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EXTENDED ARTICLE

European Association for the Study of Diabetes (EASD) Standard Operating Procedure for the development of guidelines

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Abstract

The European Association for the Study of Diabetes (EASD) has developed a Standard Operating Procedure (SOP) for the development of clinical practice guidelines, ensuring adherence to rigorous methodological standards based on the principles of the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) framework. Key components include a transparent process for managing conflicts of interest, the incorporation of multidisciplinary panels including individuals with lived experience of diabetes, an evidence synthesis based on comprehensive systematic reviews, and an explicit peer review process. This SOP delineates the roles and responsibilities of the main structures involved, including the Guidelines Oversight Committee, Guideline Development Panels, and Evidence Synthesis Teams. Additionally, the SOP describes the main stages in guideline development, namely scoping of the guideline topic, evidence synthesis, development of Evidence-to-Decision frameworks for the formulation of clear, patient-centred recommendations, writing of the guideline document and the review process.

Keywords Clinical practice guidelines · European Association for the Study of Diabetes · GRADE framework · Patient-centred care · Standard Operating Procedure

Abbreviations

AGREE	Appraisal of Guidelines, Research and Evaluation
COI	Conflict of interest
EFSD	European Foundation for the Study of Diabetes
EST	Evidence Synthesis Team
EtD	Evidence-to-Decision
GDP	Guideline Development Panel
GIN	Guidelines International Network
GOC	Guidelines Oversight Committee
GPS	Good Practice Statement
GRADE	Grading of Recommendations, Assessment, Development, and Evaluation
INGUIDE	International Guideline Development Credentialing & Certification
MOU	Memorandum of understanding
NAM	National Academy of Medicine
PICOT	Participants, Intervention, Comparator, Outcomes, Type of studies
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
RIGHT	Reporting Items for practice Guidelines in HealThcare
SOP	Standard Operating Procedure

Introduction

Clinical practice guidelines are ‘statements that include recommendations intended to optimise patient care that are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options’ [1]. Given the pivotal role that guidelines have in medical practice and their consequential impact on people’s health, it is crucial that they embody evidence-based recommendations developed through rigorous methodology. The National Academy of Medicine (NAM) and the Guidelines

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International Network (GIN) have articulated standards to ensure the production of guidelines that are trustworthy, of high quality and practically useful [1–3]. These standards encompass the formulation of guidelines by a multidisciplinary panel that includes experts and key working partners and community collaborators, consideration of important subpopulations and preferences, application of an explicit, transparent process that minimises biases and conflicts of interest (COIs), and provision of a thorough rationale for each clinical practice recommendation. Red flags compromising the integrity of guidelines, such as significant COIs among panel members, substantial industry funding, insufficient methodological expertise, inadequate external review, exclusion of the public from the development process and lack of transparency, must be rigorously avoided [4]. The Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) Working Group has created and continually refines comprehensive methodological guidance for producing guidelines that meet the high standards set by the NAM and GIN [5–7]. WHO and an expanding roster of international health associations have adopted the GRADE methodology in their own guideline development procedures [4, 8–14].

In 2023 the EASD established the Guidelines Oversight Committee (GOC) [15] to ensure that clinical practice guidelines produced by the EASD adhere to a rigorous, transparent process, ultimately yielding trustworthy, evidence-based recommendations. It is the aim of the EASD that its guidelines will align with high methodological standards, employing a systematic process consistent with NAM principles and the GRADE approach, and adhere to the domains of the Appraisal of Guidelines, Research and Evaluation (AGREE) II instrument [16]. The purpose of this Standard Operating Procedure (SOP) document is to delineate the infrastructure, methods and overarching process involved in the development of EASD guidelines under the oversight of the GOC.

Main structures involved in EASD guideline development

The main structures involved in the development of EASD guidelines are the EASD GOC, Guideline Development Panels (GDPs) and Evidence Synthesis Teams (ESTs) (Fig. 1).

Guidelines Oversight Committee The EASD GOC, with a tenure of 3 years, is composed of a chair, a co-chair and 11 additional members. The EASD Board selects the chair and co-chair, while the GOC chair and co-chair propose the remaining 11 members, who are subsequently approved by the EASD Board. Selection is based on individuals' scientific curriculum vitae, COIs, availability and motivation. A mix of geographical locations, genders and expertise (including clinical, methodological or mixed) is sought. Of the 11 additional members, four should be methodologists and four should be experts in the field of diabetes. Two serve as ex officio representatives of the EASD and the European

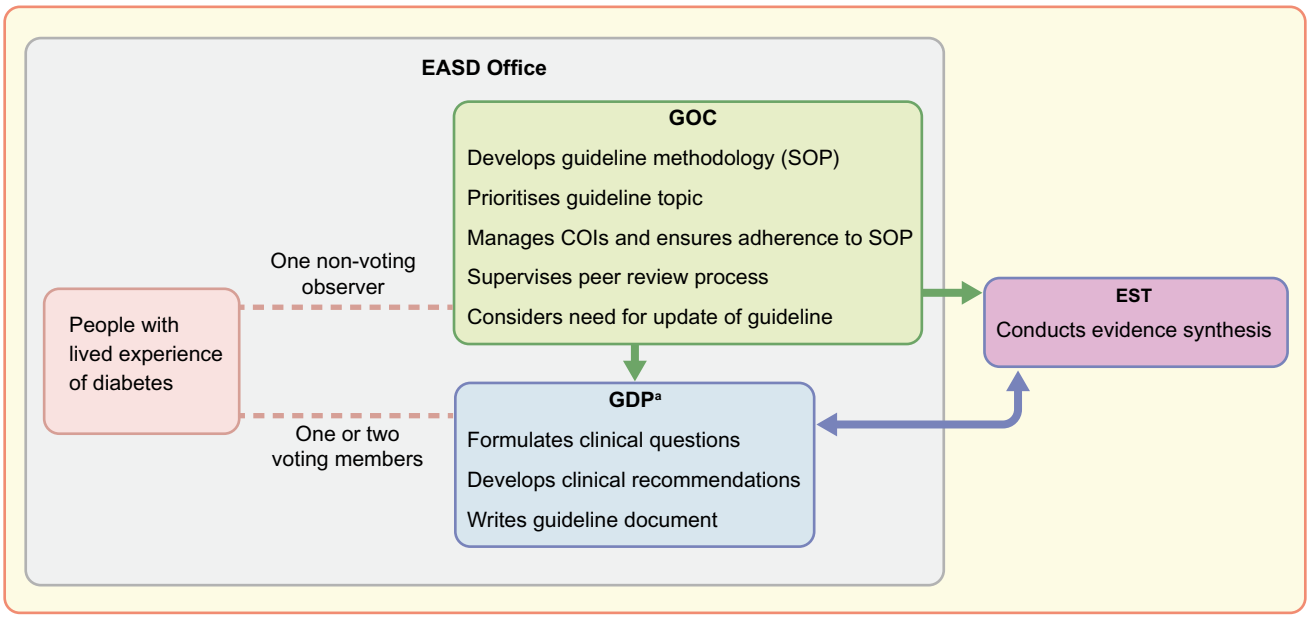

Fig. 1 Main structures and their key roles in the development of an EASD guideline. Single-headed arrows indicate the nomination of the GDP and EST by the GOC. The two-headed arrow indicates collaboration between the GDP and the EST. [a]Current policy does not prevent GOC members from also serving on a GDP

Foundation for the Study of Diabetes (EFSD), ensuring that the strategic goals of the EASD are met. Additionally, one member represents *Diabetologia*, coordinating the publication process for guideline documents and related papers while also addressing the needs and interests of the journal's readership. All GOC members are active EASD members and undergo basic formal training in the principles of guideline development and GRADE methodology (International Guideline Development Credentialing & Certification [INGUIDE] Program level 1), and members with a methodological focus also complete training for guideline methodologists (INGUIDE Program level 2) [17]. GOC members receive no financial compensation. To ensure inclusivity and to bring insights from the wider diabetes community, a member of #dedoc, an international diabetes advocacy network, is invited to attend GOC meetings as an observer. This role provides an opportunity to share perspectives from the diabetes community, fostering a patient-centred approach to guideline development. The observer is not a formal voting member of the GOC but may contribute observations and feedback during discussions.

The primary responsibility of the GOC is to supervise the development and dissemination of evidence-based clinical practice guidelines on behalf of the EASD. Specific tasks include:

- deciding to initiate a guideline for a chosen topic
- nominating the GDP for each guideline topic
- identifying and selecting ESTs for each guideline that can provide a comprehensive synthesis of the evidence
- approving the budget for each guideline within the financial constraints set in agreement with the EASD Board
- defining and overseeing the overall timeline for the production of guideline documents
- supervising the review process for guideline documents
- reviewing and providing final approval of guideline documents
- planning the publication and dissemination of guideline documents
- assessing the need for and timing of updates to existing guideline documents in collaboration with the GDP chairs
- developing and amending the EASD guidelines SOP document

Guideline Development Panel Once the GOC has decided to proceed with a guideline for a selected topic, a GDP is formed with the important task of producing a guideline document for this topic. GDPs for guidelines initiated by the EASD comprise ten members, including two GDP chairs, two guideline methodologists, one or two lay members, and four to five members recognised for their clinical expertise and experience in the specific topic. Ideally, methodologists should also possess a clinical background, while clinical/content experts will also have some methodological expertise. Inclusion of lay members—individuals with lived experience of diabetes (who either have been diagnosed with diabetes themselves or are close caregivers or family members of someone with diabetes)—is key and allows their perspectives to be incorporated at all stages of guideline development. All members have equal voting rights on clinical practice recommendations, except for methodologists, who can vote only if they also possess a clinical background relevant to diabetes. All members are regarded as equal contributors and are eligible for authorship.

For the first guideline commissioned by the EASD under the new process (guideline on diabetes distress), the GOC appointed both GDP chairs and selected two in-house EASD GOC methodologists to serve as GDP methodologists. The GDP chairs proposed additional members for the GDP, who were subsequently reviewed by and received final approval from the GOC. For subsequent guidelines, one of the two GDP chairs will be appointed directly by the GOC to ensure continuity and alignment with the strategic direction of the GOC. The second chair and other GDP members with clinical and research expertise on the guideline topic (excluding the two methodologists and lay members) will be selected through an open call process initiated by the EASD. The GOC will evaluate all applications and nominate suitable GDP members. The GDP should include a diverse group and there should be no barriers related to gender, age, race and ethnicity or nationality. The selection process for GDP lay members will be defined in future iterations of this SOP as we develop a comprehensive strategy to effectively integrate the perspectives of people with lived experience of diabetes.

Active EASD membership is a prerequisite for all GDP members, except for lay members. All GDP members receive basic (INGUIDE Program level 1) training in the GRADE methodological framework, with INGUIDE Program level 2 training additionally required for methodologists [17]. At least one of the two GDP chairs should also undergo INGUIDE Program level 2 or equivalent training to ensure a comprehensive understanding of the GRADE methodological approach. GDP members are not commissioned and receive no financial compensation for their participation, except for the two methodologists, because of the additional tasks involved, and the GDP lay members. All GDP members sign a COI form and a memorandum of understanding (MOU) document outlining their remit, confidentiality terms and authorship rules [18].

The choice of the GDP chairs is pivotal for the successful completion of a guideline document. While the GDP chairs should have comprehensive knowledge of a guideline topic, they must ensure that any pre-existing opinions on the subject do not bias the interpretation of findings arising from the evidence synthesis. Chairing a GDP requires the

ability to lead a multidisciplinary team to consensus on a given subject. The chairs are responsible for overseeing the completion of the following GDP tasks:

- framing the key clinical questions related to the specific guideline topic in a PICOT (Participants, Intervention, Comparator, Outcomes, Type of studies) format
- choosing and prioritising outcomes for each clinical question
- assessing the GRADE evidence profiles (one profile across all outcomes per clinical question) [5, 7]
- formulating recommendations based on interpretation of GRADE Evidence-to-Decision (EtD) frameworks, taking into account factors including benefits, harms, values and preferences, feasibility, and resource requirements [19]
- writing the draft guideline document
- revising the draft guideline document during the review process
- submitting the guideline document to the GOC and revising as required before submitting for publication
- participating in the update of the guideline document if required by the GOC or the EASD Board

The two GDP methodologists hold the following additional responsibilities:

- supporting the GDP to refine clinical questions in PICOT format
- conducting a preliminary literature search to assist the GDP in determining whether each clinical question necessitates a de novo systematic review or an update of an existing review
- collaborating with the EST to develop the protocol for the evidence synthesis
- ensuring that the EST conforms to the protocol for the evidence synthesis and the scope of the guideline throughout the whole process
- guiding the EST in grading the certainty (quality) of evidence per outcome [5, 7]
- preparing GRADE evidence profiles across all outcomes for each clinical question and guiding the GDP in assessing them [20]
- guiding the GDP in developing and assessing GRADE EtD frameworks, and formulating clinical practice recommendations [19]
- ensuring consistency between the GDP's recommendations and the GRADE assessments made, adhering to the wording advocated by GRADE [19, 21]

GDP lay members are to make unique and invaluable contributions such as:

- informing the GDP about how conditions and treatments affect their daily lives, ensuring that areas of concern are addressed in the clinical questions in the guidelines
- identifying important outcomes for each clinical question, which may be viewed differently by people with lived experience of diabetes
- participating in discussions assessing the benefits and harms of treatments during the formulation of EtD frameworks
- assisting in creating a lay-friendly summary of the guideline document

Evidence Synthesis Team Systematic reviews and meta-analyses form the basis for the development of evidence-based clinical recommendations [1, 2]. Therefore, the key task of an EST is to produce an evidence synthesis based on a systematic review addressing the clinical questions formulated by the GDP. The specific responsibilities of an EST include:

- collaborating with the GDP methodologists to develop a systematic review protocol based on the clinical questions formulated by the GDP
- registering the protocol in a publicly available register
- conducting a systematic review and meta-analyses in alignment with high-quality methodological standards [22, 23]
- collaborating with GDP methodologists to grade the certainty of evidence per outcome [5, 7]
- providing comprehensive technical reports to the GDP within a set time frame
- preparing a manuscript based on the systematic review and submitting it to a peer-reviewed journal

ESTs based in non-profit (ideally, academic) institutions that applied to a relevant EASD open call made in 2023 were reviewed by the GOC and shortlisted. Once a GDP has formulated the clinical questions for a guideline, the shortlisted ESTs are invited by the GOC to submit tenders for the evidence synthesis work. These tenders are scrutinised by the GOC and an EST is appointed based on the team's track record and experience in conducting high-quality systematic reviews and meta-analyses in the field of diabetes, their professionalism, motivation and readiness to undertake the required tasks, and the presence of minimal COIs. On selection, the EST is required to sign an MOU. Remuneration for the tasks performed by the EST is provided by the EASD.

Administrative support team The EASD administrative support team provides essential logistical and administrative assistance across all guideline development bodies, including the GOC, GDPs and ESTs. Although they are not formal members of these committees, their support in

coordinating communications and managing organisational tasks is vital to the smooth operation of the guideline development process.

Policy for declaration, assessment and management of COIs for GDPs and ESTs

The COI policy for GDPs and ESTs addresses all important domains outlined in the extension of the Reporting Items for practice Guidelines in HealThcare (RIGHT) statement for the reporting of COIs in policy documents of guideline organisations, including defining COIs, detailing the declaration process and specifying how COIs are assessed and managed [24]. To ensure transparency, it is mandatory for all individuals involved in EASD guideline development to adhere to the EASD COI policy. This policy requires that members of the GOC, GDPs and ESTs complete an EASD duality of interest form disclosing any COI spanning the previous 24 months (available at https://www.easd.org/guidelines/guidelines-oversight-committee.html). This form will be updated annually until the publication of a guideline document. The GOC chair and co-chair will collectively review the GDP chairs' forms, while the GOC and GDP chairs will collectively review the COI forms of the GDP and EST members. If a GDP chair is also a GOC chair, their COI form will be reviewed by an alternative member of the GOC or a member of the EASD Board. GDP COI statements will be reported in a supplementary appendix within the published guideline document.

It is required that all relationships—commercial, non-commercial, personal, institutional and other—that could potentially create a COI are disclosed. These relationships could include, but are not limited to, employment, ownership of stocks/shares/patents, role as a principal investigator in a clinical trial, receipt of research funding, provision of expert testimony, receipt of speaking honoraria, and consultancy work. Direct employment or financial interests in a pharmaceutical company that are relevant to a specific guideline, such as ownership of stocks/shares/patents, disqualify an individual from participating in a GDP or an EST. COIs are classified as either 'significant' (involving financial sums exceeding €10,000 per year or being a primary investigator in a relevant industry-sponsored study) or 'non-significant' (involving financial sums equal to or less than €10,000 per year, being a non-primary investigator in an industry-sponsored trial relevant to the specific topic or being a primary investigator in an industry-sponsored study that is not relevant to the guideline topic). At least one of the two GDP chairs should be free from significant COIs pertinent to the guideline topic. Similarly, at least 50% of the other GDP members should have no significant COIs. If a GDP member has a significant COI related to a specific clinical question in the guideline, they must abstain from the discussions and voting pertinent to the EtD framework for the respective clinical practice recommendation(s).

Selection of topics for guideline documents

Figure 2 provides an overview of the EASD guideline production procedure. Potential topics for EASD guidelines to be developed under the new process were identified through an EASD open call posted in March 2023, which invited members of the EASD to propose topics via an online survey. The survey link was included in the March 2023 EASD newsletter and an invitation to participate was also shared via social media to raise awareness. Survey participants were asked to justify the significance and timeliness

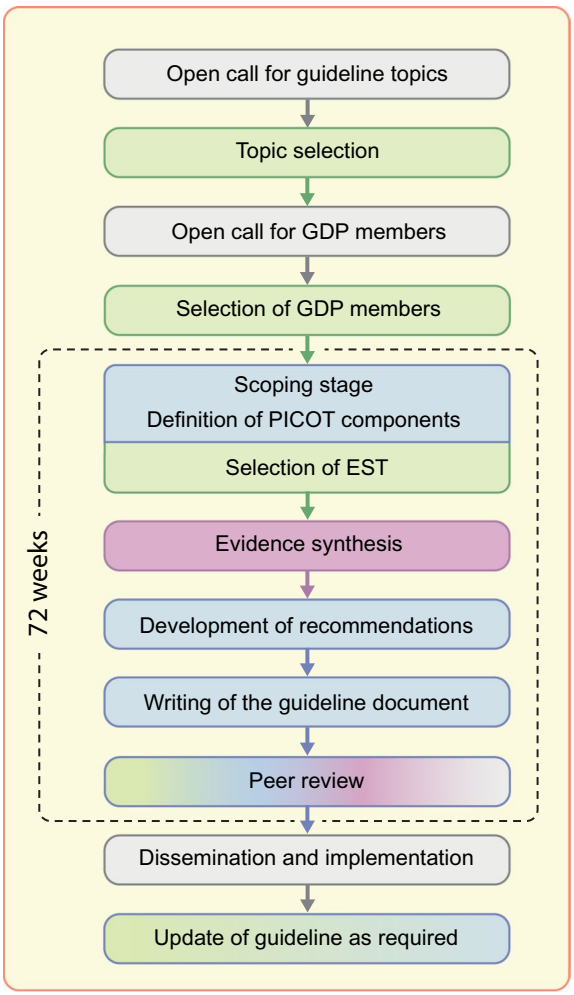

Fig. 2 Overview of the EASD guideline production procedure. Colours indicate the structures and bodies involved at each stage: grey, EASD membership; green, GOC; blue, GDP; pink, EST. Peer review is the responsibility of all four structures/bodies; updating guidelines is the responsibility of the GOC and GDP

of the topics suggested. On completion of the survey, the GOC categorised all topic proposals based on overarching themes, which were then evaluated based on their importance, potential impact and feasibility. Criteria considered in the evaluation primarily focused on clinical relevance, alongside the availability of evidence that could facilitate the development of practice recommendations and the presence of any uncertainties or controversies surrounding the topics. To ensure efficiency and avoid duplication of effort, the GOC also considered whether a proposed topic had recently been addressed by the EASD or another organisation. The prioritised themes were shortlisted and the GOC members determined the final topic selection through a voting process.

Development process for guideline documents

The development process for EASD guidelines aims to deliver evidence-based, patient-centred directives for clinical practice. The process is initiated at the first meeting of the GDP and concludes with the journal submission of the finalised guideline document. In short, this process comprises five distinct but interconnected stages: (1) scoping the guideline topic; (2) evidence synthesis; (3) formulation of clinical practice recommendations; (4) writing of the guideline document; and (5) review of the guideline document. Each of these stages plays a critical role in shaping the guideline and adheres to the GRADE approach [5–7]. Once finalised and approved by the EASD Board, the guideline document enters the publication and dissemination process to ensure that it reaches the intended audience. This section provides an overview of each stage, detailing the sequence of tasks performed, the individuals and structures involved and the expected timeline. Table 1 summarises the individual steps alongside a projected timeline for the entire process.

Stage 1: scoping the guideline topic The guideline development process begins with a scoping stage during which the GDP formulates the clinical questions related to the guideline, prioritises outcomes that are important for people with diabetes, and establishes the inclusion criteria for the studies relevant to each clinical question.

Formulating the clinical questions is a crucial step. These questions should be distinctive, addressing unique aspects of the topic, and narrow in scope, meaning that they can be answered with a manageable volume of primary evidence within the allocated time frame and with the available resources. Moreover, they should be clinically relevant and patient-centred and framed clearly using the PICOT format [6]. The clinical questions generally fall into three categories: therapeutic, diagnostic/screening and preventive. The GDP may initially draft an extensive list of potential questions but should narrow them down to the most important questions (preferably no more than ten) through discussion and a voting process. Similarly, the key outcomes for each clinical question are identified through a prioritisation process [6]. For each clinical question, a maximum of seven outcomes (including both benefits and harms) should be chosen [25]. Ideally, the GDP could also define the minimum clinically important difference for each outcome (if feasible), which will aid the grading of the certainty of evidence in the evidence synthesis phase. The next step in the scoping stage involves the refinement and clarification of the eligibility criteria for each individual PICOT domain, as well as the types of primary studies relevant to each clinical question. RCTs are generally prioritised for management questions; however, in situations where there is a scarcity of published RCTs for specific clinical questions, non-RCT studies may also be considered. This step relies on the insights and expertise of the GDP members under the methodological guidance of the GDP methodologists.

Before initiating the evidence synthesis, the GDP considers whether a de novo systematic review is necessary for each clinical question. Depending on how closely related the clinical questions are, individual questions may require separate systematic reviews or, conversely, multiple questions might be addressed within a single systematic review. Additionally, if a recent and relevant systematic review is available for a given question, it could serve as the foundation for an updated systematic review. GDP methodologists guide these decisions by performing a scoping literature search for relevant systematic reviews. However, when considering the use of an existing systematic review, the GDP, guided by its methodologists, must ascertain that the review is of adequate quality, as assessed by relevant tools such as AMSTAR 2 or ROBIS [26, 27]. Notably, an update of an existing systematic review does not merely mean revising or augmenting the existing data. In particular, the EST can use an existing high-quality systematic review to obtain components such as the search strategy, eligible studies identified up to the point of the original search, and data extracted and/or used in meta-analyses. However, this should be supplemented with additional de novo work, such as updating the literature search, expanding the search to additional databases, screening new search records, extracting data from newly eligible studies and additional outcomes, and updating meta-analyses based on new data or using more robust statistical methods. Furthermore, risk of bias assessments for all outcomes of interest may need to be repeated, along with de novo GRADE assessments, to ensure that the quality and relevance of the evidence are up to date.

Stage 2: evidence synthesis The second stage involves synthesising the relevant research evidence that addresses the clinical questions articulated during the scoping stage. The

Table 1 Summary and timeline of the development process for EASD guideline documents

Stage	Timepoint for completion (week after initiation[a])	Actions	Responsible structure(s)
1. Scoping the guideline topic	8	Formulate clinical questions (maximum of ten questions).	GDP
		Prioritise and finalise outcomes (maximum of seven for each clinical question). Ideally, define the minimum clinical important difference for each outcome.	GDP
		Frame each clinical question in a structured (PICOT) format.	GDP methodologists
		Review PICOT components and define detailed eligibility criteria and the type of primary studies that are relevant (preferably RCTs) for all clinical questions.	GDP (guided by GDP methodologists)
		Decide whether to perform a de novo systematic review or an update of an existing systematic review for each clinical question. Individual questions may require separate systematic reviews or multiple questions might be addressed within a single systematic review.	GDP (guided by GDP methodologists)
2. Evidence synthesis	32	Develop a protocol outlining all important methodological steps in the evidence synthesis.	EST and GDP methodologists
		Perform literature searches (at a minimum in MEDLINE [PubMed] and CENTRAL).	EST
		Screen the search records in duplicate and present the selection process as a PRISMA flow diagram.	EST
		Extract data from included studies.	EST
		Assess risk of bias per outcome in included studies.	EST
		Perform meta-analyses, preferably using a random-effects model. Consider providing funnel plots.	EST
		Use GRADEpro [36] to rate the certainty of evidence for each outcome for each clinical question as high, moderate, low or very low (see also Table 2) and create GRADE evidence profiles and summary of findings tables.	EST and GDP methodologists
		Deliver a detailed technical report (including but not limited to search strategies, PRISMA checklists, data extracted, forest plots and GRADE assessments) to the GDP and EASD.	EST

Table 1 (continued)

Stage	Timepoint for completion (week after initiation[a])	Actions	Responsible structure(s)
3. Formulation of clinical practice recommendations	44	Use GRADEpro to rate the overall certainty of evidence across all outcomes for each clinical question.	GDP (guided by GDP methodologists)
		For each clinical question, evaluate additional GRADE criteria, such as the balance between desirable and undesirable outcomes, values and preferences of people with diabetes, cost-effectiveness, impact on health equity, acceptability and feasibility.	GDP
		Use GRADEpro to construct EtD frameworks (one for each clinical question) based on the overall certainty of evidence and additional GRADE criteria.	GDP methodologists
		Develop recommendations, determining the direction (for or against an intervention) and strength (strong or weak/conditional) of each recommendation based on the respective GRADE EtD framework (see also Table 3). Phrase recommendations using the wording suggested in GRADE methodology.	GDP
4. Writing of the guideline document	54	Include a concise introduction followed by a methodology section.	GDP
		Include the following sections in this order for each clinical question: • formulation of clinical question • a box with respective recommendation(s) • a summary of retrieved relevant evidence • the rationale leading to specific recommendation(s).	GDP
		Include a succinct discussion and supplemental material, including GRADE evidence profiles or summary of findings tables for critical outcomes and the detailed EtD framework for each recommendation.	GDP
		Ensure compliance with the domains of the AGREE II instrument.	GDP methodologists
5. Review of the guideline document	72	Internal review of the guideline draft, considering methodological, clinical and practical aspects.	GDP and EST
		Ensure alignment with the EASD guidelines SOP and check for any contradictions with other relevant EASD guidance documents.	GOC (provide feedback), GDP (amends manuscript)
		Review by external reviewers.	External review group (provides feedback), GDP (amends manuscript)
		Final approval prior to journal submission.	GOC and EASD Board

[a]Initiation is defined as the time point of the first GDP meeting

EST is commissioned to perform this task, which involves conducting systematic reviews in accordance with high methodological standards [22, 23].

The evidence synthesis process comprises several key steps: literature search, screening of search results, data extraction, risk of bias assessment, meta-analysis, and evaluation of the certainty of the evidence for each outcome using the GRADE framework. These steps must be thoroughly outlined in a protocol developed by the EST and GDP methodologists, which should also be registered in a publicly available register. The literature search should be performed, at a minimum, in MEDLINE (PubMed) and the Cochrane Central Register of Controlled Trials (CENTRAL), although additional databases may be searched depending on the guideline topic. The screening process, which consists of a title/abstract phase and a full-text phase, should be conducted in duplicate by at least two EST members independently based on prespecified eligibility criteria and should be documented using a Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram [23]. Automation tools may be employed for the screening and/or data extraction steps to increase efficiency, provided their use is approved by the GOC. Suitable tools should be used to assess the risk of bias in eligible studies, such as Cochrane's RoB 2 for RCTs, ROBINS-I for non-RCTs, QUADAS-2 for diagnostic accuracy studies, and QUIPS for prognostic studies [28–31]. Subsequently, meta-analyses for each clinical question should be conducted, either conventional pairwise meta-analyses or network meta-analyses when there are limited primary studies directly comparing the interventions of interest or when there are multiple competing interventions. In this step, it is important to perform clinically relevant subgroup analyses, which ideally should be predefined in the protocol, and interpret their findings through robust methodology [32, 33]. In the final step, the EST, in collaboration with GDP methodologists, should use GRADE criteria to rate the certainty of evidence at the outcome level (separately for each outcome) as high, moderate, low or very low (Table 2) [5, 7, 20]. Each PICOT question should be accompanied by one GRADE evidence profile and a summary of findings table [25, 34]. At this stage, input from the GDP on the minimum clinically important difference for each outcome can enhance the validity of the GRADE assessments.

ESTs are tasked with submitting a comprehensive technical report to the GDP and the EASD within the specified time frame. This report should encompass detailed data from all individual stages of the evidence synthesis, including but not limited to the search strategies, PRISMA checklists, data extracted, forest plots and GRADE assessments. The intellectual property of this technical report is owned by the EASD and will be instrumental for the GDP in formulating the guideline recommendations. Journal submission of individual systematic reviews is the purview of the respective EST. As well as the EST members, the author list for such submissions should include GDP members who contributed to the evidence synthesis process. The order of authors should be mutually agreed on between the contributing authors.

Stage 3: formulation of clinical practice recommendations The third stage focuses on the formulation of clinical practice recommendations by the GDP, employing the GRADE EtD frameworks [19, 21, 35]. This stage begins once the certainty of evidence for each outcome has been individually rated by the EST and the GDP methodologists. At this point, an overall judgement regarding the certainty of evidence across all outcomes for each clinical question must be determined. This assessment is based on the individual GRADE ratings for the outcomes related to a specific clinical question. Overall certainty of evidence can range from high to moderate, low or very low and is usually dictated by the lowest certainty of evidence assigned to any of the critical outcomes [20].

In addition to the overall certainty of evidence, the GRADE approach requires consideration of additional determinants before making a recommendation for each clinical question. These may include the balance between desirable and undesirable outcomes, the values and preferences of people affected by the condition of interest, cost-effectiveness, the impact on health equity, acceptability and feasibility [19, 21, 35]. The GRADE approach encapsulates

Table 2 Levels of certainty of evidence according to the GRADE framework

Certainty of evidence	Explanation
High	We are very confident that the true effect lies close to that of the estimate of the effect
Moderate	We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low	Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low	We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Adapted from GRADE guideline 3 [7] with permission

these factors within the EtD criteria, which the GDP should assess. While these assessments typically follow the overall assessment of GRADE certainty of evidence, the GDP can also evaluate individual criteria concurrently with the evidence synthesis carried out by the EST. Ideally, these assessments should be supported by relevant literature, such as cost-effectiveness studies or research on patient preferences. The GDP methodologists guide the GDP to complete these judgements, using the GRADEpro GDT web-based application [36] to construct the EtD tables, which form the basis for crafting clinical practice recommendations [19]. The EtD tables serve a critical role in enhancing transparency, focusing the GDP's discussions and documenting the decisions made regarding each determinant and its influence on the recommendation. The GDP methodologists prepare the EtD tables, which the GDP discusses under the GDP chairs' leadership. Following a comprehensive assessment of all determinants, a draft recommendation is proposed for each clinical question through a voting process. Based on the GDP's assessments, four potential types of recommendations can be made, based on the direction (for or against an intervention) and strength (strong or weak/conditional) of the recommendation, as shown in Table 3 [19, 21, 35]. Recommendations are formulated through voting among all GDP members. Members with a significant COI pertaining to a particular recommendation are required to abstain from voting on that recommendation. Final recommendations should be reached by consensus through GDP discussions. The entire process, including discussions, votes and any abstentions due to COIs, should be comprehensively documented. In case of significant disagreement regarding the strength or direction of a recommendation, a conditional recommendation is deemed appropriate. Additionally, the GDP methodologists must ensure that all recommendations are articulated in an active voice, using the phrasing suggested by the GRADE approach. Specifically, strong recommendations should be stated as 'We recommend for/against ...' and weak recommendations as 'We suggest for/against ...' [19, 21]. Outcomes should generally not be mentioned in a recommendation to prevent misinterpretation that only single outcomes were considered.

The GDP's primary aim is to develop recommendations for clinically important questions based on available comparative evidence, including RCTs or high-quality comparative observational studies. These recommendations are graded using the GRADE methodology and rely on systematic reviews as already described. However, for some questions, a formal GRADE process may be impractical, unnecessary or not feasible. In these cases, the GDP may issue Good Practice Statements (GPSs) or Recommendations based on Ungraded Evidence to provide guidance. GPSs are reserved for universally accepted recommendations that are essential for effective healthcare. GPSs apply to actions that are ethically imperative and clearly beneficial and for which further evidence is unlikely to alter a recommendation. A GPS is warranted only if it meets these criteria: the recommendation is necessary for safe, effective healthcare; the expected net benefit is substantial and clear; and conducting a formal evidence synthesis would be an inefficient use of resources due to high opportunity costs [37, 38]. For GPSs, a formal literature search is conducted but is focused on existing summaries of evidence, such as systematic reviews, high-quality evidence-based reviews or relevant observational data that may indirectly support the GPS without requiring new evidence synthesis. To ensure clarity, each GPS is labelled as an 'Ungraded Good Practice Statement'. Where applicable, a brief rationale is included to support the statement, explaining the basis and any indirect evidence or ethical considerations that substantiate the recommendation. Recommendations based on Ungraded Evidence are issued when comparative studies are unavailable or minimal, yet guidance is necessary to address a clinical

Table 3 Types of recommendations based on their direction and strength

Type of recommendation	Explanation[a]
Strong for an intervention	Desirable effects of an intervention clearly outweigh undesirable effects
Weak/conditional for an intervention	Desirable effects of an intervention probably outweigh undesirable effects but uncertainty exists (e.g. because of low certainty of evidence or because desirable and undesirable effects are closely balanced)
Strong against an intervention	Undesirable effects of an intervention clearly outweigh desirable effects
Weak/conditional against an intervention	Undesirable effects of an intervention probably outweigh desirable effects but uncertainty exists (e.g. because of low certainty of evidence or because desirable and undesirable effects are closely balanced)

[a]Desirable and undesirable effects refer to all relevant GRADE EtD framework determinants, including overall certainty of evidence on the effect of an intervention on critical outcomes, balance between desirable and undesirable outcomes, values and preferences of people with the condition of interest (e.g. specific type of diabetes), cost-effectiveness, health equity, acceptability and feasibility

Based on GRADE guidelines 14 and 15 [21, 35]

question. As such, these recommendations are primarily based on the collective expertise and clinical judgement of the GDP members in the absence of robust evidence [39, 40]. Each statement is explicitly labelled as a 'Recommendation based on Ungraded Evidence' and is phrased as 'We suggest …' to indicate that it reflects an advisory level, distinct from GRADEd recommendations.

Stage 4: writing of the guideline document The content of the guideline document should align with the EASD guidelines process and adhere to GRADE methodology [1–3, 16], and follow the international RIGHT statement and checklist [41]. The title of an EASD guideline document should start with 'European Association for the Study of Diabetes (EASD) Guidelines for …'. The title page should be followed by an abstract and an accompanying lay-friendly summary (and infographic) of the guideline. The main text of the guideline document should start with a concise introduction that underscores the clinical significance of the guideline topic and presents the individual clinical questions. Subsequently, a methodology section should be outlined, detailing the GDP's composition, the management of COIs and a summary of the major methodological steps employed, such as the scoping stage, evidence synthesis and application of GRADE EtD frameworks. After the methodology section, each recommendation should be presented separately but in a consistent manner. Each should begin with the formulation of the respective clinical question and a clear presentation of the associated recommendation(s). Subsequently, for each clinical question, a brief overview of the retrieved and evaluated evidence should be presented, along with the rationale leading to the recommendation(s). This rationale should consider both the overall certainty of the evidence and other GRADE EtD determinants (Table 1). Once all clinical questions and respective recommendations are presented, a succinct discussion should summarise the recommendations, address the strengths and limitations of the guideline document and describe the overall clinical implications, considerations for implementation and potential need for future updates.

The responsibility for drafting the guideline document falls on the GDP, with oversight by the GDP chairs. While all GDP members contribute to drafting of the document, it is recommended that GDP methodologists take primary responsibility for structuring sections related to clinical questions and recommendations to ensure adherence to GRADE assessments and consistency in the presentation of evidence. Clinical and content experts may focus on drafting the introductory and discussion sections, where their expertise is especially valuable in contextualising the recommendations. After the manuscript has been drafted, the GDP methodologists should complete the AGREE II reporting checklist [16].

Stage 5: review of the guideline document Once the GDP has drafted the guideline document, it should undergo a thorough review process before submission for publication. This process involves both internal (the GDP, EST lead(s) and GOC) and external reviewers.

The initial review is conducted by the GDP and the EST lead(s) and involves a comprehensive examination of the guideline draft. After incorporating all comments and feedback, the GDP chairs are responsible for forwarding the manuscript to the GOC. The GOC conducts a preliminary review to ensure alignment with the EASD guidelines SOP and check for any inconsistencies with other relevant EASD guidance documents. Ideally, inconsistencies should be avoided; however, they may occasionally occur when the guideline incorporates newer evidence that diverges from existing guidance. In such cases, these differences should be explicitly acknowledged and elaborated on to clarify the rationale for the divergence. Once any comments or suggestions from the GOC have been appropriately addressed by the GDP, the manuscript is forwarded to the external review group.

The external review group is selected by the GOC and comprises individuals with expertise and interest in the guideline topic, as well as working partners and community collaborators directly affected by the clinical practice recommendations. In addition to healthcare professionals and experts in the field of diabetes, the external review group should also include a patient advisory group to address any potential limitations that arise from having a limited number of lay members in the GDP, thus mitigating the risk of tokenism. While it may not be practical to include a large patient advisory group in the GDP because of logistical and methodological constraints, the input and viewpoints of such individuals are deemed crucial in the external review phase. The external review group should be diverse in terms of geography and gender diversity and provide a range of perspectives. If certain perspectives or important working partners and community collaborators are not included in the GDP, they should be included in the external review group. In addition, a period of public consultation should be incorporated into the external review process to gather broader feedback and insights. The external reviewers' role is to identify errors, highlight missing data, comment on clarity and assess implications for implementation. However, they should not alter the recommendations set by the GDP. External reviewers are required to declare any COIs prior to their involvement, and they should be acknowledged in the final document.

Following receipt of feedback from the external reviewers, this information is passed to the GDP for consideration. While the GDP does not need to respond to each comment individually, it is crucial to inform the GOC about how the comments were addressed. This involves providing a revised

version of the guideline manuscript along with a summary of the revisions made. On approval by the GOC and endorsement of this decision by the EASD Board, the GDP can proceed with journal submission. In addition, a dissemination plan for each guideline should be developed, including strategies for sharing through the EASD and potential partner organisations' websites and e-learning platforms; social media; and graphical abstracts, lay language summaries, decision aids and non-English language translations and 'GRADE-Adolopment' (adoption, adaptation and, as needed, de novo development of recommendations) versions [42].

Authorship and publication policy

In the finalised guideline documents, the GDP chairs will serve as joint first authors. The remaining authors will comprise all members of the GDP and the lead(s) of the EST. Following final approval by the GOC and EASD Board, the GDP chairs will be authorised to submit the manuscript for publication, with *Diabetologia* being the preferred journal. All intellectual property rights and copyrights associated with guideline documents will be solely and exclusively owned by the EASD. Contributors to guidelines will be obliged to formally assign their respective rights to the EASD, allowing for unrestricted use and distribution by the EASD. On submission, *Diabetologia* will subject a manuscript to its standard editorial process, and the ultimate decision on publication will rest with its Editor-in-Chief. In cases where guidelines are jointly developed, parallel publication in other journal(s) (in addition to *Diabetologia*) may be considered but will require contractual agreement.

Additionally, the EASD encourages other international and national organisations to endorse its guidelines or translate them into other languages. Moreover, the EASD encourages the adaptation of its guideline recommendations to fit country-specific healthcare settings. However, any such adaptations must adhere to the GRADE-adolopment approach [42] and receive approval from the GOC and the EASD Board. All external translations or adaptations must clearly acknowledge that the original guideline is the work and intellectual property of the EASD. This approach is intended to promote the global dissemination of EASD guidelines while maintaining the authenticity and recognition of the original documents.

Updating guideline documents

The GOC and key representatives from the GDP, such as the GDP chairs and methodologists, will conduct an evaluation of each completed guideline to explore whether new research could substantially affect existing EASD recommendations. In particular, EASD guidelines will be reviewed by the GOC every 3 years after their initial publication to determine whether an update is necessary. The decision to initiate an update will be made by the GOC and, if an update is warranted, the update process will begin with the first meeting of the GDP responsible for the update. However, if compelling evidence likely to alter the recommendations of the original guideline is published prior to the 3 year review, an expedited update may be considered. Updates may involve revising clinical questions, adding or amending outcomes and incorporating subgroup analyses, especially when new research underscores these needs. For updated questions and outcomes, systematic reviews and EtD tables will be revised accordingly. Additionally, all updates will include a summary of significant revisions and a brief description of their rationale compared with the previous version. Moreover, an update may be required only for specific recommendations and not for an entire guideline document. It should be noted that any update will require additional funding, albeit generally less than the funding required for creating the original guideline.

The EASD aspires to evolve its guidelines into 'living documents', with individual recommendations ('living recommendations') updated in real-time, rather than on a 3 year basis, as pertinent new data become available [43]. However, achieving this dynamic approach will necessitate the establishment of additional funding and specialised infrastructures and methodologies. This will involve coordinated efforts between the GDP conducting the living guideline and the ESTs generating living systematic reviews. The availability of a detailed, comprehensive technical report of the evidence synthesis and relevant datasets will significantly facilitate and expedite this transition. Moreover, these resources could also reduce the affiliated budget compared with that needed for a full update of a guideline, making the process more cost-effective. Additional requirements for this approach will include the use or development of tools and platforms that facilitate a living process, a platform that allows publication of updates of individual recommendations (or clusters of recommendations), a continuous peer review system and an associated funding strategy [43].

Cooperation with other associations on guideline documents

The EASD is open to collaborating with other healthcare associations, societies and organisations for the development of joint guideline documents. For any such collaborative effort to proceed, it is essential that the guideline development adheres to the core trustworthiness standards set by the NAM and GIN, as well as meeting the key domains outlined in the AGREE II instrument [1, 2, 16]. Specifically, prerequisites for collaboration include:

- Transparent declaration, evaluation and management of COIs, aligned with the procedures detailed in this SOP. For instance, a substantial proportion of panel members must be free from significant COIs, and those with relevant COIs must recuse themselves from voting on pertinent recommendations.
- The assembly of an expert, multidisciplinary panel that considers clinically relevant subpopulations and outcomes when formulating clinical questions.
- Ensuring that recommendations are informed by a systematic review of existing research, coordinated by methodologists skilled in evidence synthesis and appraisal methodologies.
- A guideline development process that is both explicit and transparent, using the GRADE approach to rate the certainty of evidence and strength of recommendations based on EtD frameworks.
- Ensuring that the completed guideline document undergoes an external peer review process.

For jointly produced guidelines, the allocation of GDP members will be negotiated between the collaborating entities. If diabetes is the primary subject matter, equitable representation from the EASD is mandatory; however, this requirement may be relaxed if diabetes is a secondary focus. The appointment of EASD representatives to a specific GDP will conform to the procedures outlined in this SOP. In joint guidelines, the use of a common glossary is encouraged to ensure consistency in terminology across collaborating organisations, supporting clear communication and shared understanding throughout the guidelines. Such a glossary can facilitate alignment, reduce ambiguities and promote coherent interpretation of key terms [44].

To ensure clarity and a shared understanding, the development of a common MOU document between the EASD and the collaborating organisation is strongly encouraged. The MOU should outline key aspects of the collaboration, as described in relevant guidance [18]:

- Scope and purpose: clearly define the aims of the collaboration and the scope of the guideline.
- Leadership and team: specify the roles, responsibilities and composition of leadership and team members from each organisation.
- Methods and commitment: detail the methodological framework to be used, the resources required and the commitment expected from both organisations.
- Review and endorsement: outline the process for internal and external reviews, including the endorsement process by the respective organisations.
- Publication and dissemination: define the approach for publishing and disseminating the guideline, including considerations for authorship, branding and intellectual property.

Funding for the development of EASD guideline documents

The EASD is the sole financial sponsor for the development of its guideline documents and the associated evidence syntheses, ensuring no industry involvement. The budget covers expenses such as face-to-face meetings involving the GOC, the GDPs and the ESTs, journal publication fees, administration costs, and remuneration for GDP methodologists, lay members of the GDPs (subject to approval by the EASD Board) and commissioned ESTs.

Preparing and updating the SOP document

The present SOP document was initially drafted and amended by the EASD GOC before undergoing unblinded peer review by external experts specialising in evidence synthesis and/or guideline development methodology selected by the GOC. The authors solicited input from six external reviewers, two of whom did not respond; four (SA, GL, EM and FR) provided detailed and valuable feedback, which was received by September 2024 and is available in the electronic supplementary material (ESM) for full transparency, with permission from the reviewers. Feedback was also received from the GDP involved in the first guideline to be developed under this process. After incorporating these expert and practical inputs and making any necessary revisions, the SOP received final approval from the GOC and the EASD Board. The SOP is subject to future revisions, which will be enacted following discussion and an agreement among GOC members. Updates to the SOP are intended to be made publicly available on the EASD website following approval by the EASD Board.

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