ALGEMEEN STRAMIEN VOOR DE ONTWIKKELING VAN AANBEVELINGEN VAN GOEDE MEDISCHE PRAKTIJKVOERING

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INHOUD

1. KEUZE VAN ONDERWERP 1

2. AUTEURS EN BEGELEIDINGSGROEP 1

3. VOORSTEL VAN PLANNING 1

4. LITERATUURONDERZOEK 2

4.1. VAN ALGEMENE DOELSTELLING NAAR KLINISCHE VRAGEN 2
4.2. STAPSGEWIJZE ZOEKSTRATEGIE 2
4.3. BEOORDELING EN VERWERKING VAN DE LITERATUURGEGEVENS 3
4.4. CONSENSUSOVERLEG 3

5. STRUCTUUR VAN AANBEVELINGSTEKSTEN VAN DOMUS MEDICA EN SSMG 3

6. UITWERKING VAN EEN ONTWERPAANBEVELING 5

7. VALIDATIE DOOR DE STUURGROEP AANBEVELINGEN 5

8. TOETSING DOOR EXPERTS 5

9. TOETSING IN LOK-GROEPEN 5

10. PATIËNTENBETROKKENHEID 6

11. NIEUW OVERLEG VOOR EEN FINALE CONSENSUS 6

12. VALIDATIE 6

13. DRUK EN VERSPREIDING 6

BIJLAGE 1 7

BIJLAGE 2 11

1. KEUZE VAN ONDERWERP

Onderwerpen voor aanbevelingen voor goede medische praktijkvoering worden gekozen in functie van verschillende criteria die worden beschreven in *bijlage 1*.

2. AUTEURS EN BEGELEIDINGSGROEP

Een aanbeveling wordt geschreven door een groep van auteurs. Deze bestaat voor het overgrote deel uit huisartsen met praktijkervaring en ervaring in het kritisch lezen van medische onderzoeksliteratuur, en vooral van klinische studies. Bij voorkeur wordt de auteursgroep uitgebreid met betrokken geneesheer-specialisten en beoefenaars uit alle relevante niet-medische beroepsgroepen.

Binnen de auteursgroep wordt ten minste één lid van de stuurgroep Aanbevelingen (Domus Medica) of "le comité scientifique du groupe de travail des RBP de la SSMG" opgenomen, met als belangrijkste taak de procedure van ontwikkeling in goede banen te leiden.

De stuurgroep Aanbevelingen van Domus Medica, of "le comité scientifique du groupe de travail des RBP de la SSMG", is eindverantwoordelijk voor het begeleiden van de ontwikkeling van de aanbeveling en voor de redactie ervan.

3. VOORSTEL VAN PLANNING

De volgende tijdsplanning wordt aan de auteursgroep voorgesteld om de aanbeveling te kunnen finaliseren op twee jaar tijd:

- Jaar 1:
    - Maanden 1-3: formuleren van doel, doelstellingen en klinische vragen, waarop de aanbeveling een antwoord moet geven. Literatuurreview naar andere richtlijnen volgens strategie zoals beschreven in *bijlage 2*.
    - Maanden 4-6: vervolledigen van literatuurstudie (meta-analyses, systematische reviews en RCT's).
    - Maanden 7-9: stramien van aanbeveling uitwerken.
    - Maand 10: eerste uitgewerkte versie door auteursgroep.
    - Maanden 11-12: verbeteringen door auteursgroep.
- Jaar 2:
    - Maand 1: pre-definitieve versie
    - Maanden 2-5: experts en toetsing in Lok's/Glems van huisartsen
    - Maanden 6-7: verwerking opmerkingen experts en Lok's via consensusbijeenkomsten, validatie
    - Maanden 8-10: redactie, finalisatie
    - Maanden 11: validatie door CEBAM
    - Finale versie op basis van opmerkingen van CEBAM, publicatie

4. LITERATUURONDERZOEK

Volgens Agree deeltje Methodologie (items 8-14) moeten het proces waarin bewijsmateriaal is verzameld en samengesteld en de gebruikte methoden om aanbevelingen op te stellen en te herzien, duidelijk zijn:

- Er zijn systematische methoden gebruikt voor het zoeken naar wetenschappelijk bewijsmateriaal.
- De criteria voor het selecteren van het wetenschappelijk bewijsmateriaal zijn duidelijk beschreven.
- De gebruikte methoden om de aanbevelingen op te stellen, zijn duidelijk beschreven.
- Gezondheidswinst, bijwerkingen en risico's zijn overwogen bij het opstellen van de aanbevelingen.
- Er bestaat een expliciet verband tussen de aanbevelingen en het onderliggende wetenschappelijke bewijsmateriaal.
- De richtlijn is voor publicatie door externe experts beoordeeld.
- Een procedure voor herziening van de richtlijn is vermeld.

4.1. Van algemene doelstelling naar klinische vragen

Allereerst wordt de algemene doelstelling voor de aanbeveling beschreven. Vervolgens worden klinische vragen opgesteld, zo mogelijk geformuleerd als PICO (*zie bijlage 2*). Klinische vragen worden vertaald naar juiste zoektermen, aan de hand van volgende bronnen of elementen:

- Relevante zoektermen op basis van klinische vragen.
- Domeinen die volgens de opinies van experts, belangrijk zijn om te includeren.
- Na eerste algemene screening van reeds bestaande richtlijnen over deze topic:
    - overzicht van relevante topics → zoektermen
    - hulp bij het bepalen van sleutel(zoek)termen (geeft ook eerste aanwijzing van het volume aan literatuur dat hierover beschikbaar is).

Meer informatie hierover in *bijlage 2*.

4.2. Stapsgewijze zoekstrategie

De zoekstrategie voor een nieuwe aanbeveling wordt steeds stapsgewijs uitgevoerd volgens de methodologie zoals beschreven in *bijlage 2*.

In eerste instantie worden bronnen geraadpleegd die gebruikmaken van gegevens uit systematische reviews, meta-analyses en oorspronkelijke studies en hierbij commentaar geven: **guidelines en Clinical Evidence**.

In een tweede stap wordt gezocht naar **relevante meta-analyse en reviews**.

In een derde stap van de zoekstrategie, wordt gezocht naar **RCT's**.

Op zoek naar systematische reviews, meta-analyses en RCT's worden ook *elektronische databanken* geraadpleegd.

Enkel bronnen die mogelijk een antwoord kunnen geven op de gestelde klinische vragen, worden geselecteerd. Daarbij worden strenge criteria van selectie gehanteerd: niet alle gevonden literatuur moet ook weerhouden worden (zie *bijlage 2*).

De zoekstrategie voor een adaptatie van een bestaande aanbeveling voor goede medische praktijk, zal gebeuren volgens de methodologie Adapte (zie *bijlage 2*).

4.3. Beoordeling en verwerking van de literatuurgegevens

a. Kritische beoordeling

De geselecteerde literatuur wordt kritisch bekeken en op kwaliteit beoordeeld.

Om de aanbevelingen te beoordelen, kunnen de auteurs gebruikmaken van de Agree-criteria.
Voor andere literatuur (systematische reviews, klinische studies, meta-analyses) heeft men beoordelingsformulieren beschikbaar op de site www.cochrane.nl. Voor de evaluatie van diagnostische studies, kan men ook het beoordelingsformulier van Quadas gebruiken. Voor verdere informatie zie *bijlage 2*.

b. Samenvatting van de gevonden evidentie

Voor de belangrijke boodschappen (antwoorden op de klinische vragen) wordt een evidentietabel opgemaakt met een niveau van evidentie per referentie. Men doet daarnaast voorstellen voor het toekennen van een graad van aanbeveling (Grade Working Group) per boodschap, door alle noodzakelijke argumenten in te brengen, waaronder economische beschouwingen (*zie c*) (voor meer details zie *bijlage 2*).

c. Economische beschouwingen (kosten & health benefits ⇔ meerwaarde voor richtlijn)

- Als een economische analyse (kostenminimalisatie, kosteneffectiviteit, kosten-nut, kosten-baten) met gegevens voor België beschikbaar is, dan is het nodig deze gegevens te valideren (Dutch Cochrane, KCE) en de resultaten ervan te vermelden.
- De kosten-vergelijkingen tussen verschillende diagnostische en therapeutische strategieën moeten zo nuttig vermeld worden. Men moet ook de voorwaarden van terugbetaling in België vermelden, zo deze van toepassing zijn.

4.4. Consensusoverleg

Op niveau van de auteursgroep

5. STRUCTUUR VAN AANBEVELINGSTEKSTEN VAN DOMUS MEDICA EN SSMG

Men moet steeds overwegen om volgende elementen in een aanbeveling op te nemen. Sommige hiervan zijn onmisbaar voor elke aanbeveling; anderen zijn dan weer niet toepasselijk voor bepaalde themata.

1. ABSTRACT
   Wezenlijke inbreng en kernboodschappen van de aanbeveling (met niveau van evidentie en aanbeveling).

2. INLEIDING
   - Motivatie voor de richtlijn (keuze van onderwerp, omschrijving van probleem, epidemiologie, etiologie, …).
   - Doel van de aanbeveling *(cfr. AGREE item 1: Het doel van de richtlijn is specifiek beschreven).*
   - Patiëntenpopulatie *(cfr AGREE item 3: De patiëntenpopulatie waarop de aanbeveling van toepassing is, is specifiek beschreven).*
   - Context waarin de aanbeveling van toepassing is (eerstelijnsgezondheidszorg) *(cfr. AGREE item 6: De beoogde gebruikers van de richtlijn zijn duidelijk benoemd).*
   - Diagnostische en therapeutische interventies waarover de aanbeveling gaat.

3. KLINISCHE VRAGEN
   Klinische vraag: precies geformuleerde vraag of besliskundig probleem *(cfr AGREE item 2: De klinische vraag/vragen die in de richtlijn aan de orde komen, is/zijn specifiek beschreven).* Formuleer de klinische vragen in de vorm van een PICO.

4. AUTEURS EN ZOEKMETHODEN
   - Vermeld de betrokken onderzoekers en auteurs die meegewerkt hebben aan de aanbeveling (*Cfr. AGREE item 4: De leden van de werkgroep die de richtlijn heeft ontwikkeld, komen uit alle relevante beroepsgroepen*) en de onafhankelijkheid van de opstellers (*Cfr AGREE items 22 en 23: De richtlijn is niet beïnvloed door de opvattingen of belangen van de financierende instantie. Conflicterende belangen van leden van de werkgroep zijn vastgelegd*).
   - Beschrijf kort de methodologie van het literatuuronderzoek (*cfr. AGREE items 8-14: Methodologie: beschrijft het proces waarin bewijsmateriaal is verzameld en samengesteld en evenals de gebruikte methoden om aanbevelingen op te stellen en te herzien*).

5. DEFINITIES EN BEGRIPPEN

6. AANBEVELING
   Eigenlijke richtlijn – met antwoorden op de verschillende klinische vragen (diagnostisch en therapeutisch).

7. INFORMATIE VOOR DE PATIENT

8. CONCLUSIE EN AANBEVELINGEN
   Voor elke aanbeveling wordt ook een steekkaart opgesteld, die de sleutelboodschappen toelicht.

9. RANDVOORWAARDEN
   Advies vanuit het werkveld van de huisarts, praktijkvoering- en implementatieaspecten, emotionele weerstanden, kennis en vaardigheden, praktijkorganisatie, materiaal en uitrusting, organisatie van de gezondheidszorg.

10. ECONOMISCHE BESCHOUWINGEN

11. RESEARCHAGENDA
    Punten waarover nog geen zekerheid bestaat, onbeantwoorde klinische onderzoeksvragen.

12. TOTSTANDKOMING
    - gecontacteerde experts
    - stuurgroep
    - toetsing op het terrein in Lok's
    - validatie
    - opdrachtgever en financiering
    - termijn en procedure voor herziening en updating

13. NOTEN

14. GLOSSARIUM

15. INHOUDSTAFEL

6. UITWERKING VAN EEN ONTWERPAANBEVELING

Door de auteursgroep, volgens het schema en structuur zoals voorgesteld in punt 5 *(Cfr. AGREE items 15 -18 Helderheid en presentatie : De aanbevelingen zijn specifiek en ondubbelzinnig. De verschillende beleidsopties zijn duidelijk vermeld. De kernaanbevelingen zijn gemakkelijk te herkennen. De toepassing van de richtlijn wordt ondersteund met hulpmiddelen).*

7. VALIDATIE DOOR DE STUURGROEP AANBEVELINGEN

Goedkeuring van de ontwerpaanbeveling door de stuurgroep aanbevelingen (Domus Medica) of het comité scientifique (SSMG).

8. TOETSING DOOR EXPERTS

De tekst wordt vervolgens ter beoordeling voorgelegd aan meerdere zorgvuldig gekozen experts uit verschillende disciplines.

De stuurgroep (Domus Medica) of het comité scientifique (SSMG) stelt een lijst op van mogelijke experts m.b.t. het onderwerp van de aanbeveling. Daar zouden ook huisartsen-experts bij moeten zijn. **De experts dienen opmerkingen te formuleren op de tekst, onderbouwd vanuit de wetenschappelijke literatuur. Enkel bij voldoende evidentie kan met deze opmerkingen rekening gehouden worden.**

Alle opmerkingen van de experts worden door de auteursgroep bekeken tijdens een consensusvergadering. In consensus worden de nodige aanpassingen aan de tekst doorgevoerd.
De aangepaste tekst wordt bezorgd aan de redactie (in casu Huisarts Nu). De redactie bekijkt de tekst kritisch op 'formuleringen', maar niet op inhoud.

9. TOETSING IN LOK-GROEPEN

Toetsing op het terrein is belangrijk om de toepasbaarheid na te gaan zoals vermeld in items 19-21 van Agree *(De mogelijke organisatorische belemmeringen bij het toepassen van de aanbevelingen zijn besproken. De mogelijke kostenimplicaties van het toepassen van de aanbevelingen zijn overwogen. De richtlijn geeft de belangrijkste criteria om na te gaan en te toetsen of de richtlijn wordt gevolgd).*

De aanbeveling wordt getest op het terrein in een aantal Lok-groepen/Glems (minimum 4 in de eigen taalrol en 2 in de andere taalrol; hiervoor wordt de ontwerpaanbeveling gedeeltelijk vertaald: kernboodschappen, casussen en inhoudelijke sheets die gebruikt worden bij toetsing.). In elke groep moet een ervaren moderator aanwezig zijn, naast iemand van de auteursgroep, die ervoor zorgt dat wat moet getoetst worden ook effectief getoetst wordt.

De aanwezige auteur maakt (in samenspraak met de moderator) een verslag waarin beschreven wordt in welke mate de huisartsen de aanbeveling menen te kunnen toepassen (de toetscasus zal daarom opgebouwd worden rond de te verwachten struikelstenen), welke weerstanden er tegen het uitvoeren van de aanbeveling zijn en welke randvoorwaarden moeten vervuld worden om de aanbeveling te kunnen uitvoeren.

Alle deelnemers van de Lok-groepen/Glems krijgen op het einde van de bijeenkomst de aanbeveling mee, met de opdracht om aan de hand van enkele concrete vragen de haalbaarheid ervan in de praktijk uit te

proberen en de mogelijkheid om inhoudelijke opmerkingen te maken. Het evaluatieformulier sturen zij nadien terug naar het secretariaat van Domus Medica of SSMG. Men kan ook een tweede bijeenkomst plannen voor de evaluatie. De respondenten krijgen hiervoor een kleine symbolische vergoeding.

Voor aanbevelingen over een beperkte topic of voor een herziening met implicaties op praktijkvoering of -gedrag, kan men ook een evaluatie doen via schriftelijke toetsing. Alle opmerkingen vanuit de Lok-groepen en ook de teruggestuurde evaluatieformulieren worden verwerkt. Tijdens een consensusbijeenkomst van de auteurs worden alle opmerkingen overlopen en wordt in consensus de tekst eventueel aangepast, en dit ook in overleg met de 'stuurgroep' of het 'comité scientifique'.

10. PATIËNTENBETROKKENHEID

Als een informatiefolder voor patiënten wordt opgesteld, moet deze geëvalueerd worden op duidelijkheid en leesbaarheid.

11. NIEUW OVERLEG VOOR EEN FINALE CONSENSUS

- Finale consensus;
- Formulering van kernaanbevelingen met evidentieniveaus en graden van aanbeveling volgens Grade;
- Bepaling van de termijn voor noodzakelijke herziening en de procedure voor updating/opvolging (verantwoordelijke auteur).

12. VALIDATIE

De aangepaste tekst wordt eerst bezorgd aan de stuurgroep of het comité scientifique en vandaar aan Cebam ter validatie.

13. DRUK EN VERSPREIDING

De door Cebam gevalideerde tekst en zijn vertaling worden herlezen door beide wetenschappelijke verenigingen. De teksten wordt bezorgd aan de redactie (voor Domus Medica aan Huisarts Nu) voor publicatie in het tijdschrift en op de website.

De kernboodschappen worden in de andere landstaal en in het Engels vertaald en op de website geplaatst.

Er wordt een koppeling gemaakt met de GIN-website.

BIJLAGE 1

CRITERIA FOR SELECTING TOPICS FOR GUIDELINES IN FAMILY PRACTICE

1 July 2007

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The objective of this document is to highlight the criteria which should guide the Belgian scientific societies of family practice for choosing new topics of guidelines.

Guidelines are designed to improve the quality of health care, to reduce the number of unnecessary interventions and to optimise the treatment of the patients at an acceptable cost (NHMRC 1999). Moreover, the topic must answer to a public health concern, i.e. either in terms of the importance of the disease or in terms of the costs for the society. The judicious choice of topics will contribute to the interest of the physician for the guideline.

Some authors have already described desirable attributes of clinical guidelines (Lohr 1994, Grimshaw 1993), i.e.:

- Validity (based on the evidence, evaluation of health outcomes)
- Reliability/reproducibility (between experts and between GPs)
- Clinical applicability
- Clinical flexibility
- Clarity
- Multidisciplinary process
- Scheduled review
- Documentation

However, the literature about criteria for choosing topics is scarce. The current paper is based on two sources of information, e.g. a literature search and information collected from organisations which are known to produce guidelines. This second source of information was quite disappointing. Some organisations who publish guidelines often depend of authorities or other payers for the choice of the topic (e.g. ANAES, Canadian guidelines). The criteria used for the choice of their topics remain unclear. Other organisations have defined criteria for the selection of their topics (e.g. AETMIS (Agence d'Evaluation des Technologies et des Modes d'Intervention en Santé), AHCPR (Agency for Health Care Policy and Research).

The priority setting for guidelines' development should consider the following points (AETMIS 2001, AHCPR 1998, Baker 1997, Beaulieu 1999, Greenhalgh 2000, Grol 1993, Grol 1995, Grol 1998, NHMRC 1999, Shekelle 1999 , Oxman 2006).

1. RELEVANCE OF THE TOPIC

Developing guidelines is time and money consuming and the available means should be reserved primarily for the most relevant topics, namely the major causes of morbidity and mortality in the population. Relevant topics are important health problems as well as problems with a high incidence or prevalence. Since the guide-lines in this project are primarily meant to assist general practitioners, topics should be relevant in primary care.

- **Important health problem**
  Important problems are problems that lead to substantial (physical or psycho-social) morbidity or mortality. The more important the problem, the greater the possible gain as consequence of improvement of care.

- **High incidence/prevalence**
  A guideline will be of more use if it can be applied to more patients in the daily practice of the general practitioner. Upper respirator infections are for example among the commonest reasons for encounter in primary care.

- **Health problem is (or should be) mainly managed in primary care**
  A guideline can only be beneficial to primary care if it concerns diagnostic procedures and/or treatments that are applicable in primary care. However, the guideline will include clear criteria for referring a patient to a specialist when needed.

2. PROBLEM AREA

- **Substantial practice variation**
  Practice variations have many sources, including health care system features (e.g. reimbursement system), differences in access to care and patient preferences. In particular, they reflect also an uncertainty regarding the most appropriate medical decision for a given medical problem. Antibiotics prescription in case of acute sore throat illustrates the large practice variations for the same condition. New guidelines will possibly rend many old processes obsolete and propose new decision models based on the available evidence. The initial analysis of the problem should therefore also take account of the potential barriers of the general practitioners to use the best available evidence.

- **Suboptimal outcome for patients**
  The problem should have a high prevalence/incidence in the population as explained above. Moreover, the current solutions (therapeutics, follow-up) applied to solve this problem should not lead to optimal results for the patient. A good example is the management of diabetic patients in any level of care. All physicians know that an appropriate follow up of the patient decreases the complication rate. However, this follow up is difficult to organise in daily practice. The guidelines developed on this topic are an instrument for daily practice to help the general practitioner to enhance the quality of care of his diabetic patients and therefore decrease undesirable outcomes.

- **Under/over consumption (investigations, prescribing, referrals)**
  There is an increased interest in the evaluation and appropriate use medical services. It appears that patients who should benefit from services do not use them whereas other ones use them too frequently. An example is the use of mammography. Women outside the recommended age group have regular controls whereas a large proportion of 50-69 year-olds have never access to this screening procedure. Decisions based on guidelines should increase the judicious use of medical products/services and decrease the useless prescriptions.

3. POTENTIAL BENEFIT

- **Possibility for improving outcome**
  Data from the literature inform about the potential benefits for the patient. These benefits might relate to health indicators, morbidity or mortality data. However, other aspects are also worthy as the well-being, satisfaction or quality of life of the patient. An illustration is the control of pain in chronic patients. Better decision-making between general practitioner and patient will enhance the quality of care through better processes and outcomes.

- **Possibility for cost saving (for patients, society)**
  Changes of practices following new guidelines lead to a more rational use of drugs and investigations. This consequence might involve greater costs for the society and the patient. The treatment of all patients eligible for statin treatment is an illustration. However, guidelines will generally lead to a more rationalised prescription with cost savings for the patient and for the society. The limited use of radiography in case of lower back pain is an example.

- **Public Health benefit**
  Changes in practices might also be beneficial for public health as a whole. The case is obvious for antibiotics prescription where unrestricted use entails resistances and the need for larger spectrums in case of serious conditions. The optimal treatment of any communicable disease will be beneficial to the health of the whole community.

4. FEASIBILITY

- **Availability of evidence of effective treatment on the topic**
  Guidelines on effective treatment are preferable based on research evidence about the topic concerned. Inevitable, the recommendations of guidelines will always be an interpretation of available research evidence. However, guidelines must enable the user to distinguish recommendations based largely on evidence from those based largely on opinion. An explicit link between each recommendation and the justification for it is important for improving adherence of the users.

- **Potential for reaching consensus**
  As mentioned above, current practice can show great variations and this often reflects uncertainty regarding the most appropriate medical decision for a given medical problem. In some cases this cannot be solved by the development of a guideline, because existing research evidence is contradictory, inconclusive or rapidly changing and expert opinions are too divergent. These topics should not be chosen as formulating clear univocal recommendations will not be possible.

- **Potential for effective implementation and evaluation**
  Grol et al. showed that guide-lines will be more easily implemented if they are compatible with existing values among the target group and are not too controversial. Neither should guide-lines demand too much change to existing routines. If compliance to a guideline affects too much the organisation of the practices, adherence is less. Although “difficult” guidelines (which demand drastic changes of current practice) should not be entirely avoided if the topic is sufficiently relevant, the likelihood of actual implementation is best also considered in the choice of a topic. Also, it should be taken into account if the actual care provided by general practitioners in the chosen health problem can be evaluated and in what way.

References

- AETMIS (Agence d’Evaluation des Technologies et des Modes d’Intervention en Santé) : http://www.aetmis.gouv.qc.ca/fr/01_manda/index.htm
- AHCPR (Agency for Health Care Policy and Research): http://www.ahcpr.gov
- Baker R, Feder G. Clinical guidelines: where next? *Int J Qual Health Care* 1997;9:399-404.
- Beaulieu MD. Les guides de pratique clinique : valides et valables à quelles conditions ? *Louvain Med* 1999;118:527-34.
- Greenhalgh T. Savoir lire un article médical pour décider. BMJ Editions RanD, 2000.
- Grimshaw J, Russell I. Achieving Health Gain through clinical guidelines. I: developing scientifically valid guidelines. *Qual Health Care* 1993;2:243-8.
- Grol R. Development of guidelines for general practice care. *Br J Gen Prat* 1993;43:146-51.
- Grol R, Dalhuijsen J, Thomas S, in’t Veld G, Rutten G, Mokkink H. Attributes of clinical guidelines that influence use of guidelines in general practice: observational study. *BMJ* 1998;317:858-61.
- Grol R. Thomas S, Roberts R. Development and implementation of guidelines for family practice: lessons from the Netherlands. *J Fam Pract* 1995;40:435-9.
- Hutchinson A, Baker R. Chap 1. What are clinical Practice guidelines? In: Guidelines in clinical practice. Oxford: Radcliff Med Press, 1999:1-13.

- Lohr K. Guidelines for clinical practice: applications for primary care. *Int J Qual Health Care* 1994;6:17-25.
- NHMRC (National Health and Medical Research Council). A guide to the development, implementation and evaluation of clinical practice guidelines. Commonwealth of Australia, 1999.
- Shekelle P, Woolf S, Eccles M, Grimshaw J. Developing guidelines. *BMJ* 1999;318:593-6.
- Oxman AD, Schüneman HJ, Fretheim A. Improving the use of research evidence in guideline development: 2. priority setting. *Health Research Policy and Systems* 2006,4:14-20.

BIJLAGE 2

METHODOLOGY LITERATURE SEARCH

DE NOVO GUIDELINES

1. From aim to clinical question(s)

To describe the **overall aim** of the guideline, one can use the "PIPOH" method[1] .
PIPOH is short for :

- P: patient population / disease characteristics
- I: intervention(s) of interest
- P: professionals targeted by the guideline
- O: outcomes and endpoints to be taken into consideration
- H: healthcare setting and context

thereby offering a framework to clarify the overall aim.

The overall aim is often translated into specific **goals** and subsequently into practical **clinical questions**. These are to be formulated and agreed upon by a multidisciplinary group of authors. To define them, one can use – if and whenever appropriate - the PICO method [2].
PICO is short for:

- P: population or patient
- I: intervention or indicator
- C: comparison or control
- O: outcomes

offering a framework to translate a certain problem or practical question into a manageable research question.

2. Search criteria

Based on the above proposed clinical questions, search criteria should be defined. Criteria might differ, depending on which source is being searching for evidence (guidelines or publications).

The 2 sets of criteria below (1 set for guidelines, 1 for publications) should be described explicitely and if applicable, appropriately stored for future use (e.g. search re-runs in view of an updating or reviewing process).

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[1] Fervers B, Burgers JS, Haugh MC, Latreille J, Mlika-Cabanne N, Paquet L, et al. Adaptation of clinical guidelines: literature review and proposition for a framework and procedure. Int J Qual Health Care. 2006;18(3):167-76.

[2]

- Van den Bruel A, Chevalier P, Vermeire E, Aertgeerts B, Buntinx F. EBM : otitis media in children : how to formulate a PICO question. *Huisarts Nu* 2003;32:331-5.
- Van den Bruel A, Chevalier P, Vermeire E, Aertgeerts B, Buntinx F. EBM : otitis media in children : how to formulate a PICO question. *Rev Med Liège* 2004;59: 671-5.

These sets of criteria are to be seen as the minimal data set to be discussed and agreed upon by the group of authors before a literature search can commence. This also implies that the below listed criteria are not limited: if required, additional criteria may be added.

2.1. Criteria for guidelines

1. *Guideline finders*

   The following sources should be searched (well known and major guideline finders):
   - G.I.N. guideline resources: www.g-i-n.net
   - NEHL guidelinefinder: http://www.library.nhs.uk/guidelinesFinder/
   - National Guideline Clearinghouse: www.guideline.gov

   ... as combining the results of these 3 guideline finders yields a very high percentage of all online available international guidelines.
   Other sources can be searched in the presence of an (argued) indication of the multidisciplinary group of authors. The reason why should be documented.

2. *Entries*

   The goals and clinical questions normally already contain the most relevant search terms. A first screening of the guideline(s) found based on these terms, also often yields relevant entry terms. Additional search terms can also be looked up in the MeSH- medical subject heading- database: typing in one of the search terms in the MeSH search engine will produce a list of possible and/or related terms.

   The multidisciplinary group of authors is responsible for the approval of the final list of search terms. If necessary or appropriate, they will report on the terms that are excluded from the final list, also stating the reason why they were not included.

   When searching, attention should be paid to possible synonyms (e.g. “guideline”, “guidance”, “recommendation”,…), and translations (e.g. “guideline”,”richtlijn”, “aanbeveling”, “standaard”, “recommendation”, leitlinine”,…). The same attention must also be given to synomyms and translations for / of the relevant search terms.

   Resulting list of search terms:

Entry 1
Entry 2
Entry 3
Entry …

3. *Time span*

   - Most available guidelines are being updated within 5 years. Therefore guidelines will be searched for within the time span of the last 5 years, unless explicitely stated otherwise by the group of authors.
   - The date of the last search performed, the so-called end date, should be explicitely reported.

4. *Languages*

   Unless explicitely stated otherwise by the multidisciplinary group of authors, searches will be restricted to the languages mastered by at least one of the authors.
   Standard:
   - Dutch

- French
- German
- English

5. *Population*

   Description of the patient population under study, e.g. human, age, sex, ...

6. *Setting / context of the health care system3*

   - Preferably search within settings / contexts of health care systems closely related to the Belgian health care system
   - Depending on the question(s) at hand, exceptions can be allowed (if relevant, explicitly state why)

2.2. Criteria for publications

1. *Sources*

   The multidisciplinary group of authors will decide upon which databases will be searched (preferably at least 2). If less / more databases need to be searched, the group will explicitely report which and if required also why.

   As most databases contain their own search strategy or engine, whenever appropriate these will be used (described in short if necessary).
   The criteria described below should thereby always be taken into account.

   Possible databases (list not limited):

   1.1 Clinical Evidence

   1.2 For systematic reviews and meta-analyses

   1.2.1 Main sources
   - Cochrane Database of Systematic Reviews
   - Medline
   - Embase
   - Medion
   - Other databases as appropriate (report)

   1.2.2 Additional sources
   - Centre for Reviews and Dissemination (CRD) website
   - Database of Abstracts of Reviews of Effects (DARE) online database
   - Health Technology Assessment (HTA) online database : databases: may be useful to analyse the utility of a treatment of diagnostic techniques via the CRD database http://www.york.ac.uk/inst/crd/crddatabases.htm which gives acces to the NHS Economic Evaluation Database (NHS EED) and the Health Technology Assessment (HTA) Database or the Canadian Coordinating Office for Health Technology Assessment (CCOHTA) http://www.cadth.ca

   1.3 For research articles
   - Medline
   - Embase: more European and non-Anglo-Saxon articles; more about pharmacotherapy, psychiatry

3 Schünemann H J, Fretheim A, Oxman AD. Improving the use of research evidence in guideline development: 10. Integrating values and consumer involvement. *Health Research Policy and Systems* 2006, 4:22.

- Cochrane Central Register of Controlled Trials
- Other databases as appropriate, e.g.:
  - PsychINFO: psychological aspects
  - CINAHL: nursing and paramedical professions
  - Pedro : physiotherapy
  - International Pharmaceutical Abstracts : drugs
  - International Society of Drug Bulletins (Revue Prescrire, Drug and Therapeutics Bulletin, Geneesmiddelen Bulletin, etc…)

For areas where there are few or no good systematic reviews or randomised controlled trials, the search may be extended towards observational studies (recommended databases: Medline and Embase databases). This also applies when it is necessary to retrieve studies on adverse effects.

2. *Entries*

The goals and clinical questions normally already contain the most relevant search terms. Depending on the databases consulted, these terms have to be "translated" into the appropriate entries used by the particular database(s). The latter often contain proper search methods to define these terms (e.g. the MeSH database).

When listing terms, attention should be paid to possible synonyms and translations.

Resulting list:

Entry a
Entry b
Entry c
Entry …

3. *Time span*

- Define the time span within which will be searched for publications.
- The date of the last search performed, the so-called end date, should be explicitely reported.

4. *Language*

Unless explicitely stated otherwise by the multidisciplinary group of authors, searches will be restricted to the languages mastered by at least one of the authors
Standard:

- Dutch
- French
- German
- English

5. *Population*

Description of the patient population under study, e.g. human, age, sex, ...

6. *Setting / context of the health care system*

- Preferably search within settings / contexts of health care systems closely related to the Belgian health care system
- Depending on the question(s) at hand, deviations can be allowed (if relevant, explicitly state why)

3. Search strategy (step-by-step approach)

GUIDELINES
→ CLINICAL EVIDENCE
→ META-ANALYSIS & SYSTEMATIC REVIEWS
→ RESEARCH ARTICLES

3.1. Strategy for guidelines

1. *Guideline search according to the above defined criteria*

2. *Inventarisation of the found guidelines (end date version)*

   E.g. in an excel file, with the following structure
   - # GL: autonumbering guidelines
   - GL name: specific name guideline
   - GL origin: guideline developers (scientific organisation, government, industry... +/- name)
   - Country: country of guideline origin / coutry where GL applies; use ISO 3166 country codes: http://www.iso.org/iso/en/prods-services/iso3166ma/
   - GL-publi: most recent date of publication
   - GL-search date: date in GL until when references were searched (GL's own specific end date)
   - GL-language: published in which language
   - GL-www: direct link to website
   - GL-remarks: e.g. first publication year (original guideline), publication status

3. *Screening / selection method*

   a. STEP 1: **Reassess** if the found guidelines indeed answer to the above pre-defined criteria.
      i. If the title / summary indicates that a guideline definitely does not match one of the above criteria it is excluded.
      ii. When in doubt and/or unable to definitely exclude a guideline using the information in the title / summary, it is included.

   b. STEP 2: **Does the guideline, based on title and/or summary, potentially answers (a part of) the proposed clinical questions?**
      i. Three investigators will independently assess this, by scoring yes (+) or no (-). If no (-), the reason why should be documented.
      ii. Guidelines that score (+) at least twice, should be kept for further assessment.

4. *Critical appraisal*

   a. STEP 1: **Quality**
   To evaluate the methodological quality of the above selected guidelines the AGREE instrument [4] will be used. With this instrument 6 different domains are scored independently.

[4] The AGREE Collaboration. AGREE instrument 2001; available at http://www.agreecollaboration.org/

- **Scope and purpose** (items 1-3): concerned with the overall aim of the guideline, the specific clinical questions and the target patient population.
- **Stakeholder involvement** (items 4-7): the extent to which the guideline represents the views of its intended users.
- **Rigour of development** (items 8-14): the process used to gather and synthesise the evidence, the methods to formulate the recommendations and to update them.
- **Clarity and presentation** (items 15-18): the language and format of the guideline.
- **Applicability** (items 19-21): the likely organisational, behavioural and costs implications of applying the guideline.
- **Editorial independence** (items 22-23): the independence of the recommendations and acknowledgement of possible conflict of interest from the guideline development group.

Three investigators will independently score the different domains for each selected guideline. These scores will be discussed after which final scores will be assigned (consensus). This process will be documented by means of evidence tables.

The most qualitative guidelines will be kept (after consensus agreement within the group of authors).

The group of authors can thereby or therefore decide to attach more/less value to certain AGREE domains. If required, the reason why for the latter should be stated explicitely.

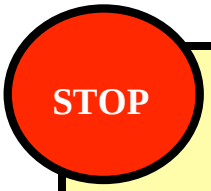
b. STEP 2: **Content**

From the selected qualitative guidelines a matrix with recommendations from these guidelines should be made.

Whenever available, the level of evidence (LeO) from each recommendation should be recorded as well.
The description of the (different) LeO system(s) used in the selected guidelines should subsequently also be documented (but not necessarily in the draft of the guideline).

Example of a matrix of recommendations.

Clinical question	**Guideline 1**		**Guideline 2**		**Guideline 3**		**Guideline ...**	
	Recomm.	LoE	Recomm.	LoE	Recomm.	LoE	Recomm.	LoE
Question 1	Recomm 1.1	LoE 1.1	Recomm 1.2	LoE 1.2	Recomm 1.3	LoE 1.3		
Question 2			Recomm 2.2	LoE 2.2				
Question 3	Recomm 3.1	LoE 3.1					Recomm 3. …	LoE 3. …
Question ...					Recomm … . 3	LoE … . 3		



ASSESS the MATRIX with RECOMMENDATIONS

"Is there a guideline that answers all the clinical questions asked?"

YES → Follow the final adaptation step below

NO → Is there one (or more) guideline(s) answering **some** of the clinical questions asked?

YES → Follow the final adaptation step below for these clinical questions

+ continue with the following search strategy for the remaining questions

NO → Continue with the following search strategy (= de novo development)

5. *Final adaptation step*

- Based on the ADAPTE procedure [5] (to be elaborated, in collaboration with the ADAPTE working group)
- Literature update.
  Whenever required, an additional search should be performed for relevant publications published ***after*** the publication of the guideline where the recommendation is taken from and ***before*** the date of the last search performed for this guideline-in-development.
  - Follow the methodology as described in this document
  - If present, consider the new evidence togheter with the existing evidence of the recommendation and agree, based on consensus within the group of authors, whether or not:
    - the recommendation should be changed (and if so, how)
    - the original assigned level of evidence for that recommmendation should be changed
    - *or* newly assign a GRADE level / recommendation (based on consensus) if no LoE was present.
- Levels for quality of evidence.
  - To allow a uniform system to be used, the different levels of evidence (LoE) of the above recommendations should be "translated" into the appropriate levels for quality of evidence of the adapted [6] GRADE system [7], resulting in either a HIGH, MODERATE or (very) LOW

[5] Fervers B, Burgers JS, Haugh MC, Latreille J, et al. Adaptation of clinical guidelines: literature review and proposition for a framework and procedure. *Int J Qual Health Care* 2006;18:167-76.

[6] Guyatt G, Gutterman DD, Baumann MH, et al. Grading strength of recommendations and quality of evidence in clinical guidelines: report from an American College of Chest Physicians Task Force. *Chest* 2006;129:174-81.

[7] http://www.gradeworkinggroup.org/index.htm

level of quality of evidence per recommendation.
- If no LoE was/were present, assign a GRADE level (based on consensus).

Example of recommendations with translated LoE's.

Clinical question	**Guideline 1**		
	Recomm.	LoE	GRADE
Question 1	Recomm 1.1	LoE 1.1	HIGH
~~Question 2~~			
Question 3	Recomm 3.1	LoE 3.1	LOW

- Strength of a recommendation.
  In order to assign the strength of a recommendation according to the GRADE system[7], resulting in a WEAK or a STRONG recommendation, some considerations should be made and/or answered before consenting on the strength of each of the recommendations:
  - Availability of the necessary expertise
  - Capability to overcome organisational barriers, if presenting
  - Necessary conditions to be met
  - Economical considerations
    - ≠ health economical analysis
    - = advantages / disadvantages / possible costs / …
  - Ability to extrapolate the recommendation to the population under study, if necessary

Example of completely GRADE'd recommendations.

Clinical question	**Guideline 1**			
	Recomm.	LoE	**GRADE**	
			(final) Quality of Evidence	Strength of Recommend.
Question 1	Recomm 1.1	LoE 1.1	HIGH	WEAK
~~Question 2~~				
Question 3	Recomm 3.1	LoE 3.1	LOW	STRONG

3.2. Strategy for Clinical Evidence

1. *Search the Clinical Evidence database according to the above defined criteria*

2. *Inventarisation*

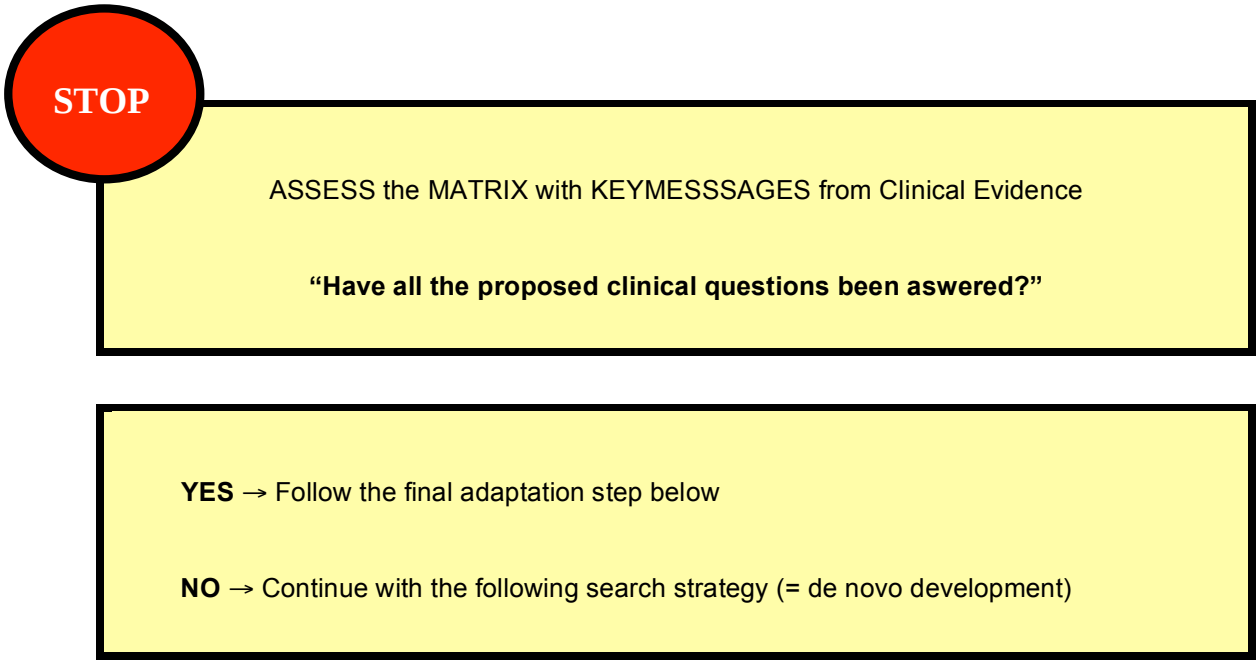
3. *Screening / selection*

   a. STEP 1: **Reassess** if the found evidence indeed answer to the above pre-defined criteria.
      i. If the title / summary indicates that the evidence definitely does not match one of the above criteria it is excluded.
      ii. When in doubt and/or unable to definitely exclude evidence using the information in the title / summary, it is included.

   b. STEP 2: **Does the evidence, based on title and/or summary, potentially answers (a part of) the proposed clinical questions?**
      i. Three investigators will independently assess this, by scoring yes (+) or no (-). If no (-), the reason should will be documented.
      ii. Evidence that scores (+) at least twice, should be kept for further assessment.

4. *Critical appraisal*

   a. The method by which the topics in the Clinical Evidence database have been assessed and appraised, is extensively described on the Clinical Evidence website (www.clinicalevidence.org: "How BMJ Clinical Evidence is put together"). As this method closely relates to the own methodology, the group of authors
      i. decided to adopt this method, implying that no additional critical appraisal will be done for the selected clinical evidence topics
      ii. unless specifically stated otherwise by the authors (with documention of the reason why).
   b. From the selected clinical evidence topics, a matrix with keymessages answering the above (remaining, unanswered) clinical questions should be made.



5. *Final adaptation step*

- Based on the ADAPTE procedure[8] (to be elaborated, in collaboration with the ADAPTE working group)
- Literature update.
  Whenever required, an additional search should be performed for relevant publications ***after*** the publication of the clinical evidence topic where the keymessage is taken from and ***before*** the date of the last search performed for this guideline-in-development.
  - Follow the methodology as described in this document
  - If present, consider the new evidence togheter with the existing evidence of the recommendation and agree, based on consensus within the group of authors, whether or not:
    - the recommendation should be changed (and if so, how)
    - the original assigned level of evidence for that keymessage should be changed
    - *or* newly assign a GRADE level / recommendation (based on consensus) if no LoE was present.
- Levels for quality of evidence.
  - If necessary "translate" the original LoE into the appropriate levels for quality of evidence of the GRADE system, resulting in either a HIGH, MODERATE or (very) LOW level of quality of evidence per recommendation
  - If no LoE was/were present, assign a GRADE level (based on consensus).
- Strength of a recommendation.
  In order to assign the strength of a recommendation according to the GRADE system, resulting in a WEAK or a STRONG recommendation, some considerations should be made and/or answered before consenting on the strength of each of the keymessages:
  - Availability of the necessary expertise
  - Capability to overcome organisational barriers, if presenting
  - Necessary conditions to be met
  - Economical considerations
    - ≠ health economical analysis
    - = advantages / disadvantages / possible costs / …
  - Ability to extrapolate the keymessage to the population under study, if necessary

3.3. Strategy for Meta-analyses & Systematic Reviews

1. *Search according to the above defined criteria*

2. *Inventarisation*

   Use e.g. Endnote library or RefMan

3. *Screening / selection*

   a. <u>STEP 1</u>: **Reassess** if the found publications indeed answer to the above pre-defined criteria.
      i. If the title / summary indicates that a publication definitely does not match one of the above criteria it is excluded.
      ii. When in doubt and/or unable to definitely exclude a publication using the information in the title / summary, it is included.

[8] Fervers B, Burgers JS, Haugh MC, Latreille J, et al. Adaptation of clinical guidelines: literature review and proposition for a framework and procedure. *Int J Qual Health Care* 2006;18:167-76.

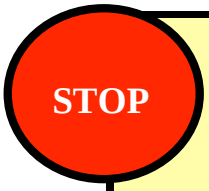
b. STEP 2: Does the publication, based on title and/or summary, potentially answers (a part of) **the proposed clinical questions?**
   i. Three investigators will independently assess this, by scoring yes (+) or no (-). If no (-), the reason why should be documented.
   ii. Publications that score (+) at least twice, should be kept for further assessment.

4. *Critical appraisal*

To further assess the selected publications the appropriate Cochrane checklists (available at http://www.cochrane.nl/index.html) should be used.
This process will be documented by means of evidence tables.

5. *Summary of findings: evidence table(s)*

a. Evidence tables should be constructed based on the above Cochrane checklists or –if accessible– by using the GRADE Working Group software (http://www.gradeworkinggroup.org/index.htm)
b. Next step:
   i. Categorize the conclusions per clinical question answered
   ii. Record the different levels of evidence (LoE) of these conclusions / recommendations (if present)



ASSESS the EVIDENCE TABLE(s) of the MA & SR

"Have all the proposed clinical questions been aswered?"

YES → Follow the final adaptation step below

NO → Continue with the following search strategy

(= complete de novo development)

6. *Final adaptation step*

- Based on the ADAPTE procedure [9] (to be elaborated, in collaboration with the ADAPTE working group)
- Literature update.
  Whenever required, an additional search should be performed for relevant publications published ***after*** the publication of the meta-analysis / systematic review where the recommendation is taken from and ***before*** the date of the last search performed for this guideline-in-development.
  - Follow the methodology as described in this document
  - If present, consider the new evidence togheter with the existing evidence of the keymessage and agree, based on consensus within the group of authors, whether or not:
    - the keymessage should be changed (and if so, how)

[9] Fervers B, Burgers JS, Haugh MC, Latreille J, et al. Adaptation of clinical guidelines: literature review and proposition for a framework and procedure. *Int J Qual Health Care* 2006;18:167-76.

        - the original assigned level of evidence for that keymessage should be changed
        - *or* newly assign a GRADE level / recommendation (based on consensus) if no LoE was present.
- Levels for quality of evidence.
    - If necessary "translate" the original LoE into the appropriate levels for quality of evidence of the GRADE system, resulting in either a HIGH, MODERATE or (very) LOW level of quality of evidence per recommendation
    - If no LoE was/were present, assign a GRADE level (based on consensus).

- Strength of a recommendation.
  In order to assign the strength of a recommendation according to the GRADE system, resulting in a WEAK or a STRONG recommendation, some considerations should be made and/or answered before consenting on the strength of each of the recommendations:
    - Availability of the necessary expertise
    - Capability to overcome organisational barriers, if presenting
    - Necessary conditions to be met
    - Economical considerations
        - ≠ health economical analysis
        - = advantages / disadvantages / possible costs / …
    - Ability to extrapolate the recommendation to the population under study, if necessary

3.4. Strategy for Research articles

1. *Search according to the above defined criteria*

2. *Inventarisation*

   Use e.g. Endnote library / RefMan

3. *Screening / selection*

   a. Does the evidence, based on title and/or content, potentially answers (a part of) the proposed clinical questions?
   b. Three investigators will independently assess this, by scoring yes (+) or no (-). If no (-), the reason why will be documented.
   c. Evidence that scores (+) at least twice, will be kept for further assessment.

4. *Critical appraisal*

   To further assess the selected publications the appropriate Cochrane checklists (available at http://www.cochrane.nl/index.html) should be used. This process will be documented by means of evidence tables.

5. *Summary of findings: evidence table(s)*

   a. Evidence tables should be constructed based on the above Cochrane checklists or –if accessible– by using the GRADE Working Group software (http://www.gradeworkinggroup.org/index.htm)
   b. Next step:
      i. Categorize the conclusions per clinical question answered
      ii. Formulate recommendations

6. *Final adaptation step*

   a. Levels for quality of evidence.
   Assign an appropriate level per recommendation according to the GRADE system (HIGH, MODERATE or (very) LOW level of evidence per recommendation), based on consensus by the group of authors.

b. Strength of a recommendation.
In order to assign the strength of a recommendation according to the GRADE system, resulting in a WEAK or a STRONG recommendation, some considerations should be made and/or answered before consenting on the strength of each of the recommendations:
- Availability of the necessary expertise
- Capability to overcome organisational barriers, if presenting
- Necessary conditions to be met
- Economical considerations
  - ≠ health economical analysis
  - = advantages / disadvantages / possible costs / …
- Ability to extrapolate the recommendation to the population under study, if necessary

UPDATING of GUIDELINES

Process

1. Updating should be performed yearly, unless otherwise stated by the authors
2. The above described methodology for literature search (search criteria and strategy) should be followed.
   - BEWARE: Time span of the update literature search: one year after the end date of the literature search of the previous version / update and the start of the new update.

REVIEWING of GUIDELINES

Process

1. Reviewing should be performed every 5 years, unless otherwise stated by the authors
2. Reviewing includes the critical assessment of the goals and clinical questions, if necessary these should be adjusted and/ or relevant topics should be added
3. The above described methodology for literature search (search criteria and strategy) should be followed.
   - BEWARE: Time span of the review literature search: between the end date of the literature search of the previous publication of the guideline and the start of the review.