Practice Guidelines in Neurorehabilitation

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ABSTRACT

Practice guidelines are scientifically based practice recommendations. They can be consensus-based and provided by a single medical society (S1 guideline) or developed by a group of national medical societies with a structured consensus process (S2k guideline). S2k guidelines are a good opportunity to develop valid practice guidelines with a broad supporting base when health topics are either complex or when clinical evidence is limited. Evidence-based guidelines rest on a systematic search and critical appraisal of the available evidence and represent the highest quality level for guidelines; they can be developed by single medical societies (S2e guideline) or jointly by several national medical societies (S3 guideline). They reflect the state of the art and generate a high degree of confidence that their recommendations support optimal treatment. The German neurorehabilitation society (DGNR) provides evidence-based guidelines for motor rehabilitation after stroke (arm, mobility, spasticity).

Introduction

According to an internationally recognized definition [1], guidelines are systematically developed statements that reflect the current state of knowledge and help physicians and patients decide on appropriate treatment in specific disease situations. Unlike directives, they are not legally binding and must be adapted to the individual case [2]. The development process of medical guidelines should be systematic and transparent. Their main purpose is the give a picture of the state of art of medical care. They offer orientation to physicians, health care workers, therapists, patients as well as relatives and other medical care providers in matters of decision-making and treatment options. While implementing the guidelines, practitioners may use their discretion to a certain extent in each specific case. Equally, patients' preferences must also be included in the decision-making process. The clinician may deviate from the recommendations of the guideline in a specific case if there are plausible reasons for doing this, including the patient's attitude to the treatment. Where health care is provided by statutory social insurance, cost efficiency of the treatment must also be taken into account.

The main importance of the guidelines is to help health care personnel to really understand the newest developments and treat patients accordingly in the context of a steadily growing amount of clinical scientific knowledge. By systematic development of guidelines, specialist societies can make transparent the state of the art information relevant to treatment in various specialist areas of medicine and describe treatment options and recommendations derived from them.

In Germany, the methodology for the development of medical guidelines and their presentation of these in the internet is guaranteed primarily by the Workshop of Scientific Medical Societies (AWMF) (see http://www.awmf.org/leitlinien.html) [3]. Scientific associations such as the German Society of Neurology (DGN) (http://www.dgn.org) and the German Society for Neurorehabilitation (DGNR) (http://www.dgnr.de) are members of the AWMF and use the instruments of the AWMF in their development and presentation of guidelines. This ensures quality control and transparency of the available guidelines.

In the following, considerations on the development of the guidelines in general, and in particular in the field of neurorehabilitation will be discussed in greater detail.

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Guidelines Methodology

According to the system of AWMF [3], guidelines are developed and classified in four development stages from S1 to S3, with S3 having the highest quality level.

- S1: The guideline has been prepared by an expert group by an informal consensus.
- S2k: A formal consensus finding has taken place across medical specialist societies and is the basis for the guideline.
- S2e: Systematic evidence search and appraisal of evidence has taken place and is the basis for the recommendations of the guideline.
- S3: The guideline has gone through all the elements of systematic development, its recommendations are based both on a systematic search of literature and evaluation of evidence as well as on consensus across the board of medical specialist societies.

The methodological quality of an S3 guideline is correspondingly higher than that of an S2 or S1 guideline. The higher the level of the methodological quality, the smaller is the number of guidelines of the AWMF, which is due to the considerable increase in the effort required to compile them, especially for evidence-based S2e and S3 guidelines. At the end of 2016, the AWMF Guidance Register comprised 417 S1 guidelines, 215 S2 guidelines, and 139 S3 guidelines.

S1 guidelines

The S1 class of guidelines is a recommendation for action by experts. Because they lack a systematic development process, they are not regarded as guidelines in the narrower sense [1]. However, the rules of the AWMF editorial independence ensure that there is disclosure of conflicts of interest as well as adoption by the participating societies and organizations [3].

In the area of neurorehabilitation, their importance lies in health care aspects for which no broad base of evidence from clinical trials can be expected, and in making transparent experience-based knowledge for use in clinical practice, agreed upon by the specialist medical societies involved. S1 guidelines can also be seen as a first step in the development of guidelines in the narrower sense when it is a matter of initiating coordination and standardization processes within a specialist medical society.

S2k guidelines

S2k guidelines are developed in a structured consensus process. Representatives of all relevant addressees and the target group of patients for whom the guidelines are being developed participate in the guideline development process. This is to ensure that different perspectives are taken into consideration. The S2k guideline is interdisciplinary, and the guideline panel should be representative in this sense. The consensus-finding process should also meet high quality standards. The aim is the clinical assessment of the meaningfulness and applicability of the evidence, weighing up of benefits and harm, comparing them with alternative approaches, clarifying different points of view, and taking into account the preferences of patients in a formal consensus procedure (e. g., nominal group process, Delphi technique). The use of formal procedures serves to avoid distortions of the recommendations by processes of group dynamics and particular interest groups. At the end of the assessment process, a recommendation is adopted, its strength given a grade, the strength of the consensus is determined, all of which give an idea as to the legitimacy of the recommendation for implementing in clinical practice [4].

S2k guidelines are suitable for use in many treatment areas. Since all the relevant medical specialist societies participate in the deliberations and the patient perspective is also taken into account, there is assurance that the recommendations have a broad base. By incorporating different perspectives, the validity, as well as the later acceptance and implementation of the guidelines can be strengthened, especially in a field like neurorehabilitation, which involves several professional groups, both physicians, nurses and therapists. Subjects without a broad evidence base from high-quality clinical trials as well as highly complex subjects for which it is difficult to provide a systematic evidence base can be dealt with well with S2k guidelines. Thus, they often represent a very good compromise between the effort invested in the development of the guidelines and the clinical benefit achieved.

S2e and S3 guidelines

The aim of the S2e and S3 guidelines development is to formulate recommendations for clinical practice based a comprehensive, systematic search for and a critical assessment of the available evidence.

S2e guidelines are developed within a medical specialist society, and S3 guidelines are interdisciplinary according to the consensus methodology of the S2k guidelines (in addition to the systematic evidence-based approach).

It is important to bear in mind that the recommendations of a guideline can only be as valid as the knowledge on which it is based. Only a systematic search for and critical appraisal of evidence allows the formulation of recommendations that demonstrably represent the state of art of the knowledge base. Systematic search and assessment of literature makes, on the one hand, the development of S2e and S3 guidelines very complex. On the other hand, S2e and S3 guidelines are of the highest scientific quality. Users of the guideline can have high confidence in the reliability of the recommendations if the methodology of the guideline development is validly applied. In order to make the task manageable, it is advisable to clearly define and delimit the issue dealt with in the S2e and S3 guideline.

In order to ensure that the critical appraisal of evidence and the process of summarizing are structured and transparent, the DGNR has chosen a standardized procedure for the development of S2e and S3 guidelines, which is outlined below [5]. This is intended to enable the reader to understand the various assessment steps and classifications underlying the evidence-based recommendations.

Reports of clinical trials are considered as original papers. Systematic reviews are overviews that systematically search for and incorporate all available clinical trials according to their clearly stated study goals, evaluate the methodology of the studies and, across studies, answer the questions raised in the systematic review. Meta-analysis is the process of subjecting the data of several studies to common statistical analysis.

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▶ **Table 1** Gradation of evidence, recommendation and consensus strength in guidelines as an expression of the degree of certainty/uncertainty of the knowledge base for the respective recommendations [according to 2].

Quality of Evidence	Study base	Symbols
High	High-quality systematic reviews (with or without meta-analysis) of randomized controlled clinical trials (RCT)	1a
	RCTs with very low distortion risk and high precision of the effect estimator (narrow confidence intervals)	1b
Moderate	High-quality systematic reviews of cohort studies	2a
	Cohort studies with very little distortion risk	2b
Low	Case control studies	3
Very low	Case series, Case reports	4
Recommendation grade	**Formulation**	
Strong recommendation	ought to/ought not to	A
Recommendation	should/should not	B
Open recommendation	can be considered	0
Consensus strength	**Poll results of the guideline committee**	
Strong consensus	In favor: > 95% of participants	
Consensus	In favor: > 75–95 % of participants	
Majority agreement	In favor: > 50–75 % of participants	
No consensus	In favor: < 50 % of participants	

The following are the steps taken from assessment of evidence to formulation of recommendation (compare Table 1 for further explanation):

(I) For each source (original papers, systematic reviews and meta-analyses)

(1) evaluation of the methodology (the validity)

(2) classification of evidence level of each source (1a to 5 according to the "Oxford Center for Evidence-Based Medicine - Levels of Evidence", last version from March 2009, http://www.cebm.net/Oxford-centre-evidence-based-medicine):levels-evidence, March-2009 /)

(3) summarizing the conclusions of the results, and deriving recommendations from the individual sources

(II) For summarizing data from all sources on a specific issue (for example, therapy method) (original papers, systematic reviews and meta-analyses)

(4) summarized assessment (quality of evidence) of the sources included in the sense of the resulting confidence in the estimation of the effect strength (of a therapy) and

(5) grading of the derived recommendation.

The quality of evidence for a particular question or a target parameter of a guideline is grouped into 4 categories according to the "GRADE" system ("Grades of Recommendation, Assessment, Development and Evaluation, GRADE", www.gradeworkinggroup.org) [6]:

- High quality – further research is unlikely to affect our confidence in the estimation of the (therapeutic) effect or prognosis.
- Medium quality – further research is likely to affect our confidence in the estimation of the (therapeutic) effect or prognosis and may alter the estimate.
- Low quality – further research will most likely influence our confidence in the estimation of the (therapeutic) effect or prognosis and will probably change the estimate.
- Very low quality – any estimation of the (therapy) effect or prognosis is very uncertain.

The evaluation of "quality" in this sense (GRADE) is intended to make it clear how stable the data situation for a particular therapeutic option is. High-quality meta-analyses enable very reliable assessment of effect strength of therapies across several randomized controlled trials with high patient numbers and low variability results and furthermore, one can assume that additional studies are unlikely to the change this assessment. At the other end of the evaluation spectrum, there are situations in which, e. g., no controlled studies are available, which allow the therapy effect to be assessed with a certain degree of certainty; here one can assume a "very low quality" of evidence.

Only if the entire data situation based on clinical studies, systematic reviews and meta-analyses is known and has been critically appraised, can one assess "quality" in this context. The final assessment of quality in this sense is essential for clinical decision and thus the formulation of a recommendation.

The recommendation for or against a particular intervention/target criterion is determined only after ascertaining the above-mentioned summary evidence on a specific issue.

The methodology then envisages the allocation of degrees of recommendation by the members of the Guidelines Group through a formal consensus procedure. In addition to the GRADE criteria, additional criteria for the clinical assessment of the applicability and transferability of the evidence are explicitly specified [7]:

- benefit-risk assessment
- effect size of study results
- clinical relevance (suitability of the efficacy measures of the study for the care, adequacy of the control groups and dosages used)
- pathophysiological and clinical plausibility

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- the feasibility of the guideline implementation in therapeutic routine (including resource requirements and utilization etc., structural quality not yet available)
- ethical obligations (necessity of action)

The grading of the recommendations of the guidelines corresponds to the categories "ought to" (A), "should" (B) or "can" (0).

Guidelines of the DGNR

In the last few years, the DGNR had focused in particular on the preparation of S2e guidelines (see also http://www.dgnr.de/Leitlinien-Evidenztabellen.29858.html). It is in this way that the S2e guidelines for motor rehabilitation of the arm after stroke [among others- [8], rehabilitation of mobility after stroke (ReMoS) [9], and the treatment of spasticity after stroke [10] were developed. Worldwide, these systematic evidence-based guidelines for motor rehabilitation after stroke have a unique position. They show, for example, that there is no lack of evidence regarding neurorehabilitation. The therapeutic aspects of arm rehabilitation guidelines alone included the results of 106 randomized controlled trials as well as 12 systematic reviews. A revision of this guideline is currently being prepared as an S3 guideline. For this purpose, 299 publications of randomized controlled studies have been evaluated and about 100 systematic reviews are available for evaluation. The ReMoS guideline makes a reference to 272 published reports and the spasticity guideline to 111.

There is therefore no lack of evidence, at least in some areas of neurorehabilitation. On the contrary, on some questions, there are so many extensive clinical studies that one can justifiably ask if, without a systematic evidence-based approach, healthcare is being or can be offered in keeping with the current state of knowledge. Anyone involved in neurorehabilitation is unable to keep pace with the extensive and rapidly expanding evidence for all treatment measures and to ensure their immediate implementation in clinical practice. Each study requires a standardized critical appraisal. The results of studies that address a question must be summarized in the sense of a creating a synthesis of the best available evidence. On the basis of knowledge of the entire evidence base, valid recommendations for clinical practice can then be derived and, according to the state of the art, the decision for the optimal therapy can be made.

Evidence-based S2e and future S3 guidelines of the DGNR ensure that systematically developed recommendations such as guidelines on motor rehabilitation after stroke for use in neurorehabilitation, an expanding field with high clinical impact, demonstrably reflect the current state of knowledge and make it easy for the physicians and therapists as well as their patients to make decisions on goal-oriented and effective treatment.

This can be achieved by limiting the individual guideline to a circumscribed subject area, namely just one syndrome (e. g., paralysis of the arm) and a disease entity (e. g., stroke). Even linking motor rehabilitation of the arm and mobility after stroke, let alone rehabilitation covering these aspects for different disease, would implement an S2e or S3 guideline, which can neither be worked out from a manageable group of guideline developers, nor would it have a format that would be well understood by the reader because of the abundance and complexity of the information.

Accordingly, it may be useful to supplement the more focused S2e and S3 guidelines with overview guidelines such as the S2k guideline "Rehabilitation of sensory motor disorders" of the DGN (AWMF register number: 030/123; http://www.awmf.org/Guidelines/detail/ll/030-123.html), which focuses on arm motion and mobility in patients with brain damage, as in (but not limited to) stroke. More global guidelines, such as the S3 guideline "Stroke" of the German Society for General Medicine and Family Medicine (DEGAM) (AWMF Register number: 053/011, http://www.awmf.org/uploads/tx_szleitlinien/053-011l_S3_Schlaganfall_2012-expired.pdf), have an even broader focus, as they address rehabilitation issues only in a very condesed form.

This means that there are, on the one hand, guidelines that are more focused and, possibly of higher quality, which are useful when differentiated recommendations are needed, and, on the other, there are also guidelines that are thematically broader that provide an overview of the recommendations given. It is important that the validity of the broader guidelines is not lower than that of the more focused evidence-based recommendations. This can be achieved, in particular, if members of the group involved in the development of the more focused evidence-based guidelines participate in the development and support the formulation of the thematically broader guidelines, thus ensuring that a recommendation across all guidelines has the same high quality.

There are also many topics of neurorehabilitation, for which there is no broad evidence base. Here, it is desirable to work out good clinical practice according to current evidence and clinical experience in consensus with the participating medical societies in order to provide as valid recommendations as possible for clinical practice. A positive example of this approach is the recently completed S2k guideline "Prolonged Weaning in Neurological Neurosurgical Early Rehabilitation" of the DGNR (as the lead Society) (AWMF register number: 080/002, http://www.awmf.Org/guidelines/detail/registration/1/ll/080-002.html). Prolonged weaning of patients with neurological disorders has its own specific features; these should be addressed in a separate set of guidelines which supplement the current S2k guideline of the German Society for Pneumology and Respiratory Medicine (DGP) (AWMF register number: 020/015, http://www.awmf.org/uploads /tx_szleitlinien/020-015l_S2k_Prolonged_Weaning_2014_01_verlaengert.pdf). In particular, special attention is to be given to patients with central disturbances of respiratory regulation (e. g., brain stem lesions), swallowing (neurogenic dysphagia), neuromuscular problems (e. g., critical illness neuropathy, Guillain-Barre syndrome, paraplegia, myasthenia gravis) or cognitive disorders (e. g., consciousness and vigilance disorders, severe communication disorders), whose care during the weaning of ventilation requires, in addition to competence in intensive medical care, neurological or neurosurgical and neurorehabilitation expertise.

Conclusions for Practice

Guidelines are scientifically based, practice-oriented recommendations for action. Their main purpose is to give a picture of the state of the art medical care. They give orientation to physicians, health care workers, therapists, patients as well as their relatives

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and other medical care providers in terms of decision-making and treatment options.

For some areas in neurorehabilitation, there is extensive clinical evidence from clinical trials. Systematic collation of data, their critical appraisal, formulation and consensus-supported evidence-based practice recommendations place high demands on the development of the guidelines. For the users, however, they represent a guarantee that, with respect to the clinical problems they address, by orienting to the guideline (S2e or S3 level), they make the clinically best and effective treatment choice, demonstrably in keeping with the state of the art knowledge.

The evidence-based guidelines of the DGNR are of high quality and currently are available in the areas of arm rehabilitation, rehabilitation of mobility and treatment of spasticity after stroke.

For other subjects for which there is no broad evidence base, it is recommended that standards of good clinical practice according to available evidence and clinical experience in consensus with the participating specialist groups are developed in order to provide as reliable recommendations as possible for use in the clinical practice (S2k level). An example of this is the S2k guideline "Prolonged Weaning in the Neurological-Neurosurgical Early Rehabilitation" of the DGNR, the Society that plays a leading role in the area of neurological rehabilitation.

Acknowledgements

Conflict of interest

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