

**Norwegian Institute of Public Health and Division for Health Services [case number 2]**

<b>Institution: Norwegian Institute of Public Health</b>
<b>Administrative unit:</b> Cluster for systematic reviews and health technology assessments
<b>Title of case study:</b> Development and impact of the GRADE approach for assessing the confidence in effect estimates to make the findings of systematic reviews more useable in evidence-based decision-making processes
<b>Period when the underpinning research was undertaken:</b> 2000- current date
<b>Period when staff involved in the underpinning research were employed by the submitting institution:</b> 2000- current date
<b>Period when the impact occurred:</b> 2004-current date

**1. Summary of the impact**

In this impact case we describe the participation of our employees in the global working group who developed and implemented the use of [GRADE](#) (Grading of Recommendations Assessment, Development and Evaluation). GRADE is a methodological approach for assessing the quality of the evidence/ confidence in the results of a systematic review and the strength of recommendations in a guidelines process. We then describe the impact that the implementation of GRADE has had on increasing the transparency of reporting of findings for systematic reviews, and in guidelines processes. Furthermore, GRADE has become the gold standard for systematic reviews in international groups such as the [Cochrane Collaboration](#), the [WHO](#) and the National Institute for Health Care and Excellence ([NICE](#)) in the United Kingdom.

This impact case will focus on the impact of using GRADE to assess the confidence in the results from a systematic review.

**2. Underpinning research**

Before GRADE there were many different ways to assess the confidence in findings from a systematic review. These approaches were not transparent and were less systematic.

Methodological work to develop GRADE started in 2000 and continues to this day. Implementation of the GRADE approach in systematic reviews and guidelines started in approximately 2004.

The GRADE working group took the following approach to developing GRADE:

1. The GRADE working group started by mapping and assessing the current ways of assessing the confidence in the quality of the evidence.
2. The team used an evidence-based approach to develop the new tool through an iterative process of surveys, and user testing of examples. Everything that was included in the final tool worked well in user testing and had been understood by participants in multiple tests before being included.

The final GRADE assessment tool encourages researchers to make transparent, systematic and consistent assessments. After implementing the initial tool with evidence profiles where researcher decisions are explained, the GRADE working group introduced Summary of Findings (SoF) tables. This further increased the level and detail of decision reporting and communication. GRADE also provides a transparent and equal approach for decision makers to understand the findings of systematic reviews and how much trust they can place in the effect estimates when making informed decisions.

The development of the GRADE tool led to the publication of scientific articles, a handbook and a multitude of freely available teaching materials. These include:

- [GRADE Handbook](#)
- [GRADEpro](#)
- Two chapters in the [Cochrane handbook](#) for systematic reviews of interventions
- More than 30 academic publications (including a [series](#) of 6 articles in BMJ followed by a still ongoing series in J clin epi)
- Thousands of published systematic reviews that have implemented GRADE assessments
- Webinars, teaching materials, integrated into systematic review teaching, website, included in Cochrane training

GRADE has also encouraged further methods development to assess the confidence in the findings of qualitative evidences synthesis ([GRADE CERQual](#)), software to support the assessment process ([GRADEpro](#), [iSoQ](#)), support for guidelines processes ([MAGIC](#)) and a project to make systematic review findings available to the general public ([SUPPORT summaries \(kort oppsummert\)](#)). There is currently a worldwide network of researchers using and further developing these methods.

GRADE has also been used in hundreds of guidelines processes across a large number of institutions, for example, the WHO. Since 2009, the WHO has had mandatory use of GRADE in systematic reviews underpinning their recommendations, as well as standard use of the GRADE evidence-to-decision framework for determining the strength of recommendations. More than [110 organizations from 19 countries around the world have endorsed or are using GRADE](#).

The GRADE working group is a global network with global collaboration amongst members and institutions. Our employees played a key role in the development, testing and implementation of the method.

- Signe Flottorp and Andy Oxman were the initiators of the idea that led to the collaboration that became the GRADE working group. The informal meeting in 2000 with several other international collaborators where this discussion started is considered the first meeting, Gunn Vist joined at the second meeting later in 2000. All three are still employed in the Area for Health Services.
- Annhild Mosdøl (employed until 2019) was a member of the GRADE Equity Group.
- A number of current employees are members of GRADE Scandinavia.
- GRADE inspired GRADE CERQual for use in qualitative evidence synthesis. Many researchers in the Area for the Health Services at NIPH have been involved in its development since 2012; Claire Glenton (employed until 2022), Simon Lewin (employed until 2022), Signe Flottorp, Andy Oxman, Rigmor Berg and Heather Munthe-Kaas.
- GRADE also inspired the MAGIC app development led by Per Olav Vandvik (employed until 2024). Stijn van der Velde (employed until 2023) joined the MAGIC group a short time later.

### 3. References to the research

Schünemann HJ, Higgins JPT, Vist GE, Glasziou P, Akl EA, Skoetz N, Guyatt GH. Chapter 14: Completing 'Summary of findings' tables and grading the certainty of the evidence. In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). *Cochrane Handbook for Systematic Reviews of Interventions* version 6.4 (updated August 2023). Cochrane, 2023. Available from [www.training.cochrane.org/handbook](http://www.training.cochrane.org/handbook).

Schünemann HJ, Vist GE, Higgins JPT, Santesso N, Deeks JJ, Glasziou P, Akl EA, Guyatt GH. Chapter 15: Interpreting results and drawing conclusions. In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). *Cochrane Handbook for Systematic Reviews of Interventions* version 6.4 (updated August 2023). Cochrane, 2023. Available from [www.training.cochrane.org/handbook](http://www.training.cochrane.org/handbook).

Schünemann HJ, Santesso N, Vist GE, Cuello C, Lotfi T, Flottorp S, Davoli M, Mustafa R, Meerpohl JJ, AlonsoCoello P, Akl EA. Using GRADE in situations of emergencies and urgencies: Certainty in evidence and recommendations matters during the COVID-19 pandemic, now more than ever and no matter what. *Journal of Clinical Epidemiology* 127 (2020) 202e207.

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Schünemann HJ, Mustafa RA, Brozek J, Steingart KR, Leeflang M, Murad MH, Bossuyt P, Glasziou P, Jaeschke R, Lange S, Meerpohl J, Langendam M, Hultcrantz M, Vist GE, Akl EA, Helfand M, Santesso N, Hooft L, Scholten R, Rosen M, Rutjes A, Crowther M, Muti P, Ratz H, Ansari MT, Williams J, Kunz R, Harris J, Rodriguez IA, Kohli M, Guyatt GH, for the GRADE Working Group, GRADE guidelines: 21 part 1. Study design, risk of bias and indirectness in rating the certainty across a body of evidence for test accuracy, *Journal of Clinical Epidemiology* (2020), doi: <https://doi.org/10.1016/j.jclinepi.2019.12.020>. [https://www.jclinepi.com/article/S0895-4356\(19\)30673-0/pdf](https://www.jclinepi.com/article/S0895-4356(19)30673-0/pdf)

Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, Schünemann HJ. GRADE: an emerging consensus on rating quality of evidence and strength of recommendation. *BMJ* 2008; 336: 924-926. doi:10.1136/bmj.39489.470347.AD.

#### 4. Details of the impact

The GRADE Working Group is a network of international collaborators who participated in discussions and testing of examples while developing this methodological approach (see table below). Three of our employees were key members of the core working group during the formative years of the development of the approach. In addition to participating in the discussions and tests, our people were deeply involved in making progress through planning, developing, preparing and conducting the tests, assessing and writing. The examples used for developing and testing the GRADE approach were selected from discussions and suggestions from within this group and therefore often by default relevant to the participating institutions.

##### **Table over key participating institutions**

American University of Beirut, Lebanon	Hospital de Sant Pau, Universidad Autonoma de Barcelona, Spain	The Swedish Agency for Health Technology Assessment and Assessment of Social services (SBU), Sweden
Bond University, Australia	Kyoto University Graduate School of Medicine/School of Public Health, Japan	Universidad San Sebastian, Chile
Case Western Reserve University, USA	Manchester University NHS Foundation Trust, UK	University Hospital Basel, Switzerland
Copenhagen University Hospital, Denmark	Mayo Clinic, USA	University Medical Center Freiburg, Germany
Duke University Medical Center and Durham Veterans Affairs Center for Health Services Research in Primary Care, USA	McMaster University, Canada	University of Florida, College of Medicine, USA
German Hospital, Argentina	Oregon Health and Science University, USA	University of Modena and Reggio Emilia, Italy

Guide2Guidance, The Netherlands	State University of New York at Buffalo, USA	University of Toronto, Canada
Harvard Medical School, USA		West China Second University Hospital, Sichuan University and Key Laboratory of Birth Defects and Related Disease of Women and Children, China

The participation of many different organizations with employees focused on different aspects of the systematic review and guidelines process (systematic review producers, guideline producers, and global networks across medical and public health disciplines) was helpful for implementing and disseminating of the GRADE approach.

A key dissemination activity was workshops at Cochrane Colloquium. These provided access to the target user group for the GRADE approach as well as an arena for feedback on implementation of GRADE and its ease of use. The active participation of anyone interested in GRADE at workshops during Cochrane Colloquiums encouraged the participation of relevant people and expertise as well as aiding dissemination to and input from experienced systematic review methodologists. As a result of these workshops, implementation of the GRADE approach in Cochrane systematic reviews was made easier.

#### **Beneficiaries**

The clear beneficiaries of the GRADE tool are the producers of, and users of systematic reviews and guideline recommendations. These groups benefit from the increased transparency, systematic approach, and consistency in judgements around the confidence in the results of a systematic review that using the GRADE tool provides. A further beneficiary is the general public as GRADE has increased the transparency of the decision-making process for guidelines in implementation of new methods in the health care sector and beyond. GRADE allows for end users to follow the decision trail of a recommendation back to the original evidence and see which other factors influence the guideline panel's decision.

#### **Nature of the impact**

Impact of the GRADE approach began about 2004 and continues to grow, both in systematic reviews and guidelines processes. The GRADE working group continues to explore new methodological innovations linked to using the GRADE tool allowing the tool to adapt to the changing landscape of systematic reviews and guidelines. As GRADE has become standard practice in leading institutions worldwide (WHO, NICE), other institutions have become aware of the benefits of transparent and systematic evaluation of the evidence and begun to implement the approach. This continued implementation has happened at the country level and is also happening at the municipal level in Norway through the *Supporting municipalities to make informed decisions* project at the NIPH.

#### **Evidence or indicators of the extent of the impact (with dates)**

- Since 2004 it has become standard practice to use GRADE in systematic reviews
- GRADE has been used in Norwegian guidelines processes, for example related to changes in treatment for [multiple sclerosis](#), the dangers of [using snus](#) and e-cigarettes, or [how best to communicate about children's weight status to parents](#).
- GRADE is a required component of all systematic reviews contributing to [WHO guidelines](#). Most recently employees in our cluster contributed key evidence to a [guideline on non-](#)

[surgical management of chronic primary low back pain in adults in primary and community care settings.](#)

**5. Sources to corroborate the impact** (indicative maximum of ten references)

An example with considerable impact in Norway is the [HTA-report with a network meta-analysis on disease modifying treatment for relapsing remitting multiple sclerosis](#) (using GRADE).

An international example involving the use of GRADE with a global impact are the [WHO living guidelines on Covid 19 drugs](#)

The impact from the GRADE working group is clearly demonstrated by the inclusion of this methodological approach in the assessment of the confidence in results from systematic reviews by the Cochrane collaboration's Handbook for Systematic Reviews of Interventions, chapter 14 and 15, [Cochrane Handbook for Systematic Reviews of Interventions | Cochrane Training](#)

Another clear demonstration of impact and uptake is the adoption of the GRADE approach by leading international guideline producers such as

-The WHO Handbook for Guideline Development, [GRC Handbook - second edition \(who.int\)](#) chapter 9 and 10.

-WHO Guidelines handbook that clearly describes and highlights GRADE as a mandatory part of the process: <https://www.who.int/publications/i/item/9789241548960>

-NICE, [Developing NICE guidelines: the manual](#), chapter 6.

- [Canada's Drug and Health Technology Assessment Agency](#) (CADTH) requires the use of GRADE in their reports.

Finally, our national Directorate of Health has adopted the use of GRADE in Norwegian guidelines processes through the Norwegian National Guide for Developing Guidelines ([Veileder for utvikling av kunnskapsbaserte retningslinjer \(fullversjon\).pdf \(helsedirektoratet.no\)](#)). This guidance on the use of GRADE (from page 28), is only available in Norwegian. However, we think it has had an important impact in Norway and has improved the methodology used for Norwegian National Guidelines for Health.