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SPECIAL ARTICLE

Guidance for the preparation of neurological management guidelines by EFNS scientific task forces – revised recommendations 2004*

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Since the publication of the first EFNS task force reports in 1997, a total of 20 evidence-based guidelines for the treatment and management of neurological diseases have been published by the EFNS (www.efns.org/guidelines). In 2001, recommendations for the preparation of neurological guidelines were issued by the EFNS Scientific Committee (Eur J Neurol 2001; 8: 549–550). These have now been updated and revised. More unified criteria for standards of reporting are set up which include classes of scientific evidence and predefined levels of recommendation. These criteria as well as others listed below should be used for all working groups that aim at recommending treatment, diagnostic procedures or other interventions within the framework of the EFNS.

Neurological treatment guidelines/ management recommendations on a European scale – by EFNS

Neurological diseases and disability are a primary concern worldwide. In a global survey, it was found that of the leading 10 disabling diseases, eight were caused by diseases of the brain (Üstün *et al*., 1999). In Europe, brain diseases cause a loss of 23% of the years of healthy life and 50% of years lived with disability. Thus 35% of the total burden of disability-adjusted life years is caused by brain diseases alone (Olesen and Leonardi, 2003). In Europe, both mortality and morbidity due to neurological causes are increasing and the health expenditure for this burden is also growing rapidly. In contrast, part of the cost is due to treatments that have become established without scientific evidence. Although the situation varies from country to country, this is the case not only for many treatments for common diseases such as stroke, migraine and other headaches, parkinsonism and epilepsy, but also for other conditions including many segments of neurological prevention and neurorehabilitation.

The European Federation of Neurological Societies (EFNS) has recognized the demands for the development of European standards for the management and treatment of neurological diseases and has – since 1997 – published some 20 such guidelines. They have been distributed widely on the web and as printed material. Several of them have been translated into other European languages for use of national neurological societies. The task force applications and practice recommendations published within the framework of the EFNS (www.efns.org) have increased and therefore underwent a critical review. To meet the needs of future task forces preparing guidelines, more specific instructions than the previous guidance (Hughes *et al*., 2001) seemed necessary and this paper responds to that need.

Aim of guidelines

The aim of an EFNS neurological management guideline is to provide evidence-based guidance for clinical neurologists, other health care professionals and health care providers about important aspects of management of neurological disease. It provides the view of an expert task force appointed by the Scientific Committee of the EFNS. It represents a peer-reviewed statement of minimum desirable standards for the guidance of practice based on the best available evidence. It is not intended to have legally binding implications in individual cases.

Scientific basis of guidelines

The increasing burden of neurological diseases and disability can only be met by implementing measures of prevention and treatment that are scientifically proven

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and based upon evidence-based criteria. Sets of treatment recommendations and management guidelines have been prepared by the EFNS and similarly by the American Academy of Neurology (AAN), Quality Standards Subcommittee (1999). The critical standards used in both organizations aim to:

- Evaluate the scientific evidence according to prespecified levels of certainty;
- Grade the recommendations according to the strength of available scientific evidence.

This Subcommittee of the EFNS recommends the use of such classes of evidence and grades of recommendations in the way developed by the AAN. They have been applied for a therapeutic measure (Hirtz *et al.*, 2003) and a diagnostic measure (Shevell *et al.*, 2003) within the AAN practice guidelines groups. The definitions and requirements for the classes of evidence and levels of recommendations from the AAN have been adapted and slightly modified and are listed in Tables 1 and 2.

Some of the issues under discussion include the question of classifying secondary endpoints from large, randomized, controlled trials as either first or second class evidence. The Subcommittee members agree that these secondary endpoints should usually not have the same scientific weight as the primary ones. This becomes relevant when the primary and secondary endpoints are both positive (or negative), implying that they both bear statistically significant results in favour of (or contrary to) the intervention under investigation. To name but one example: many intervention trials with cardiovascular endpoints (e.g. myocardial infarction) also have a secondary neurological endpoint (e.g. stroke). Assuming that both are positive, this does not imply that the treatment is effective for both cardiac and cerebral endpoints with equal scientific certainty, because the inclusion parameters, endpoint definitions and the diagnostic work-up regularly differ in precision and in absolute numbers of cases for both endpoints and usually heavily favour the primary one. These issues have not been handled uniformly in the past and therefore these new, extended guidelines have been revised.

One other issue to be discussed within the framework of each task force when evaluating scientific evidence refers to important clinical areas for which no high class evidence is available or likely to become available in the near future. In such cases – which should be marked as exceptional – it may be possible to recommend best practice based on the experience of the guideline development group. An example of such an important area is the problem of recommendations for driving after stroke where it is not easily conceivable to gather a large body of randomized evidence. Such 'good practice points' have been used by the Scottish Intercollegiate Guidelines Network (SIGN) and make the recommendations more useful for health workers (SIGN, 2002). But such 'good practice points' should not imply that they are based on more than class IV evidence which implies large clinical uncertainty. No impression is intended that a randomized trial to test the intervention can be avoided by assigning such points to a specific recommendation.

Critical review of guidelines

Current methods of developing guidelines have improved from the informal consensus (TOBSAT = the old boys sat at a table; see Grilli *et al.*, 2000) and adapted to formal consensus methods, which use a systematic approach to assess the experts' opinion and

Table 1 Evidence classification scheme for a therapeutic intervention

Class I: An adequately powered prospective, randomized, controlled clinical trial with masked outcome assessment in a representative population or an adequately powered systematic review of prospective randomized controlled clinical trials with masked outcome assessment in representative populations. The following are required:

(a) randomization concealment

(b) primary outcome(s) is/are clearly defined

(c) exclusion/inclusion criteria are clearly defined

(d) adequate accounting for dropouts and crossovers with numbers sufficiently low to have minimal potential for bias

(e) relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences

Class II: Prospective matched-group cohort study in a representative population with masked outcome assessment that meets a–e above *or* a randomized, controlled trial in a representative population that lacks one criteria a–e

Class III: All other controlled trials (including well-defined natural history controls or patients serving as own controls) in a representative population, where outcome assessment is independent of patient treatment

Class IV: Evidence from uncontrolled studies, case series, case reports, or expert opinion

Rating of recommendations

Level A rating (established as effective, ineffective, or harmful) requires at least one convincing class I study or at least two consistent, convincing class II studies

Level B rating (probably effective, ineffective, or harmful) requires at least one convincing class II study or overwhelming class III evidence

Level C (possibly effective, ineffective, or harmful) rating requires at least two convincing class III studies

Table 2 Evidence classification scheme for a diagnostic measure

Class I: A prospective study in a broad spectrum of persons with the suspected condition, using a 'gold standard' for case definition, where the test is applied in a blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy
Class II: A prospective study of a narrow spectrum of persons with the suspected condition, or a well-designed retrospective study of a broad spectrum of persons with an established condition (by 'gold standard') compared to a broad spectrum of controls, where test is applied in a blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy
Class III: Evidence provided by a retrospective study where either persons with the established condition or controls are of a narrow spectrum, and where test is applied in a blinded evaluation
Class IV: Any design where test is not applied in blinded evaluation OR evidence provided by expert opinion alone or in descriptive case series (without controls)
Rating of recommendations
Level A rating (established as useful/predictive or not useful/predictive) requires at least one convincing class I study or at least two consistent, convincing class II studies
Level B rating (established as probably useful/predictive or not useful/predictive) requires at least one convincing class II study or overwhelming class III evidence
Level C rating (established as possibly useful/predictive or not useful/predictive) requires at least two convincing class III studies

reach an agreement on recommendation. The evidence-based consensus links its work directly to scientific evidence (Shaneyfelt *et al*., 1999). According to the AAN, the strength of the 'guideline development process aims at the evidence-based category, with little use for expert opinion' in order to reduce the likelihood of severe bias when relying on informal consensus alone (Franklin and Zahn, 2002). Consequently, guideline development has also been subjected to systematic evaluation. Following a systematic search, practice guidelines published in peer-reviewed medical literature between 1985 and 1997 were assessed with a 25-item measurement instrument which included the use of levels of evidence. From 279 guidelines investigated, the mean overall adherence to such levels of evidence was 43% but improved significantly between 1985 and 1997 (36.9% versus 50.4%; $P < 0.001$) (Shaneyfelt *et al*., 1999). Grilli *et al*. (2000) found similar discrepancies when investigating 431 guidelines between 1988 and 1998. The authors suggest the development of common standards of reporting, similar to the CONSORT statement for reporting the results of clinical trials (Moher *et al*., 2001). A more recent review of guidelines for stroke prevention has shown that there are notable differences on information about panel selection, funding source, and consensus methods. Thus it concludes that current stroke prevention guidelines do not provide adequate information to permit assessment of their quality (Hart and Bailey, 2002).

Guideline recommendations should also include the description of methods used for synthesizing individual judgements. The development of the consensus reached is important but minority statements should also be included when necessary (Black *et al*., 1999). All critical reviews are recommended to make use of a systematic and formal procedure of establishing guidelines. One recent and major effort was published by a Conference on Guideline Standardization (COGS) that produced a checklist to be used prospectively by developers to enable standardized recommendations (Shiffman *et al*., 2003). This was achieved by means of a reiterative method (mostly several rounds of balloting by panel experts who gave differing weights to different pieces of scientific evidence). This method has reproducible results and is less likely to be biased by individual opinion. It involves stricter definitions for collecting and synthesizing evidence about potential harms, benefits and patients' preferences, and more effective considerations for implementation. Unfortunately, this COGS method would be very laborious. The EFNS guidance proposed here captures the most important elements of the COGS proposals.

In addition to management guidelines, appropriate methods are needed to develop expert consensus on the process of care. Examples include the timely referral for diagnostic procedures (e.g. nerve conduction velocity testing in carpal tunnel syndrome) and measures to improve patient satisfaction (Franklin and Zahn, 2002). Such process-related guidelines must take patient preferences into account and are no less important than treatment guidelines. Finally, there is evidence that adherence to guidelines improves patient outcome. This has been shown, e.g. for post-acute rehabilitation following stroke indicating that such guidelines can also be used as quality of care indicators (Duncan *et al*., 2002).

As a result of these quality issues, the goals and the process of the task force work are described in more detail below. These will be reviewed every 4 years and updated if necessary by the Subcommittee.

Collection of scientific data

1 The Cochrane Library, should be consulted by every person or group planning to develop a guideline. For many therapeutic options, there is little randomized evidence and non-randomized studies also have to be

considered. Authors of treatment guidelines should liaise with the coordinating editors of the appropriate Cochrane review group and review the list of registered titles of the Cochrane systematic reviews which have not yet been converted into protocols (www.cochrane.no/titles). The EFNS and the AAN have agreed to share their list of practice parameters or management guidelines under preparation.

2 Collection of data from original scientific papers in referee-based scientific journals are the cornerstone for evaluation of scientific evidence. Such papers can be identified from several bibliographic databases. It is important to use specific and sensitive keywords as well as combinations of keywords. One keyword is rarely sufficient. Both older and new scientific papers should be included. It is always necessary to collect the data from the paper itself, not from secondary literature. The full paper should always be read, not only the abstract. Data can be included from papers which have been accepted but not yet published, but not usually before acceptance. In accordance with the Cochrane Library, unpublished data from randomized trials can be used provided they are of high quality. Such exceptions should be explained in the synthesizing evidence section of the report.

3 Collection of papers containing any previous meta-analyses of the same or similar topics should always be undertaken. Such papers are always helpful, but they usually do not give the full and final conclusion for a task force.

4 Collection of review/overview papers is done from the same bibliographic databases. Such reviews are usually well known by the experts in the field, and may be included in the work of the task force. The conclusions of such papers should never be used without independently evaluating the scientific evidence of the papers from the original data.

5 Scientific data from papers published in refereed journals not included in the main databases may be included. As such papers are more difficult to identify, it is not a prerequisite for a task force to collect them.

6 Scientific data from non-refereed journals, books or other publications should usually not influence recommendations and conclusions. They are therefore not important to collect.

7 Previous guideline documents and recommendations should be sought from MEDLINE, EMBASE and other sources including national and international neurology organizations, patient organizations, and national or supranational health-related bodies. Although task force conclusions should rely on quality-assured scientific data alone, it is appropriate to discuss previous guidelines and recommendations (which may be registered by the International Network of Agencies for Health Technology Assessment, www.inahta.org).

Recommendations for the process of proposing, planning and writing a guideline†

1 Neurological Management Guidelines will be produced by Task Forces appointed by the Scientific Committee.

2 Proposals for Task Forces concerning neurological management should be submitted to the Scientific Committee. The proposal should include the title, objectives, membership, conflict of interests, short (100–300 words) explanation of why the guideline is needed, already existing guidelines on same or related topic, search strategy, method for reaching consensus, and time frame for accomplishment. Task Forces will usually be appointed following a proposal from the chairperson of a Scientific Panel to the Scientific Committee.

3 The Task Force will consist of a chairperson and at least six but not usually more than 12 members. No more than two members should usually come from any one country. Conflicts of interest must be declared by members at the time of the formation of the Task Force. The chairperson should be free from conflicts of interest. If feasible, the group should include a patient advocate (normally an officer from a European patient organization if the Task Force deals with a clinically relevant topic) and other relevant specialists (such as a statistician) and health professionals. If Task Forces have a budget, they must nominate a secretary and treasurer and submit an annual account to the Management Committee.

4 The Task Force will review the available evidence and include within its report the search strategy employed. Where appropriate, the evidence concerning health care interventions must be based on a thorough systematic literature search and review. The report should include a structured summary that contains the main conclusions. Irreconcilable differences between group members should be referred to the Scientific Committee through its chairman.

5 Existing guidelines prepared by other organizations (including European neurology subspeciality societies, European national neurological societies, non-European neurological societies, and other organizations) will be sought and where appropriate adopted in part or whole with appropriate acknowledgement and respect for copyright rules.

6 The format of the guidelines will use the style of the *European Journal of Neurology* and follow a template with these sections:

†This guidance was approved by the EFNS Scientific Committee.

(1) Title. *This should read:* EFNS Guideline on ……Report of an EFNS Task Force on …… (title of Task Force, if different from the topic of the guideline);
(2) Structured abstract;
(3) Membership of task force;
(4) Objectives;
(5) Background;
(6) Search strategy;
(7) Method for reaching consensus;
(8) Results;
(9) Recommendations;
(10) Statement of the likely time when the guidelines will need to be updated;
(11) Conflicts of interest;
(12) References.

7 The length of the guideline report should not be more than eight printed pages including references (4000 words). Supplementary material may be published on the EFNS website. The authors will be the EFNS Task Force on *management/diagnosis/other of condition*. The authors will be listed as Members of the Task Force with the chairman first and the other authors in alphabetical order.

8 The task force should submit the completed guideline for approval to the chairperson of the Scientific Committee.

9 The Scientific Committee will have the proposed management guideline reviewed by its members, the president of the EFNS and the chairpersons of any Scientist Panels which might be affected by the guidelines but where not involved in the preparation of them. Additional external peer reviewing may be sought especially in areas where few neurological experts are available. Within eight weeks of submission, the chairperson of the Scientific Committee will advise the chairperson of the Task Force whether the guidelines have been accepted as the official guidelines of the EFNS or not. If revision is needed, the Task Force will prepare a revised version and submit this to the review process again, highlighting the revisions and documenting the responses to each of the referees' comments.

10 Following approval, the management guidelines will be submitted by the chairperson of the Task Force to the editor/s of the *European Journal of Neurology* with a view to publication. The editor will have the power to accept or reject the guidelines for publication and may make minor editorial changes.

11 The validity of published guidelines will be reviewed by the chairpersons of the Task Force and the relevant Scientist Panel at least every 2 years.

12 Guidelines will be published on the EFNS web and in the *European Journal of Neurology*.

13 National societies will be encouraged to translate guidelines for dissemination in their own countries.

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