



Interdisziplinäres Stoffwechsel-Centrum: Endokrinologie, Diabetes und Stoffwechsel - Kompetenzzentrum Seltene Stoffwechselkrankheiten, Charité,



European
Reference
Network

for rare or low prevalence
complex diseases

Network
Hereditary Metabolic
Disorders (MetabERN)

Center of Excellence for Rare Metabolic Diseases in Adults

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Guidelines within the framework of ERNs

Definition

Guideline

Target group

Set-up

Quality

Guidelines in Rare Diseases

Definition - What is a guideline?

Health care guidelines are

- **systematically** developed statements by
- a **systematic review** of evidence and
- an assessment of the benefits and harms of alternative care options

which assist **target groups** to make

- informed decisions about **appropriate health care** for specific circumstances
- Health care guidelines provide **recommendations** that describe in detail what the recommended action is and under what circumstances it should be performed



Plates 6/7 of the Edwin Smith Papyrus (~17th century BC), among the earliest medical guidelines

www.rarebestpractices.eu/pagine-23-glossary



Definition - Guideline

Additional objectives

- Standardization of care,
- Quality of care ↑
- Risk ↓ (patient, healthcare provider)
- balance cost and medical parameters (i.e. effectiveness, specificity, sensitivity, etc.)

Please note:

GL may have legal consequences



https://en.wikipedia.org/wiki/Medical_guideline
<http://presse.beck.de/beckextra-das-magazin/justitia-fakten.aspx>



Please be aware

Health care guidelines are NOT

- Consensus Statements
- Reviews
- **Clinical Pathway Recommendations/
Clinical Practice Guidelines**

www.rarebestpractices.eu/pagine-23-glossary





defining **Target Groups** (stakeholders) for guidelines -1-

Medical community

(Basic researcher)
(Clinical scientist)



Clinically active physician
General practitioner
Internal medicine
Neurologist
Surgeon etc.



Health personal
Nurse
Dietitian
Physical therapist etc.



defining **Target Groups** (stakeholders) for guidelines -2-

Medical administration

Insurance companies
Governmental/Hospital administration



 **Patient**

Patient support groups
Individual patient
Patient's family



https://www.123rf.com/stock-photo/public_administration.html?sti=m9bumzv1wr912zcdog|&mediapopup=56446025

<https://s4sbxng1g31g0qgc3q2ogrh0-wpengine.netdna-ssl.com/wp-content/uploads/support-hands-small-1024x565.jpg>



Why is it important to define a Target Groups?

Issues not influenced:

Methodology/

Historical and pathophysiological issues

Topics dependent on target groups

Focus

Medical community Diagnosis, therapy, follow-up

Non-medical com. Supportive therapy
Administration Social needs

Administration

Epidemiology
Cost / Infrastructure
Documentation



Language

Medical community
Administration
Patients





Methodology -1- Standards

National/European/International Standards

NICE (UK)
AWMF (Germany)
Council of Europe

Initiation and Responsibility

Medical Scientific Societies
Governmental bodies

providing information via national clearinghouses
(USA: National GL Clearinghouse, UK: NICE Nat. Institute for Health and Care Excellence, Germany: German Agency for Quality in Medicine)

Council of Europe. Developing a methodology for drawing up guidelines on best medical practice. Recommendation Rec(2001)13 and explanatory memorandum. Strasbourg: Council of Europe Publishing, 2002.



Methodology -2- Development

General Methodology

Delphi Process

Re-iterated process of manuscript development deals with



specific topic
quality of sources
conflict of interests

Transparency

Stakeholders involved

Financial support

Target groups

Sources and the quality of sources

<http://www.mspguide.org/tool/delphi>





Methodology -3- Quality

Quality of Sources

Reviews

Consensus statements

Primary data

(Clinical trials

Basic research)

AGREE

GRADING

APPRAISAL OF GUIDELINES
FOR RESEARCH & EVALUATION **II**



AGREE II

INSTRUMENT

The AGREE Next Steps Consortium
May 2009

Grading quality of evidence and strength of recommendations

Grades of Recommendation, Assessment, Development, and Evaluation (GRADE) Working Group

Clinical guidelines are only as good as the evidence and judgments they are based on. The GRADE approach aims to make it easier for users to assess the judgments behind recommendations

Healthcare workers using clinical practice guidelines and other recommendations need to know how much confidence they can place in the recommendations. Systematic and explicit methods of making judgments can reduce errors and improve communication. We have developed a system for grading the quality of evidence and the strength of recommendations that can be applied across a wide range of interventions and contexts. In this article we present a summary of our approach from the perspective of users of guidelines.



What makes a good guideline?

Judgments about evidence and recommendations are complex. Consider, for example, the choice between

"Development and validation of an international appraisal instrument for assessing the quality of clinical practice guidelines: the AGREE project". Qual of Health Care. **12**: 18–23. PMC 1743672 . PMID 12571340.

Council of Europe. Developing a methodology for drawing up guidelines on best medical practice. Recommendation Rec(2001)13 and explanatory memorandum. Strasbourg: Council of Europe Publishing, 2002.





Definition - Guideline - Example

Circulation

HOME ABOUT THIS JOURNAL ALL ISSUES SUBJECTS BROWSE FEATURES RESOURCES AHA JOURNALS

AHA GUIDELINE

Prevention of Infective Endocarditis

Guidelines From the American Heart Association: A Guideline From the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee, Council on Cardiovascular Disease in the Young, and the Council on Clinical Cardiology, Council on Cardiovascular Surgery and Anesthesia, and the Quality of Care and Outcomes Research Interdisciplinary Working Group

Walter Wilson, Kathryn A. Taubert, Michael Gewitz, Peter B. Lockhart, Larry M. Baddour, Matthew Levison, Ann Bolger, Christopher H. Cabell, Masato Takahashi, Robert S. Baltimore, Jane W. Newburger, Brian L. Strom, Lloyd Y. Tani, Michael Gerber, Robert O. Bonow, Thomas Pallasch, Stanford T. Shulman, Anne H. Rowley, Jane C. Burns, Patricia Ferrieri, Timothy Gardner, David Goff, David T. Durack,

The Council on Scientific Affairs of the American Dental Association has approved the guideline as it relates to dentistry. In addition, this guideline has been endorsed by the American Academy of Pediatric Dentistry.

[Download PDF](#) <https://doi.org/10.1161/CIRCULATIONAHA.106.183095>
Circulation. 2007;116:1736-1754
Originally published October 8, 2007

18 pages

Including: History, methodology, pathogenesis etc

Nine pages to read before finding the first recommendation on what to do

- Article
 - Abstract
 - History of AHA Statements on Prevention of IE
 - Rationale for Revising the 1997 Document
 - Potential Consequences of Substantive Changes in Recommendations
 - Pathogenesis of IE
 - Rationale for or Against Prophylaxis of IE
 - Cardiac Conditions and Endocarditis
 - Antibiotic Regimens
 - Specific Situations and Circumstances
 - Other Considerations
 - Future Considerations
 - Acknowledgments
 - Footnotes
 - References
- Figures & Tables
- Supplemental Materials
- Info & Metrics

<http://circ.ahajournals.org/content/116/15/1736.long#sec-30>





Conclusion 1

Guidelines could and should be
a reliable source of in-depth information
delivering systematic evidence for specific target groups and
health care problems

Characterized by **transparency** on
target groups
authors/initiators/stakeholders
finances
quality of sources
methodology



Conclusion 2

Setting up Guidelines is

Time consuming

Costly

10-20 medical specialists

Timeline rarely < 1 year

Time increases with the number of stakeholders

Problems with Rare Diseases

~ 7000 rare diseases

Probably more than there are specialists on rare diseases

Evidence may be lacking (*remember GL are to be set up within the framework of evidence-based medicine*)

Each GL has to consider SPECIFIC TOPICS related

children

adults

emergencies

pregnancies

As well as the different target groups



Conclusion 3



Guidelines rarely provide easy, formalized access, providing

- short, distinct information on how to proceed
- schedules that can be used without further ado



Clinical Pathway Recommendations

TIME is of essence



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Thank you for listening



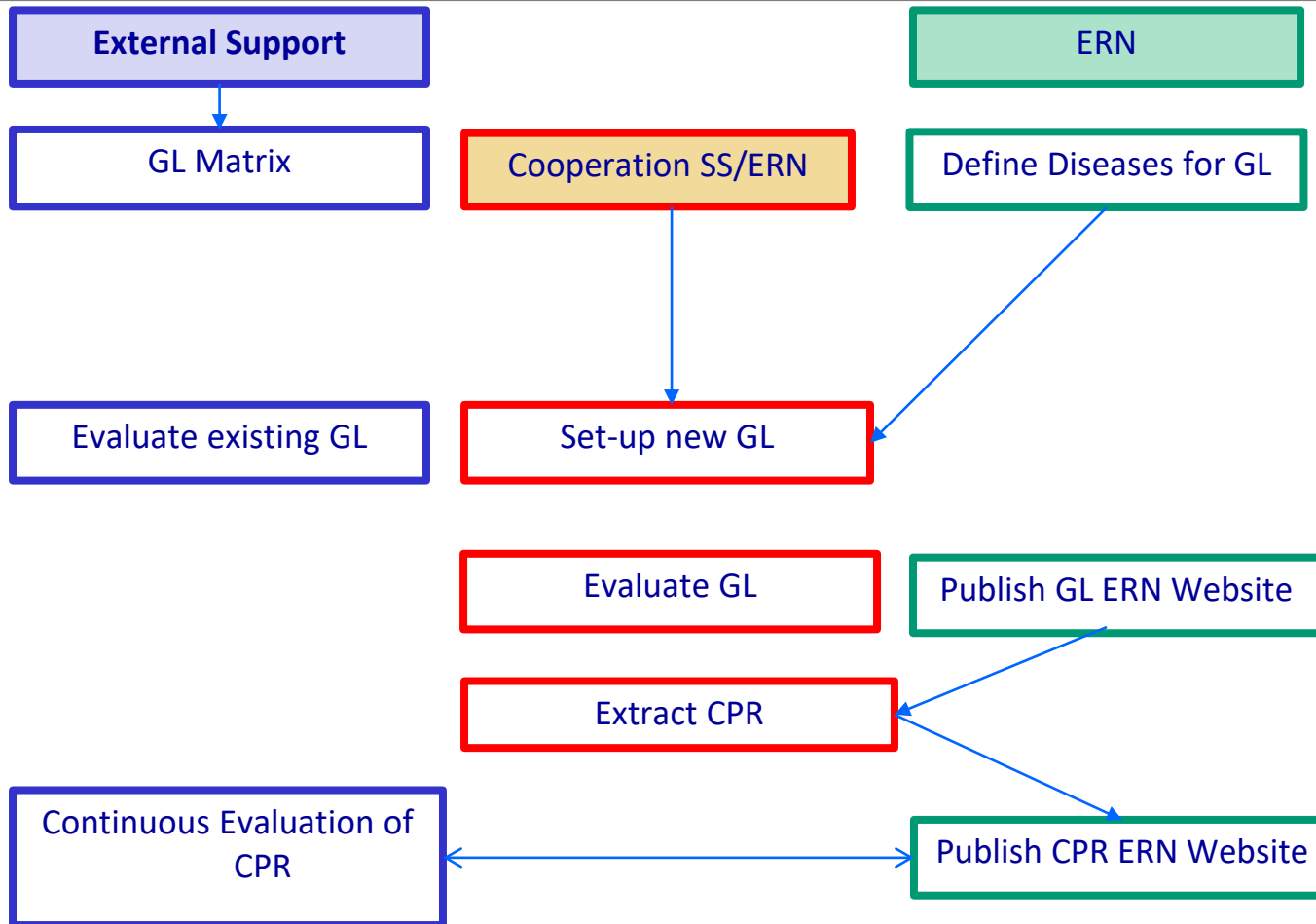


Suggested Workflow

Step 1	Matrix for GL	Criteria: Quality / Transparency / Standardized / easy to use Set up Standardizes way in GL evaluation EU Tender for support
Step 2a	Define Diseases for GL	Suggestion from ERN/ Cooperation with Scientific Societies
Step 2b	Check existing GL	see Criteria Step 1 Evaluation
Step 3	Evaluate GL	for formal criteria see Step 1 Certify GL according to ERN quality criteria „ERN CERTIFICATE“
Step 4	Publish GI	certified GL made available via ERN Websites
Step 5	Extract CPR clinical pathway rec.	According to set-up standards of quality /transparency/Layout Publish on ERN Website
Step 6	Continuous evaluation	make evaluation of CPRs compulsory for users (Ranking / Improvement)



Suggested Workflow





Definition - Consensus Statement

In health care consensus process is an approach that enables the multidisciplinary group to reach an agreement on a particular issue

Consensus statement

- a public statement on a particular aspect of medical knowledge that a **representative group of experts** agree to be **evidence-based** and **state of the art** knowledge.
- to counsel on the best possible/acceptable way of diagnosis/therapy. Re-evaluation if necessary.
- Written by an independent panel of experts, convened by a medical association/governmental authority.

Consensus statements differ from Guidelines:

"Consensus statements **synthesize new information**, from recent or ongoing research, that has implications for reevaluation of routine medical practices. They do not give specific algorithms or guidelines for practice. (NIH) "

https://en.wikipedia.org/wiki/Review_article; Woodward, A. M. (1977). The Roles of Reviews in Information Transfer. Journal of the American Society for Information Science, 175-180



Definition - Review

Reviews

Summarizes

...A clearly formulated question using systematic and explicit methods to identify, select, and critically appraise relevant research, and to collect and analyze data from the studies that are included in the review.

Statistical methods (meta-analysis) may or may not be used to analyze and summarize the results of the included studies.

Systematic reviews

- determine an objective list of criteria,
- find all previously published original experimental papers that meet the criteria;
- then compare the results presented in these papers.



Clinical pathway (CP) – a tool for ERN?

Challenges

Content of CP

disease specific subnetworks

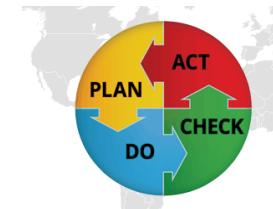
Standardization

CP groups (WP4 in MetabERN)

ANY MOVE TOWARD STANDARDIZATION IS A MOVE IN THE RIGHT DIRECTION.

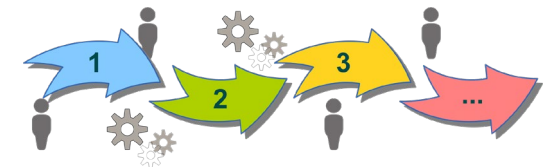
Quality

AGREE II standards for Guidelines
GRADING criteria for other publications used to set-up CPs



Transparency

standardized, open process
all literature available
internet based platform



Corporate identity (ERN)

Schemes, schedules, working material provided by CP groups

<http://www.quotehd.com/quotes/dave-williamson-quote-any-move-toward-standardization-is-a-move-in-the-right>; <http://i.imgur.com/lZeoE37.png>;
<http://clipart-library.com/clipart/277994.htm>