ERKNet
The European Rare Kidney Disease Reference Network

european society for paediatric nephrology

IPNA

Type and quality of a new guideline

- The potential benefits of practice guidelines are only as good as the quality of the practice guidelines themselves.
- High level of quality & strength (usually based on large RCTs) → Guidelines
- Fair / poor level of quality & strength → Clinical Practice Recommendations(CPR) or Consensus Papers
- Poor guideline development process → Poor Guideline or Recommendation

Practical Organization of Clinical Practice Recommendations (SOP)

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Methodology

- Pragmatic & standardized approach (SOP available online)
- Focus on clinical usefulness
- Suggestions will be made where there is no RCT to guide evidence based practice
- Use the **GRADE** method (e.g. define **PICO questions**) & follow the recommendations of the **Right Statement** (checklist)
- Set a schedule & adapt it during the process
- Goal: finish guideline within 1 year (otherwise it is outdated by the time of publication)

RESEARCH AND REPORTING METHODS Annals of Internal Medicine

A Reporting Tool for Practice Guidelines in Health Care: The RIGHT Statement

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The quality of reporting practice guidelines is often poor, and there is no widely accepted guidance or standards for such reporting in health care. The international RIGHT (Reporting Items for practice Guidelines in HealThcare) Working Group was established to address this gap. The group followed an existing framework for developing guidelines for health research reporting and the EQUATOR (Enhancing the QUAlity and Transparency Of health Research) Network approach. It developed a checklist and an explanation and elaboration statement. The RIGHT checklist includes 22 items that are considered essential for good reporting of practice guidelines: basic information (items 1 to 4), background (items 5 to 9), evidence (items 10 to 12), recommendations (items 13 to 15), review and quality assurance (items 16 and 17), funding and declaration and management of interests (items 18 and 19), and other information (items 20 to 22). The RIGHT checklist can assist developers in reporting guidelines, support journal editors and peer reviewers when considering guideline reports, and help health care practitioners understand and implement a guideline.

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† Members of the RIGHT Working Group are listed in **Appendix 1** (available at www.annals.org); their contributions are listed in **Appendix 2** (available at www.annals.org).

Table. RIGHT Checklist

Evidence		
Health care questions	10a	State the key questions that were the basis for the recommendations in PICO (population, intervention, comparator, and outcome) or other format as appropriate.
	10b	Indicate how the outcomes were selected and sorted.
Systematic reviews	11a	Indicate whether the guideline is based on new systematic reviews done specifically for this guideline or whether existing systematic reviews were used.
	11b	If the guideline developers used existing systematic reviews, reference these and describe how those reviews were identified and assessed (provide the search strategies and the selection criteria, and describe how the risk of bias was evaluated) and whether they were updated.
Assessment of the certainty of the body of evidence	12	Describe the approach used to assess the certainty of the body of evidence.
Recommendations		
Recommendations	13a	Provide clear, precise, and actionable recommendations.
	13b	Present separate recommendations for important subgroups if the evidence suggests that there are important differences in factors influencing recommendations, particularly the balance of benefits and harms across subgroups.
	13c	Indicate the strength of recommendations and the certainty of the supporting evidence.
Rationale/explanation for recommendations	14a	Describe whether values and preferences of the target population(s) were considered in the formulation of each recommendation. If yes, describe the approaches and methods used to elicit or identify these values and preferences. If values and preferences were not considered, provide an explanation.
	14b	Describe whether cost and resource implications were considered in the formulation of recommendations. If yes, describe the specific approaches and methods used (such as cost-effectiveness analysis) and summarize the results. If resource issues were not considered, provide an explanation.
	14c	Describe other factors taken into consideration when formulating the recommendations, such as equity, feasibility, and acceptability.
Evidence to decision processes	15	Describe the processes and approaches used by the guideline development group to make decisions, particularly the formulation of recommendations (such as how consensus was defined and achieved and whether voting was used).
Review and quality assurance		
External review	16	Indicate whether the draft guideline underwent independent review and, if so, how this was executed and the comments considered and addressed.
Quality assurance	17	Indicate whether the guideline was subjected to a quality assurance process. If yes, describe the process.

Continued on following page

Table–Continued

Section/Topic	Number	Item
Funding and declaration and management of interests		
Funding source(s) and role(s) of the funder	18a	Describe the specific sources of funding for all stages of guideline development.
	18b	Describe the role of funder(s) in the different stages of guideline development and in the dissemination and implementation of the recommendations.
Declaration and management of interests	19a	Describe what types of conflicts (financial and nonfinancial) were relevant to guideline development.
	19b	Describe how conflicts of interest were evaluated and managed and how users of the guideline can access the declarations.
Other information		
Access	20	Describe where the guideline, its appendices, and other related documents can be accessed.
Suggestions for further research	21	Describe the gaps in the evidence and/or provide suggestions for future research.
Limitations of the guideline	22	Describe any limitations in the guideline development process (such as the development groups were not multidisciplinary or patients' values and preferences were not sought), and indicate how these limitations might have affected the validity of the recommendations.

RIGHT = Reporting Items for practice Guidelines in HealThcare.

12 Steps in guideline development

1. Select the topic & define the population covered (1 coordinator)
2. Define type of guideline: consensus paper – CPR – (guideline)
3. Define working groups for guideline preparation:
   - Core group: approx. 10 members; include all specialities needed; include a patient representative; Try to balance between countries/centers within ERKNet; Associate experts from other ERNs or other Scientific societies if needed
   - External expert group: preferentially from European Networks or Societies
   - Voting group: ERKNet and other WGs, e.g. ESPN WGs
4. Ask the right questions – selecting the right outcomes
   - Define PICO questions
   - Each question gets allocated to a subgroup of 2-4 core group members

Steps 1-4 may be done within a 2-3 hour face to face meeting

Asking the right questions

Are speeding cameras good?

- Depends on what is meant by good...
- Speeding tickets can be good for
  - reducing traffic accidents
  - reducing damage from accidents
  - reducing human damage from accidents
  - increase tax income

→ Not everyone values these outcomes the same way...

PICO Questions

The P.I.C.O. Model for Clinical Questions

P	**P**atient, **P**opulation, or **P**roblem	How would I describe a group of patients similar to mine?
I	**I**ntervention, Prognostic Factor, or Exposure	Which main intervention, prognostic factor, or exposure am I considering?
C	**C**omparison or Intervention (if appropriate)	What is the main alternative to compare with the intervention?
O	**O**utcome you would like to measure or achieve	What can I hope to accomplish, measure, improve, or affect?
	What **T**ype of question are you asking?	Diagnosis, Etiology/Harm, Therapy, Prognosis, Prevention
	Type of **S**tudy you want to find	What would be the best study design/methodology?

PICO Questions
Example

What duration of prednisone should a child receive in the initial episode of NS?

- **Patient (or Population) to whon the recommendation will apply:**
  Children ages 1-18 years with newly diagnoses idiopathic NS
- **Intervention being considered:**
  Prednisone 60 mg/m2 for 2 months
- **Comparison (which may be "no action" or an alternative intervention):**
  Prednisone 60 mg/m2 for more than 2 months
- **Outcomes affected by the intervention:**
  Time to remission, time to relapse, number with FRNS/SDNS by 2 yrs…

- Type of question: treatment
- Type of study design RCTs

12 Steps in guideline development

5. Systematic literature review (RCTs, non-controlled / observational studies)
   - Prepare evidence tables
   - Check for risk of bias for an outcome in individual studies
   - Check for quality of evidence for each outcome across studies
   - Epidemiological support will provided by ERKNet
6. Plan a one-day face to face meeting (support by ERKNet)
   - Half day meeting may be fine for consensus papers
7. Before the meeting: subgroups are requested to prepare a preliminary answer & evidence text for each PICO question. This should be as concise and brief as possible (<1 page)
8. At the meeting:
   - Formulate recommendations & evidence text
   - During this process new (sub)questions may arise
   - Grade recommendations (AAP system)

12 Steps in guideline development

9. Editing of draft by core group (within 3 months)
10. Draft sent out to external experts & voting group (4 week deadline)
    - Delphi process for grading and changes
11. Consider to endorse the guideline by other ERNs or Societies before submission
12. Publication ☺

Thereafter: Distribution & Implementation

Grading of the recommendations

Strength of recommendation

Aggregate evidence quality	Benefit or harm predominates	Benefit and harm balanced
Level A • Intervention: well-designed and conducted trials, meta-analyses on applicable populations • Diagnosis: independent gold-standard studies of applicable populations	Strong recommendation	Weak recommendation (based on balance of benefit and harm)
Level B Trials or diagnostic studies with minor limitations; consistent findings from multiple observational studies	Moderate recommendation	
Level C Single or few observational studies or multiple studies with inconsistent findings or major limitations		
Level D Expert opinion, case reports, reasoning from first principles	Weak recommendation (based on low-quality evidence)	No recommendation may be made
Level X Exceptional situations where validating studies cannot be performed and benefit or harm clearly predominates	Moderate recommendation / Strong recommendation	

American Academy of Pediatrics Grading Matrix

Phrasing the recommendations

Choose your words

- 1-2 (4) concice phrases with clear recommendation (specify patient group & situtation)
- Short paragraphs to explain rationale (whole sentences if possible)
- Mention level of evidence where possible

➢ Please write independent paragraphs

➢ Be creative with your agenda

Phrasing the recommendations

- Imperative recommendations

  "genetic testing must not be performed without consent"

- Strong recommendations
  - We recommend….
  - …should be performed

- Weaker recommendations
  - We suggest…
  - …consider the treatment with…

Aggregate evidence quality	Benefit or harm predominates	Benefit and harm balanced
Level A • Intervention: well-designed and conducted trials, meta-analyses on applicable populations • Diagnosis: independent gold-standard studies of applicable populations	Strong recommendation	Weak recommendation (based on balance of benefit and harm)
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Level C Single or few observational studies or multiple studies with inconsistent findings or major limitations		
Level D Expert opinion, case reports, reasoning from first principles	Weak recommendation (based on low-quality evidence)	No recommendation may be made
Level X Exceptional situations where validating studies cannot be performed and benefit or harm clearly predominates	Strong recommendation Moderate recommendation	

Phrasing your rational

- Cite studies rather than reviews
- Good to refer to existing recommendations

Suggestion for further research

- Collect as you go along
- Prioritize at the end

Plain English

- **Avoid** 'may' and 'can'
- **Avoid** general statements: 'is recommended', 'is useful/helpful', 'is needed', 'treatment options include'
- **Avoid** ambigiuous phrases: 'clinically appropriate', 'if necessary'
- **Use an active verb** that tells reader what they should do , and indicate the strength of recommendation

- 'intervention X may be offered' → 'consider the intervention'
- 'intervention X is recommended' → 'offer the intervention'
- 'intervention X is helpful' → 'offer the intervention' or 'consider the intervention'

Example

4. Treatment schedule for GH therapy and monitoring

Recommendation:

1.We recommend that GH should be given at doses of 0.045 to 0.05 mg/kg body weight per day by subcutaneous injections in the evening (grade B, moderate recommendation).

2.We recommend both GH reference and GH biosimilar products for use in short children with CKD (grade B, moderate recommendation).

3.We suggest three to six monthly clinic visits to monitor stature, height velocity, pubertal development, skeletal maturation on wrist X-ray, renal function, thyroid hormone levels, serum glucose, calcium, phosphate, bicarbonate, and PTH levels (grade D, weak recommendation).

4.If height velocity in the first year of GH treatment is less than 2 cm/year over baseline, we recommend to assess patient adherence to GH therapy including measurement of serum IGF-I levels, weight-adjusted GH dosage and nutritional and metabolic factors, as recommended before initiation of GH therapy (grade B, moderate recommendation).

5.We recommend stopping GH when the patient reaches his genetic target height, when epiphyseal closure is demonstrated, at the time of renal transplantation and when the patient does not adequately respond to GH treatment despite optimal nutritional and metabolic control (grade B, moderate recommendation).

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Example

Evidence and rationale:

GH dosage

The GH dosage used in the available RCTs and observational studies was 28-30 IU/m^2/week (equivalent to 0.045 to 0.05 mg/kg/day) by daily subcutaneous injections (**Suppl. tables 4-6**).

Six RCTs [29,44,64,69,70,71,72,73,74,75] compared doses of 14 IU/m^2/week (equivalent to 0.023 mg/kg/day) to 28 IU/m^2/week (5 studies) [76,77,78,79,80] or 28 IU to 56 IU/m^2/week (equivalent to 0.09 mg/kg/day; 1 study) [61]. A recent meta-analysis demonstrated that in the 28 IU/m^2/week group increase in height velocity was 1.18 cm/year (95% CI 0.52 to 1.84) higher compared to the 14 IU/m^2/week group and height velocity SDS after one year of treatment was

1.48 higher (95% CI 0.03 to 2.93) [43]. In the one study comparing 28 IU/m^2/week with 56 IU/m^2/week no significant difference between groups in the mean height SDS change and mean height velocity was shown. Therefore, we recommend a dosage of 0.045 to 0.05 mg/kg/day, with dose adjustment according to body weight on regular intervals.

Frequency of administration

In healthy controls as well as in patients with GH deficiency, bioavailability of GH after subcutaneous injection is around 80%, independent of sex. T_{max} is 3 to 6 hours, and half-life 2 to 3 hours according tot he data provided fort he US Food and Drug Administration (FDA) [81].

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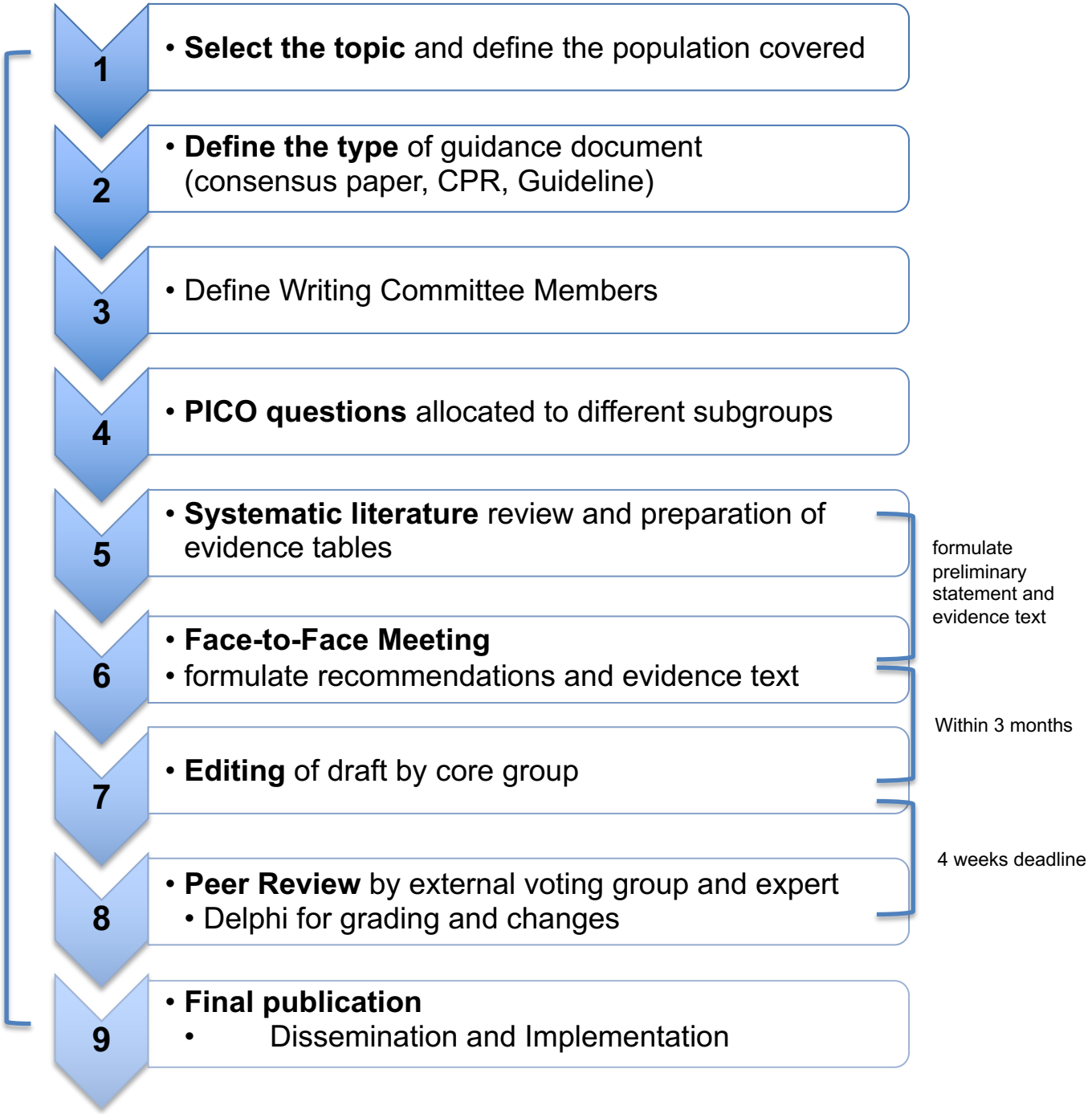
1
• Select the topic and define the population covered
2
• Define the type of guidance document (consensus paper, CPR, Guideline)
3
• Define Writing Committee Members
4
• PICO questions allocated to different subgroups
5
• Systematic literature review and preparation of evidence tables
6
• Face-to-Face Meeting
• formulate recommendations and evidence text
7
• Editing of draft by core group
8
• Peer Review by external voting group and expert
• Delphi for grading and changes
9
• Final publication
• Dissemination and Implementation
formulate preliminary statement and evidence text
Within 3 months
4 weeks deadline