

## 5. Materials and methods

---

Despite an increase in the number of publications of CPG (clinical practice guidelines), it is well known that the recommendations contained therein are not followed and often fail to become integrated in daily clinical practice. Moreover, many of them continue to be based on non-systematic reviews of the literature and on the opinions of “experts” or “authorities” on the subject, without specifying the criteria upon which the recommendations are decided.

With the development of the concepts of evidence-based medicine, more structured and explicit methods have been set up to elaborate these guidelines, with recommendations that are linked to scientific evidence.

The Institute of Medicine<sup>36</sup> defined CPGs as a set of recommendations that is systematically developed to aid physicians and patients in decision-making as to the best care for his/her specific clinical condition. It also proposed the main features that guidelines should have in order to enhance their possibilities of being scientifically rig-

orous and useful, so that they can truly aid in achieving the desired outcomes in patients' health: the four content-related features of the guidelines (scientific validity, reproducibility, clinical applicability, and flexibility), and four that have to do with the process of development and presentation (clarity, multi-disciplinary process, scheduled revision, and explicit presentation of the documentation used).

Many CPG quality rating instruments that have been subsequently elaborated have maintained most of these features, adding implementation strategies, their implications, and the evaluation of the process, as stated in the AGREE project<sup>37</sup>.

This guide for clinical practice seeks to provide an answer to the problem of PMNE in childhood. It is structured in two basic sections (diagnosis and treatment), with a summary of the evidence on which specific recommendations are made. The choice of the problem to be addressed is based on the low level of diagnosis and treatment for this condition in Primary Care pediatrics. It at-

tempts to contribute to improving the quality of care and outcomes in patients, to the extent that the recommended procedures and decisions have demonstrated their effectiveness both empirically and on the basis of sound scientific evidence.

In doing the recommendations, the guidelines have focused mainly on diagnosis and the clinical effectiveness of the different treatments. We have taken into account the fact that the recommendations should be applicable in Primary Care. The cost of the interventions has not been assessed.

### **Formulation of clinical questions**

- The clinical questions were clearly defined and all alternatives to the decision and expected outcomes were identified.
- All existing evidence was located systematically, then evaluated critically, and classified according to evidence-based medicine<sup>38</sup> criteria, summarizing the best scientific evidence on each aspect.
- Each of the decision points was identified where it was necessary to integrate this valid evidence with the clinician's expertise and patient preferences. Hence, the present guide is not of a regula-

tory nature, it sets out to accurately identify the range of potential decisions and to provide evidence that, together with clinical judgment, patient values and expectations, and the center's conditions, should make it easier to make the most appropriate decision in each case.

The authors identified areas of uncertainty regarding associated factors, diagnosis, and treatment of PMNE.

### **Questions identified**

The areas of uncertainty were specified in the following questions:

#### **Risk factors associated with enuresis**

1. Is there any physical condition that is associated with PMNE?
2. Is there any psychiatric condition that is associated with PMNE?

#### **Diagnosis**

1. Does a urine culture or dipstick urinalysis need to be performed on all children with PMNE seeking care at the Healthcare Center?
2. Do other diagnostic tests need to be carried out in children with PMNE seeking care at the Healthcare Center?

## Treatment

1. How efficacious is behavioral therapy?
2. How efficacious is alarm behavioral therapy for enuresis?
3. How efficacious is drug treatment with desmopressin?
4. Have risk factors for treatment failure been described for the different treatments?

## Follow-up:

1. For how long should treatment be continued?
2. What is the most effective treatment withdrawal guideline?
3. What are the indications for referral to an urologist?

## Systematic strategy for the bibliographic search

The systematic review of the literature only covered studies reported in Spanish, English and French. Searches were made in:

### A) Secondary sources of information:

Major:

1. Cochrane Collaboration
2. Clinical practice guides:
  - Centers that prepare CPGs:

*American Academy of Pediatrics, New Zealand Guidelines Group, Cincinnati Children's Hospital Medical Center.*

– CPG storage centers:

*National Guidelines Clearinghouse, CMA Infobase, Primary care Clinical Practice Guidelines, NeLH Guideline Finder.*

3. Reports by Health Technology Assessment Agencies: Health Technology Assessment Database-HTA.

Minor:

4. Journals with structured abstracts: ACP Journal Club, Clinical Evidence on line, Bandolier.
5. Files of critically appraised topics: AEPap, CATs.

Global:

6. EBM databases: TRIP/SUMSearch and The Database of Abstracts of Reviews of Effectiveness-DARE).

### B) Primary sources of information:

1. Traditional bibliographic databases: Medline with its electronic version PubMed, Embase, IME.
2. Traditional medical journals.
3. Textbooks.

### C) Grey literature / manual search

### **Selection criteria (inclusion-exclusion)**

Studies were selected according to the following criteria in the searches:

- They should deal with children and adolescents. PubMed goes up to 18 years of age (in exceptional cases, and when there was no data exclusively obtained on children and adolescents, we have accepted mixed inclusion with adults, with explicit reference made in the text).
- They should deal with PMNE.
- Outpatient setting:

If specific information was not available according to these criteria, studies with general criteria were included, e.g.: hospital setting, different types of enuresis..., but this was always specified in the results.

- Quality criteria: The highest quality articles have always been selected on each aspect evaluated.

Any content whose scientific evidence was insufficient is referred to explicitly. In these cases, a recommendation was reached by consensus on the basis of standard of care in our setting.

The authors decided to use the “Centre for Evidence-Based Medicine (CEBM) of Oxford”<sup>38</sup> classification to grade the evidence (Annex 1). We considered there were potentially clinical differences with the target population of our guidelines when the studies scenario wasn’t the community but rather the hospital or any other scenario different from Primary Care, or if they included a type of enuresis different from PMNE. In this case we applied the extrapolation criterion to graduate recommendations.

- Years of searches: Searches were made in databases from the lower limit of each one up to August 2004.

## **Types of studies included**

---

### **Studies of associated factors in PMNE**

- Systematic reviews.
- Cohort studies.
- Case-control studies.
- Case studies.
- Population surveys.

### **Diagnostic studies**

- Validation of diagnostic tests.
- Systematic reviews.
- Cohort studies.
- Case-control and cross-sectional studies.

### **Treatment studies**

- Systematic reviews and meta-analyses.
- Controlled clinical trials.
- Cohort and case-control studies.
- Case studies.

## **Timeline of the elaboration of the guidelines**

---

The working meetings took place from January 2004 to May 2005, approximately every two weeks and outside of working hours. The external review took place between January and February 2005 and the assessment of applicability to Primary Care is still pending completion.

## **Declaration of conflicts of interest**

---

All authors work for the Agencia Valenciana de Salud (Valencian Regional Government Health Authority) of the Generalitat Valenciana (Valencian Regional Government). They have no relationship whatsoever with private commercial entities involved in the treatment of enuresis nor have they received any external public or private assistance in relation to these guidelines. These guidelines have been promoted and carried out by the authors without any external financial support.