Guidelines, evidence, and cultural factors

Comparison of four European guidelines on uncomplicated cystitis

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Objectives – To compare four recent guidelines on uncomplicated cystitis and to examine how cultural factors may have affected recommendations. Design – Descriptive study with a qualitative analysis of authors’ reasons for recommendations. Material – Guidelines for general practitioners published 1999–2000 from Germany, The Netherlands, Norway, and Belgium on diagnosis and treatment of uncomplicated cystitis. Opinions of the guideline authors on the influence of local factors on the recommendations were collected before and after feedback on the differences between the guidelines. Results – Few cited references were shared between the guidelines, and recommendations differed substantially, especially on diagnostic strategies and referral criteria. The authors attributed parts of the differences to local factors. German and Belgian authors stressed the need for safety in their diagnostic and therapeutic approach, while Dutch authors felt confident in their gatekeeper role and the Norwegian authors mainly relied on “the evidence”. German and Belgian authors perceived patients to hold power, German authors referred to the power of the sub-specialists, while the Norwegians aimed to share power with the patient through a patient-centred approach. Conclusion – There are substantial differences even between high-standard guidelines on the same well-defined clinical entity. The selection of literature data, and diagnostic and therapeutic recommendations, seemed to be influenced by such cultural aspects as habits, the patient’s expectations, and the structure of the healthcare system.

Key words: cystitis, guidelines, general practice, uncomplicated lower urinary tract infection.

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In this study we compared these four guidelines, and aimed at describing how the authors perceived the influence of cultural factors in their guidelines.

MATERIAL AND METHODS
We selected four recent North European guidelines for general practice targeting similar populations: adult women with uncomplicated cystitis. The guidelines

Evidence-based guidelines have been developed in several countries to assist GPs in daily practice.

- Cultural factors play a role in clinical decision-making. This study demonstrates that authors of guidelines are often not aware of these cultural influences.
- Once confronted with differences between guidelines from other countries, the guidelines’ authors provide scientific arguments as well as cultural arguments.
- Differences in selection of evidence between guidelines are striking and need more research.
were published in 1999 in Germany and The Netherlands (11,12) and in 2000 in Norway and Belgium (13,14). All guidelines were developed by professional organizations for general practitioners.

We compared the references used in the guidelines as well as the specific recommendations on diagnosis and treatment. The authors were asked by e-mail how they perceived the influence of cultural factors in their guidelines (“Which cultural influences influenced (a) the process of guideline development, (b) the formulation of the concrete diagnostic, and (c) the therapeutic strategy recommended in the guideline?”). After having received the answers to these questions, we confronted the authors with the differences between the guidelines, and asked them again whether and to what extent these differences could be attributed to cultural factors. One of us (TC) was the first author of the Belgian guideline. Therefore we sent the questionnaires to the second author of this guideline.

In the questionnaire, cultural factors were defined as “a mixture of beliefs of patients and practitioners, local habits, the influence of medical experts from hospital-based disciplines, expectations of patients, historical evolutions in medical practice, and organization of care”. We have used the concept taking the same meaning in the following text.

Analysis
Differences in the guidelines are described. The authors’ explanations for differences between the guidelines were analysed qualitatively using a pragmatic approach to Giorgi’s phenomenological method as modified by Malterud (16). The resulting categories are presented.

RESULTS
A comparison of the number of references and their overlap is presented in Table I. Of the 205 literature citations, only 7 were shared between 3 guidelines, and only 1 by all 4 guidelines. More references were shared in the therapeutic sections than in the diagnostic sections.

The diagnostic recommendations varied from no further examination in patients with suggestive symptoms to always combining illness history with urinalysis by use of chemical strip testing or microscopic examination (Table II). Even the same diagnostic tests were interpreted differently with important consequences in the proportion of women labelled as having cystitis.

The drug choice was in agreement in three guidelines but with different dosage schedules (see Table II). The Norwegian guideline did not select a first-choice drug. Referral strategies also varied. The German guideline advocated referral of all women with recurrence of symptoms, while other guidelines recommended referral only if complicating factors are suspected (B), or if prophylactic therapy failed (NL).

Authors’ explanations for differences between the guidelines could by qualitative analysis be broken down to the following three concepts.

Need for safety
Both German and Belgian authors stressed the need for safety, i.e. not missing diagnoses, and the need for adherence to local procedures even if they are not fully evidence based. Norwegian authors feel confident in relying on evidence, whereas Dutch authors build their confidence on their key role in the healthcare system.

... the need to exclude even far-fetched, but potentially serious differential diagnoses. (G)

... a general practitioner can not miss a diagnosis. (B)

... there has been quite a great resistance against the recommendation to ... (but) our recommendations are based on systematic search of evidence. (N)

... guideline development by GPs for GPs. (NL)

Who is perceived as holding power?
German authors described how (sub-)specialists and their traditions of being on the safe side strongly influenced the content of the guideline. In contrast, the Dutch authors claimed that the general practitioners are confident in their contact with patients, provided that they treat their patients fast and efficiently. The Belgian authors aimed at anticipating patients’ reactions in their guideline, while the Norwegian authors believed that evidence-based recommendations might facilitate shared decision-making.

... we needed to deal with both the consensus requirement (with) and the open access to specialists. (G)
patients can consult without referral a specialist. This is a very sensitive item with general practitioners and patients (B).

I personally think it is important ... (in the case of uncertainty) ... to give the patients an opportunity to participate in the decision-making. (N)

Best evidence for which decision? Between the countries there were distinct differences in which recommendations based on “best evidence” were made by authors. While the Norwegian authors advocated the possibility of no treatment as an alternative to discuss with the patient, the other authors discarded this possibility.

We do not have obvious evidence to support a statement that all uncomplicated UTIs should be treated by antimicrobials. (N)

There is no evidence that favours non-treatment. Treatment is relatively harmless and cheap, and people do have complaints. (NL)

Why would she go to the doctor if she doesn’t want treatment? (G) [In the patients’ view] if a disease is not cured immediately, it is the fault of the doctor, more than the natural history of the disease. (B)

Three guidelines (N, NL, B) reported sufficient evidence for advocating self-initiated treatment for patients with recurrent cystitis. German and Belgian

Table II. Diagnostic and therapeutic strategies advised in the 4 GP guidelines on uncomplicated lower urinary tract infections.

<table>
<thead>
<tr>
<th>Germany</th>
<th>Netherlands</th>
<th>Norway</th>
<th>Belgium</th>
</tr>
</thead>
<tbody>
<tr>
<td>DIAGNOSIS</td>
<td>Symptoms + urinalysis</td>
<td>Symptoms + urinalysis</td>
<td>Symptoms ONLY</td>
</tr>
<tr>
<td>Urine sample:</td>
<td>Urine sample:</td>
<td>Urine sample:</td>
<td>Urine sample:</td>
</tr>
<tr>
<td>No midstream, no cleansing, spread labia</td>
<td>Midstream, no cleansing, spread labia</td>
<td>NO Urine sample</td>
<td>Midstream, no cleansing, spread labia</td>
</tr>
<tr>
<td>Urinalysis:</td>
<td>Urinalysis:</td>
<td>NO Urinalysis</td>
<td>Urinalysis:</td>
</tr>
<tr>
<td>→ Stick: Nitrite AND LE</td>
<td>→ Stick Nitrite (N)</td>
<td>N Pos → UTI</td>
<td>N Neg → LE-test</td>
</tr>
<tr>
<td>N AND LE Pos → UTI</td>
<td>N Pos → UTI</td>
<td>N Neg → Dipslide culture</td>
<td>N AND LE + → NO UTI</td>
</tr>
<tr>
<td>N OR LE Neg → culture</td>
<td>N Neg → Dipslide culture</td>
<td>OR microscopic detection of bacteria in unspun urine</td>
<td>N→ AND LE + → doubt; ask patient’s preference</td>
</tr>
<tr>
<td>Culture:</td>
<td>Culture:</td>
<td>Culture:</td>
<td>Culture:</td>
</tr>
<tr>
<td>Only in:</td>
<td>Only in:</td>
<td>Only in:</td>
<td>Only in:</td>
</tr>
<tr>
<td>– Doubts (N OR LE neg)</td>
<td>– Complicated UTI</td>
<td>– Treatment failure</td>
<td>– Complicated UTI or pregnancy</td>
</tr>
<tr>
<td>– Patients at risk</td>
<td>– Treatment failure of two antibiotic courses</td>
<td>– Recurrent UTI within 4 weeks</td>
<td>– Recurrent infection</td>
</tr>
<tr>
<td>– Upper UTI</td>
<td>Risk of complicated UTI</td>
<td>Treatment failure</td>
<td>Treatment failure</td>
</tr>
<tr>
<td>Criterion : &gt;10^2 cfu/ml</td>
<td>Criterion : &gt;10^3 cfu/ml</td>
<td>Criterion : &gt;10^4 cfu/ml</td>
<td>Criterion : &gt;10^5 cfu/ml</td>
</tr>
<tr>
<td>TREATMENT</td>
<td>Selection:</td>
<td>Selection:</td>
<td>Selection:</td>
</tr>
<tr>
<td>NF 100 mg 2dd OR NF 100 mg 2dd</td>
<td>TMP 300 mg 1dd OR OR NF 50 mg 4dd or 100 mg 2dd</td>
<td>NO DRUG SELECTED</td>
<td>TMP 300 mg 1dd OR</td>
</tr>
<tr>
<td>3 days</td>
<td>3 days</td>
<td>3 days</td>
<td>NF 100 mg 3dd</td>
</tr>
<tr>
<td>Failure:</td>
<td>Failure:</td>
<td>Failure:</td>
<td>3 days</td>
</tr>
<tr>
<td>Change NF to TMP or vice versa for 10 days</td>
<td>Change NF to TMP or vice versa for 3 days</td>
<td>NO recommendations</td>
<td>Change NF to TMP or vice versa for 3 days</td>
</tr>
<tr>
<td>Recurrent infections:</td>
<td>Recurrent infections:</td>
<td>Recurrent infections:</td>
<td>Recurrent infections:</td>
</tr>
<tr>
<td>TMP or NF at bedtime or post-coitus</td>
<td>TMP or NF noite or post-coitus</td>
<td>Self-treatment</td>
<td>TMP or NF at bedtime or post-coitus</td>
</tr>
<tr>
<td>For 6 months</td>
<td>For 3 months OR self-treatment</td>
<td></td>
<td>For 6 months OR self-treatment</td>
</tr>
<tr>
<td>Referral: All Recurrent UTI (≥3x/year) → urologist</td>
<td>Referral: Failure of prophylactic therapy in recurrent UTI</td>
<td>Referral: Not mentioned</td>
<td>Referral: Only if complicating factors are suspected in recurrent UTI</td>
</tr>
</tbody>
</table>

N = nitrite test; LE = leukocyte-esterase test; Pos = positive; Neg = negative; UTI = urinary tract infection; NF = nitrofurantoin; TMP = trimethoprim.
authors stated that this practice met with some resistance from the doctors.

*Treatment without investigation of the urine is defendable if complaints are clear... (NL)*

*We [doctors] don't want to leave it completely in the hands of the patient. (B)*

*I think there is no sound evidence for self-treatment. ... The cultural thing is that self-treatment of any kind is perceived as very problematic by German doctors... (G)*

**DISCUSSION**

Our study suggests that cultural factors play a substantial role in the production of guidelines, both in selection of literature and in formulation of recommendations.

The four selected guidelines were all systematically developed in accordance with accepted strategies (15). They were developed by expert general practitioners and peer-reviewed by groups of general practitioners and external experts, and three of them were tested in practice. Consequently, the development process was largely the same for the selected guidelines.

The selected guidelines were ideal for comparison for references as they addressed the same disease, and were all published within the same period. The systematic literature search described by the authors was rather similar, so the potential sources of evidence were shared. Nevertheless, there was little overlap in evidence cited by the guidelines. This illustrates that other factors, beyond the guideline development process, may influence the selection of evidence. Authors of the guidelines seemed to select literature that was most in accordance with the local conditions and their norms and values. Consequently, “guidelines for guidelines” do not guarantee a standardized outcome.

Most differences between the guidelines were found in the diagnostic recommendations. This divergence may partly be due to the lack of diagnostic trials in general practice (17). Most available data come from microbiological studies, which cannot be extrapolated to general practice. Even the definition of UTI in a clinical setting is controversial. Only symptoms as well as results of urinalysis or urine culture may be used as criteria (9,18). When there are conflicting definitions and lack of evidence, local traditions in the healthcare system could influence the decisions on diagnostic procedures. For instance, in Norway diagnosis by telephone was optional, as typical symptoms alone were regarded as sufficient for the diagnosis (13).

Others have recently supported this standpoint (9,18). The Norwegian authors also considered this as empowering the patient. Relying on symptoms alone was not acceptable for German or Belgian GPs: they felt need for more “safety” in the diagnostic process and therefore advocated urinalysis and other diagnostic tests for diagnosing UTI. In Belgium, patients expect home visits by their GP, and a diagnostic strategy feasible at home was preferred (19).

For the therapy of uncomplicated UTI a large number of trials indicate the effectiveness of a variety of drugs. Therefore the ultimate choice of the first-line drug is based on consensus. The Norwegian guideline did not recommend any specific drug and left the choice to the individual GP. In Germany, The Netherlands, and Belgium, the same choice was made for 3 days' treatment with TMP and NFX, illustrating more a Northern European consensus on well-known and cheap drugs rather than strong evidence (20).

Self-treatment was an option in all guidelines except the German, in the case of recurrent cystitis. The German guideline recommended referral to a urologist instead. This may also be an illustration of the need for safety.

Both needs for safety and perception of who holds power may be influenced by the healthcare system. In The Netherlands and Norway, the GP is a “gatekeeper” and patients can only consult a specialist after referral by a GP. Both Dutch and Norwegian authors displayed the self-confidence of GPs in their answers. The Dutch authors focused on their role in the system, while the Norwegian authors focused on staying evidence-based and on building grounds for patient-centred strategies. In contrast, Belgian and German GPs are subjected to a system where patients may freely consult other specialists. This may have resulted in a more defensive attitude in the guideline (21), especially in the diagnostic recommendations and referral criteria.

The interaction between the two factors “need for safety” and “perception of who holds power” may depend heavily on local conditions. Authors of the German and the Belgian guidelines perceived the differences to stem from pressure: from the subspecialists in Germany and from the patients in Belgium, respectively. The Dutch and the Norwegian authors stated that their argumentation was evidence-based, but still results differed.

Our data clearly illustrate how the same evidence may be used for diametrically opposite conclusions depending on the authors’ conceptual framework. The impact of current best evidence was used to support the recommendation that all patients with uncomplicated cystitis should be treated, while its limitations were used to justify the option of no treatment. The
specific evidence-based pros and cons seemed to arise from conceptions of what was desirable or possible under local conditions. This may be a general difficulty in any guideline development. Rogers, in a recent paper on guidelines and ethics, points to the importance of the priority-setting process, and points out that we need a way of setting priorities in an explicit and transparent process as the effects of group composition on final recommendations are well documented (22,23).

The transparency of a guideline is improved by providing levels of evidence and grades of recommendations (24), as in the German and Norwegian guidelines. If the recommendations are based on consensus or expert opinion, the supportive arguments could be explicitly described in the text. This might help the guideline user to distinguish evidence-based from culture-based statements. Another possibility for improvement is to adopt an external review asking guideline developers in other countries to comment on draft guidelines in order to explore the cultural and local influences (23). In particular, if existing international guidelines are used for local adaptation, as recently proposed by Bro and Waldorff for the Scandinavian countries, there is a strong need for transparency (25).

Finally, international collaboration in guideline production, as in Cochrane groups or international scientific societies, may increase the possibility to disclose cultural influences. Once disclosed, differences could be worked on, or the authors could at least keep track of them in the guideline.

In conclusion, there are substantial differences even between high-standard guidelines on the same well-defined clinical entity. The selection of literature data, and diagnostic and therapeutic recommendations, seemed to be influenced by such cultural aspects as habits, the patient’s, expectations and the structure of the healthcare system.

REFERENCES