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Subfertility guidelines in Europe: the quantity and quality of intrauterine insemination guidelines

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BACKGROUND: International collaboration could facilitate systematic development of guidelines to regulate and improve clinical practice. To promote European collaboration in guideline development in reproductive medicine, insight into existing subfertility guidelines in Europe is essential. The study aim was to explore the number and quality of clinical practice guidelines on homologous intrauterine insemination (IUI) in Europe. METHODS: To identify IUI guidelines in Europe, electronic databases and Internet were systematically searched and key experts on assisted reproduction in 25 European countries were questioned. The quality of IUI guidelines was systematically assessed with the internationally validated Appraisal of Guidelines for Research and Evaluation (AGREE) Instrument. Qualitative methods were used to appraise IUI guideline recommendations and references. RESULTS: National guidelines on IUI are available in four of 25 European countries. The quality of IUI guidelines in Europe is moderate to high, but the recommendations and references differ considerably. CONCLUSIONS: The number of IUI guidelines in Europe is surprisingly small, and differences in their recommendations and references are considerable. To overcome these deficiencies in clinical guidance on IUI care in Europe, a central body with expertise in up-to-date guideline development methodology and sufficient resources could be established in Europe for central selection and international exchange of evidence to support guideline recommendations.

Key words: Europe/guidelines/intrauterine insemination/quality/subfertility

Introduction

Assisted reproduction raises complex ethical, legal and social dilemmas. Controversial issues in reproductive medicine concern the restriction of assisted reproduction techniques (ARTs) based on age or sexual orientation, the impact of multiple births on health and healthcare resources, the donation of gametes or embryos, the cryopreservation of gametes, embryos or gonadal tissues and the preimplantation genetic screening of embryos (Kääriäinen *et al*., 2005). Criticism of assisted reproduction arises in the context of a broad spectrum of cultural, religious and social attitudes in societies towards technical intervention in human reproduction (Fasouliotis and Schenker, 2000).

Although the necessity for some form of regulation in reproductive medicine is obvious, there has been an ongoing debate in society regarding the best approach to regulate assisted reproduction (Fasouliotis and Schenker, 1999). Many countries have opted for national legislation on assisted reproduction (Boggio, 2005). The recent legislative interventions of the Italian government to regulate reproductive medicine, restricting and banning several common procedures to assist human reproduction, are well known (Turone, 2004; Ragni *et al*., 2005). Although restrictive reproductive laws can impose strict limitations on the practice of assisted reproduction, it is argued that legislation is inappropriate to deal adequately with the continuing rapid technological advances in reproductive medicine (Fasouliotis and Schenker, 1999).

The development of clinical practice guidelines may be a more effective approach to regulate assisted reproduction. On the one hand, subfertility guidelines can be regarded as a means of external control of ethical, legal and social issues in reproductive medicine (Grol *et al*., 2005). On the other hand, subfertility guidelines can assist healthcare professionals and patients in the decision-making process regarding appropriate, safe and cost-effective care and improve the quality of subfertility care (Field and Lohr, 1990; Woolf *et al*., 1999). Therefore, both authorities and healthcare professionals are interested in clinical practice guidelines and increasingly support the development of guidelines for reproductive medicine.

Given the potential detrimental consequences of low-quality guidelines for reproductive medicine, such guidelines should meet basic quality criteria (The AGREE Collaboration, 2003).

However, the development of high-quality guidelines requires specific expertise and considerable resources (Grol *et al*., 2005). International collaboration offers opportunities for sharing some elements of the expensive and time-consuming process of guideline development (Fervers *et al*., 2003; Burgers *et al*., 2004). To promote European collaboration in guideline development activities in reproductive medicine, insight into existing subfertility guidelines in different European countries is essential. However, little is known about subfertility guidelines in Europe. Therefore, we explored in which European countries subfertility guidelines are available and evaluated the methodological quality, recommendations and references of the identified guidelines. In this study, we focused on clinical practice guidelines for homologous intrauterine insemination (IUI), because of the expected high availability of clinical guidance in Europe on this frequently used technique to assist human reproduction.

Materials and methods

Selection of guidelines

To identify IUI guidelines in Europe, three systematic search methods were used. First, we searched Medline and PubMed up to May 2005 for IUI guidelines using the keywords 'fertility', 'fertility problems', 'infertility', 'subfertility' and 'intrauterine insemination', combined with 'guidelines', 'clinical practice guidelines' or 'recommendations'.

Second, we performed an Internet search in May 2005 to obtain IUI guidelines, using the previously mentioned keywords, in the search engines Google, Altavista and Yahoo. We also searched for IUI guidelines on the websites of (inter)national professional societies in the fields of obstetrics and gynaecology, and reproductive medicine (e.g. www.figo.org, www.nfog.org, www.iffs-reproduction.org, www.eshre.com and www.nordicfs.org), and on the websites of (inter) national institutes involved in guideline development (e.g. www.g-i-n.net, www.guideline.gov and www.cbo.nl). Searches were extended using links when available. Organizations were contacted by e-mail to retrieve possible IUI guidelines not published on the Internet.

Last, one author (J.A.M.K.) asked all 24 fellow members of the European IVF Monitoring (EIM) Consortium by e-mail for IUI guidelines. The European Society of Human Reproduction and Embryology (ESHRE) established the EIM Consortium in 1999 to start a collaborative data-collection programme for IVF in Europe. Members play a leading role or have lengthy experience in IVF programmes in their respective country and presumably in other aspects of assisted reproduction as well. Two and four weeks after the initial mailing, reminders were sent to non-responders. During the annual meeting of the EIM Consortium in June 2005, non-responders were asked once more to participate. If EIM members failed to respond, other key experts on assisted reproduction in these European countries were contacted. The online search utility to find members in the ESHRE membership file was used to obtain their contact details.

We used the following criteria to select guidelines for appraisal:

(i) National guidelines from European countries;

(ii) Clinical practice guidelines or separate sections of clinical practice guidelines, containing specific recommendations to assist clinical decision-making on homologous IUI care in secondary or tertiary healthcare settings, thus excluding systematic reviews and legal documents;

(iii) Information available in the guideline or in a separate document about the guideline development process.

Selected IUI guidelines not published in Dutch or English were translated into Dutch.

Appraisal of methodological quality of guidelines

To evaluate the methodological quality of the selected IUI guidelines, we used the Appraisal of Guidelines for Research and Evaluation (AGREE) Instrument. The AGREE Instrument is an internationally validated, generic tool to assess the methodological quality of clinical practice guidelines on 23 key items, categorized in six domains: scope and purpose (three items), stakeholder involvement (four items), rigour of development (seven items), clarity and presentation (four items), applicability (three items) and editorial independence (two items) (The AGREE Collaboration, 2003). Detailed information about the AGREE Instrument is available on the website of the AGREE Collaboration (http://www.agreecollaboration.org). Four investigators appraised the selected IUI guidelines independently by scoring each item of the AGREE Instrument on a four-point Likert scale (1 = strongly disagree, 2 = disagree, 3 = agree and 4 = strongly agree). Differences in ratings of more than one point per item were discussed to achieve consensus. We calculated six domain scores for each guideline by adding up the scores of the individual items in a domain given by the four appraisers and standardizing the total as a percentage of the maximum possible score for that domain (range 0–100%). The final step in guideline appraisal with the AGREE Instrument involved an overall judgement about the usefulness of each guideline, based on the ratings of individual items and the balance between the domains. The overall assessment was scored on a four-point categorical scale [strongly recommended, recommended (with provisos or alterations), not recommended and unsure].

Appraisal of guideline recommendations

To appraise the recommendations of the IUI guidelines, four authors extracted independently the key recommendations of each guideline. Discrepancies in recommendation extraction were discussed to reach agreement. Subsequently, we investigated whether systems to grade the quality of evidence and the strength of recommendations were used in the guideline development process. We also explored the scope of each IUI guideline, and we compared the recommendations to assess the extent of variation between the selected IUI guidelines.

Appraisal of guideline references

To evaluate the references on which the key recommendations of the IUI guidelines are based, we assessed the publication dates and origin of the references and the number of references shared with the other selected IUI guidelines.

Results

Selection of guidelines

After our search for IUI guidelines in Europe, we included four IUI guidelines, one each from Denmark, England and Wales, France and the Netherlands (Table I). We verified that in 21 other European countries, IUI guidelines were not available (Table II).

The IUI guidelines from England and Wales, France and the Netherlands are peer-reviewed publications and in their respective language available on the Internet (Table I). The Danish IUI guideline is a first draft of the update of a previous IUI guideline from 1997 and not yet published. Governmental agencies produced the IUI guidelines from England and Wales and France, whereas the Danish and Dutch IUI guidelines are developed by national professional organizations.

Table I. Characteristics of intrauterine insemination (IUI) guidelines from Denmark, England and Wales, France and the Netherlands

Country	Organization responsible for guideline development	Title	Year of publication	Web site
Denmark	Danish Society of Obstetrics and Gynaecology (DSOG) and Danish Fertility Society (DFS)	Homologous intrauterine insemination[a]	Version 2004	Not yet online
England and Wales	National Collaborating Centre for Women's and Children's Health, commissioned by the National Institute for Health and Clinical Excellence (NICE)	Fertility: assessment and treatment for people with fertility problems Chapter 10: Intrauterine insemination	2004	http://www.ncc-wch.org.uk http://www.nice.org.uk http://www.rcog.org.uk
France	National Agency for Accreditation and Evaluation in Healthcare (ANAES)	Infertility of a couple	1996	http://www.anaes.fr
Netherlands	Dutch Society of Obstetrics and Gynaecology (NVOG)	Intrauterine insemination	2000	http://www.nvog.nl

[a]First draft of the update of a previous IUI guideline from 1997.

Table II. Response of informants from 21 European countries without intrauterine insemination (IUI) guidelines

Country	Additional comments
Response: 'No IUI guidelines'	
Belgium	'Current development of subfertility guidelines by Flemish Society of Obstetrics and Gynaecology' 'Other documents about subfertility available'[a]
Czech Republic	'No guideline development activities due to lack of collaboration between professional societies, the government and insurance companies'
Finland	'No legislation on assisted reproduction available' 'Other documents about subfertility available'[b]
Germany	'No national guidelines, because Germany is divided in different states, each with different regulations' 'Other documents about subfertility available'[c]
Greece	'No guideline development activities due to lack of a guideline development programme of the Greek Infertility Society, and, up to recently, lack of a central health body'
Iceland	'No national guidelines, because there is only one fertility clinic in Iceland' 'Other documents about subfertility available'[b]
Ireland	'Other documents about subfertility available'[d]
Italy	'Development of IUI guidelines is planned in the near future, as part of national legislation on assisted reproduction'
Poland	'Development of IUI guidelines is considered by Polish Fertility and Sterility Society'
Portugal	–
Slovakia	'Other documents about subfertility available'[e]
Spain	'Current development of subfertility guidelines by Spanish Fertility Society'
Switzerland	–
Response: 'No IUI guidelines; legislation on assisted reproduction available'	
Austria	'Other documents about subfertility available'[f]
Hungary	–
Latvia	'Current development of subfertility guidelines by Latvian Association of Gynaecologists and Obstetricians'
Norway	'Other documents about subfertility available'[b]
Russia	–
Slovenia	–
Sweden	'Local guidelines on assisted reproduction available' 'Other documents about subfertility available'[b]
Ukraine	–

[a]'Perspective on ovulation induction' and 'perspective on ovarian hyperstimulation syndrome', published by the Flemish Society of Obstetrics and Gynaecology (VVOG) (http://www.vvog.be).
[b]'Clinical and laboratory guidelines for ART in the Nordic countries', published by the Nordic Federation of Societies of Obstetrics and Gynaecology (NFOG) (http://www.nfog.org).
[c]'Guideline for psychosomatic oriented assessment and treatment for fertility problems', 'recommendation for assessment of infections and infection prophylaxis in ART', 'perspective on ART: ovarian hyperstimulation treatment with gonadotrophins or anti-oestrogens and risk for ovarian cancer' and 'perspective on the comparison of recombinant FSH and urinary-derived FSH', published by the German Society of Gynaecology and Obstetrics (DGGG) (http://www.dggg.de).
[d]'Report on possible approaches to the regulation of all aspects of assisted human reproduction and the social, ethical and legal factors involved in determining public policy', published by the Commission on Assisted Human Reproduction (http://www.dodc.ie).
[e]'Guideline for subfertility management', including a specific part about medical management of subfertility.
[f]'Guideline for assessment of subfertility with opportunities and limitations for treatment in gynaecology departments without IVF', published by the Austrian Society of Gynaecology and Obstetrics (OEGGG) (http://www.oeggg.at).

Eight of the 21 informants from European countries without IUI guidelines reported that national laws regulate assisted reproduction (Table II). Nine informants mentioned the existence of other documents regulating reproductive medicine. Informants from Belgium, Latvia and Spain reported that a professional society in their country is currently developing subfertility guidelines. Informants from Italy and Poland mentioned plans for the development of IUI guidelines in the near future.

Appraisal of methodological quality of guidelines

The results of appraisal of the methodological quality of the selected IUI guidelines with the AGREE Instrument are summarized in Table III. The IUI guideline from England and Wales rated high on the majority of AGREE criteria, and the domain scores varied between 58 and 96%, which indicates a high overall guideline quality. According to the results of AGREE appraisal, this IUI guideline is strongly recommended for use in daily healthcare practice. The French and Dutch IUI guidelines scored high as well as low on a similar number of AGREE criteria, and most domain scores were between 30 and 60%, which indicates a moderate overall guideline quality. We were not able to appraise the Danish IUI guideline on two domains of the AGREE Instrument, that is, stakeholder involvement and editorial independence, owing to the draft status of this guideline. Assessment of the Danish IUI guideline on four other domains showed a moderate overall guideline quality.

Appraisal with the AGREE Instrument revealed several flaws in the methodological quality of the Danish, French and Dutch IUI guidelines. It was unclear in the French and Dutch IUI guidelines whether patients participated in guideline development, causing low domain scores for stakeholder involvement. Neither the criteria for selecting evidence nor the methods used to formulate the recommendations were explicitly described in the Danish and Dutch IUI guidelines, lowering domain scores for the rigour of development. None of the IUI guidelines from Denmark, France and the Netherlands considered cost implications of applying the recommendations, resulting in low domain scores for applicability. Finally, the French and Dutch IUI guidelines failed to mention whether the funding body influenced guideline development, and whether members of the guideline development group had conflicts of interest, causing poor domain scores for editorial independence. Overall, the IUI guidelines from Denmark, France and the Netherlands could be recommended for use in practice if alterations are made to overcome these particular flaws.

Appraisal of guideline recommendations

Systems to grade the quality of evidence and the strength of recommendations were used to develop the IUI guidelines from Denmark and England and Wales. Each recommendation in these guidelines was based on the best evidence available, graded according to the strength of the underlying evidence and explicitly linked to the supporting evidence. Recommendations in the French and Dutch IUI guidelines were not graded according to the strength of the underlying evidence, and the link between the recommendations and the supporting evidence was less clear. Therefore, it was not apparent whether the recommendations in the French and Dutch IUI guidelines were based on the best evidence available or on weak research data, personal opinions or common practice.

The IUI guidelines differed in the number of key recommendations and in their coverage. The IUI guidelines from Denmark and England and Wales comprised of a limited set of evidence-based recommendations, whereas the French and Dutch IUI guidelines included considerably more recommendations. These differences were particularly apparent for the IUI guideline from England and Wales, consisting of eight key recommendations, and the Dutch IUI guideline, consisting of 31 key recommendations and covering topics that were outside the scope of the IUI guideline from England and Wales, mainly management and organizational aspects of IUI care. For example, four key recommendations of the Dutch IUI guideline covered timing in IUI treatment (‘IUI should be performed 20–30 h after luteinizing hormone surge’) and four other Dutch key recommendations were related to practice facilities for IUI care (‘IUI treatment results should be evaluated yearly’).

Table III. Standardized domain scores[a] of intrauterine insemination (IUI) guidelines from Denmark, England and Wales, France and the Netherlands assessed with the Appraisal of Guidelines for Research and Evaluation (AGREE) Instrument

AGREE Instrument domains	Denmark	England and Wales	France	Netherlands
Scope and purpose (%)	50	67	61	53
Stakeholder involvement (%)	No score[b]	79	35	33
Rigour of development (%)	51	96	73	52
Clarity and presentation (%)	77	83	52	63
Applicability (%)	31	58	17	31
Editorial independence (%)	No score[b]	67	13	8
Overall assessment	Recommended[c]	Strongly recommended[d]	Recommended[c]	Recommended[c]

[a]Standardized domain scores are calculated by adding up item scores in a domain and standardizing the total as a percentage of the maximum possible domain score (range 0–100%).
[b]Not possible to score the items in this domain in the first draft of the update of the Danish IUI guideline from 1997.
[c]Recommended with provisos or alterations to overcome insufficient or lacking information on the guideline development method.
[d]Strongly recommended without provisos or alterations.

For detailed exploration of similarities and discrepancies between guideline recommendations, we compared the key recommendations of the IUI guideline with the best methodological quality (i.e. the IUI guideline from England and Wales) with the recommendations of the other IUI guidelines (Table IV). The content of the key recommendations of the IUI guidelines differed considerably. For example, the IUI guidelines were not consistent in their recommendations to offer ovarian stimulation in IUI treatment. The IUI guideline from England and Wales explicitly stated that ovarian stimulation should not be offered to couples with mild male-factor and unexplained subfertility, whereas others recommended stimulated IUI to manage these fertility problems. Furthermore, consensus was lacking for the suggested total number of IUI cycles. The IUI guideline from England and Wales and the Netherlands recommended up to six IUI cycles for couples with unexplained subfertility, whereas the Danish IUI guideline suggested three to six IUI cycles and the French IUI guideline at least six IUI cycles.

Appraisal of guideline references

The total number of references in the selected IUI guidelines ranged between 11 and 38 (Table V). The majority of first authors of studies cited in the Dutch IUI guideline (73%) originated from the Netherlands. The French IUI guideline also cited a high proportion of studies from authors of their own country (33%). References in the IUI guidelines from Denmark and England and Wales were predominantly from the USA, the Netherlands and Canada. No references were shared by all four IUI guidelines, and only three references were present in three guidelines. The IUI guidelines from Denmark and England and Wales had the most references in common (n = 11), whereas the French IUI guideline shared just one reference with the Danish IUI guideline.

Discussion

This is the first study to provide insight into the number and quality of subfertility guidelines in Europe. National clinical practice guidelines on homologous IUI are currently only available in four of 25 European countries. The methodological quality of the IUI guidelines in Europe is moderate to high, but the recommendations and references of these guidelines differ considerably.

Table IV. Comparison of recommendations of the intrauterine insemination (IUI) guideline from England and Wales (n = 8) with recommendations of IUI guidelines from Denmark, France and the Netherlands

Recommendation topics	Denmark	England and Wales	France	Netherlands
Indications for (un)stimulated IUI[a]				
Male-factor subfertility	Stimulated IUI	Unstimulated IUI	Stimulated IUI	Stimulated IUI in mild male-factor subfertility[b] Unstimulated IUI in severe male-factor subfertility[c]
Unexplained subfertility	Stimulated IUI	Unstimulated IUI	Stimulated IUI	Stimulated IUI
Minimal to mild endometriosis	Stimulated IUI	(Un)stimulated IUI	Stimulated IUI	Not mentioned
Indication for IUI or FSP	FSP in unexplained subfertility	FSP in unexplained subfertility	Not mentioned	Not mentioned
Single versus double IUI	Single IUI per cycle	Single IUI per cycle	Not mentioned	Not mentioned
Total number of IUI cycles				
Male-factor subfertility	3–6	Up to 6	Up to 6	Up to 6
Unexplained subfertility	3–6	Up to 6	At least 6	Up to 6
Minimal to mild endometriosis	3–6	Up to 6	Not mentioned	Not mentioned

FSP, Fallopian sperm perfusion.
[a]Stimulated IUI, IUI following stimulation of the ovaries using oral anti-estrogens or gonadotrophins; unstimulated IUI, IUI in natural cycles.
[b]More than 10×10^6 motile sperm available after sperm preparation.
[c]Less than 10×10^6 motile sperm available after sperm preparation.

Table V. Characteristics of references in IUI guidelines from Denmark, England and Wales, France and the Netherlands

Guideline references	Denmark	England and Wales	France	Netherlands
Total number of references	38	27	30	11
Number of references published after 2000 (%)	10 (26)	5 (19)	–	–
Origin of references[a]				
References from own country (%)	2 (5)	4 (15)	10 (33)	8 (73)
Top three references from other countries (%)	11 (29) USA 6 (16) Netherlands 4 (11) Canada	8 (30) USA 3 (11) Netherlands 3 (11) Canada	7 (23) UK 6 (20) USA 2 (7) Australia/Italy	1 (9) USA 1 (9) Canada 1 (9) International
Number of references shared with other guidelines				
Denmark	–	11	1	4
England and Wales	11	–	0	3
France	1	0	–	0
Netherlands	4	3	0	–

[a]Origin of first author of cited study.

The strong point of our study is the systematic and rigorous approach to identify IUI guidelines in Europe. Furthermore, the 100% response rate in our survey among key experts on assisted reproduction guarantees the scientific validity of our results on the availability, or otherwise, of IUI guidelines in 25 European countries. Another strength of our study is the systematic appraisal of the methodological quality of the IUI guidelines with the internationally validated AGREE Instrument.

Our study also has some limitations. First, in contrast with the systematic appraisal of the methodological quality of the IUI guidelines, we were not able to use a framework to evaluate the quality of individual guideline recommendations. Currently, no validated appraisal instruments for individual guideline recommendations are available.

Second, our appraisal of the references of the IUI guidelines may seem limited, because we did not examine the quality of the cited studies nor the consistency between study conclusions and guideline recommendations. In other areas of medicine, numerous investigators showed deficiencies in methods used to search and select evidence and formulate guideline recommendations (Grimshaw *et al*., 1995; Shaneyfelt *et al*., 1999). As a result, clinical practice guidelines are not always based on a systematic review of literature, discrepancies exist between evidence and guideline recommendations, and few references are shared among guidelines on the same topic (Antman *et al*., 1992; Lacasse *et al*., 2001; Christiaens *et al*., 2004). However, it is beyond the scope of our study to test the generality of these previous findings for reproductive medicine.

The small number of IUI guidelines in Europe is surprising. For years, IUI has been a frequently used therapeutic modality in reproductive medicine across Europe (Duran *et al*., 2002). In contrast with other ARTs, homologous IUI is not prohibited by legislation throughout Europe (Schenker, 1997; Andersen *et al*., 2005). Thus, prohibitive laws do not account for the lack of IUI guidelines in the majority of European countries. Although some European countries have set down a legal framework within which homologous IUI treatment may take place, these laws do not support clinical decision-making in day-to-day subfertility care and cannot substitute for clinical practice guidelines. Furthermore, the small number of IUI guidelines in Europe contrasts with the large number of guidelines on other medical issues, such as breast cancer or diabetes mellitus (Eisinger *et al*., 1999; Burgers *et al*., 2002, 2004). Clearly, further research is necessary to elucidate underlying reasons for the lack of IUI guidelines in most European countries.

Despite the overall moderate-to-high methodological quality of IUI guidelines in Europe, some striking flaws in their methodological quality were identified with the AGREE Instrument. When interpreting these flaws, we must keep in mind that the perspectives on optimal methods for guideline development changed over time (Grol *et al*., 2005). In fact, internationally recognized standards for development and reporting of clinical practice guidelines were just recently established by the AGREE Collaboration. Therefore, flaws in the methodological quality of the IUI guidelines may result from the use of different methods for guideline development at different moments in time. This supports our observation that the most recently published IUI guideline from England and Wales used more advanced methods for guideline development and scored highest on AGREE appraisal. Moreover, flaws in the methodological quality of the more dated IUI guidelines from France and the Netherlands mainly concern aspects of guideline quality that gained importance over the past few years, such as integrating patient preferences and opinions, economic evidence and statements regarding editorial independence in clinical practice guidelines.

Flaws in the methodological quality of the IUI guidelines may also be attributable to the differences in resources. Professional societies generally have smaller budgets for guideline development than governmental agencies, which could explain the lower scores for the rigour of development on AGREE appraisal of the IUI guidelines produced by the Danish and Dutch professional organizations (Burgers *et al*., 2003).

Both the number and content of the key recommendations of the IUI guidelines in Europe differed considerably. Differences in the recommendations of guidelines on the same topic are common and mainly attributable to the selection of different evidence to support guideline recommendations (Shaneyfelt *et al*., 1999; Burgers *et al*., 2002). This corresponds with the minimal overlap in references cited in the IUI guidelines. Some variation in references can be explained by the different publication dates of the IUI guidelines. However, previous studies reported that political and cultural factors, socioeconomic aspects and characteristics of healthcare systems are more important influences on the choice of evidence for guideline development (Burgers *et al*., 2002; Christiaens *et al*., 2004). It is not imaginary that such factors also compromise the selection of evidence for guideline development in reproductive medicine.

In conclusion, this study revealed that the number of IUI guidelines in Europe is surprisingly small and that the differences in the recommendations and references cited in these guidelines are considerable. How can we overcome these deficiencies in clinical guidance on IUI care in Europe? We suggest the establishment of a central body in Europe with expertise in up-to-date guideline development methodology and sufficient resources to select the best evidence available to support guideline recommendations. Subsequently, the evidence selected on a central level could be shared internationally in the form of evidence tables, summarizing the content of the selected studies and indicating the level of evidence according to validated evidence-level structures. In the context of reproductive medicine in Europe, this strategy for central selection and international exchange of evidence to support guideline recommendations may very well increase the number of subfertility guidelines in Europe, improve their scientific validity, promote international consensus on their clinical content and reduce duplication of effort and inefficient use of resources (Burgers *et al*., 2003; Fervers *et al*., 2003). Interestingly, ESHRE recently applied this approach to select evidence on a European level for the development of recommendations on the diagnosis and treatment of endometriosis (Kennedy *et al*., 2005). The issue of whether or not ESHRE will continue to act

as a central body to select evidence for the development of guidelines on other clinical subjects in reproductive medicine should be discussed internationally. Proposals regarding other eligible European organizations to select and share evidence for guideline development in Europe should also be brought forward in an international debate. Clearly, establishment of a central body will be an important first step to facilitate systematic guideline development to promote best practice in reproductive medicine as well as in other healthcare settings.

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