order to identify breakthrough therapies that should be available in all countries and socioeconomic contexts.

The impact of any guideline on health outcomes can be physician-focused (satisfaction, guideline uptake), patient-focused (quality of life, survival) and health system-focused (optimal allocation of resources, expenses and benefits) [14]. To date, ESMO has not explored the systematic investigation of the implementation and impact of its guideline products, nor has it pursued a formal independent audit of their quality. It is not clear at the moment whether ESMO should proceed on its own to audit the quality, implementation and impact on health outcomes of its guidelines [13, 15]. This task involves allocation of resources, cooperation with multiple partners and consideration of the distinct organisational, financial and social features of each European country [7, 12]. Moreover, several external initiatives on the subject are already underway [16, 17]. Finally, there is ample room for lobbying for establishing ESMO Guidelines as a training tool in pre- or post-graduate training, as a certification tool for completion of the medical oncology specialty or as the recommendation repository and performance benchmark for quality cancer care by regulatory authorities.

threats
As threats, we define parameters or strategies that may undermine the clarity, accuracy and acceptance of ESMO Guidelines, degrade their impact on health outcomes or render them less competitive than other similar projects.

We believe that ESMO guidelines should not be transformed to bulky reference tools for health economics/health technology assessment studies or for formal reimbursement decisions. Poor production, update, dissemination, alienation with patients would affect their quality and impact and should be avoided at all costs. Cooperation with other societies for joint production of multi-disciplinary guidelines should be encouraged, while simultaneously adhering to ESMO SOPs and brand. Independence from governments and pharmaceutical industry has been a defining feature of ESMO Guidelines from their inaugural day and should remain so. Lobbying for use by European authorities in accreditation/certification and quality cancer care schemes is an ongoing effort that stems from the quality and acceptance of ESMO Guidelines.

The ESMO Guidelines should adapt to the new reality of ‘transitions’: print to electronic; average medicine for tumour site-specific populations to stratified medicine for focused tumour groups to personalised medicine for the single patient. Finally, we should always use as guiding principle the focusing axiom of any successful guideline: What it intends to do, for Whom and in Which clinical circumstances.
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references