human reproduction

Selection of key recommendations for the management of women with endometriosis by an international panel of patients and professionals

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STUDY QUESTION: Can the differences in patients' and professionals' perspective regarding essential endometriosis care be accommodated in one set of key recommendations?

SUMMARY ANSWER: Consensus between patients and professions on a key set of recommendations for essential endometriosis care was achieved.

WHAT IS KNOWN ALREADY: Guideline development alone will not lead to healthcare improvement. Quality indicators are needed to monitor actual care and guideline adherence. These can help with better implementation of the ESHRE guidelines in European hospitals and thereby improve the quality of endometriosis care. The first step in the development of quality indicators is to select a compact set of key recommendations.

STUDY DESIGN, SIZE AND DURATION: Using a RAND modified Delphi method, this study reports the systematic selection of key recommendations based on the ESHRE guideline 'Management of Women with Endometriosis' by an international expert panel of both patients and professionals during the study period of September 2015 and December 2015.

PARTICIPANTS, SETTING, METHODS: An international panel of patients ($n = 10$) and medical professionals ($n = 11$) rated and prioritized the 83 recommendations extracted from the ESHRE guideline for relevance in three rounds. A strict consensus methodology was used to select key recommendations. The main outcome measure was one set of key recommendations for endometriosis care.

MAIN RESULTS AND THE ROLE OF CHANCE: A representative set of 17 key recommendations was selected from the preliminary set of 83 recommendations. This selection covers all dimensions of endometriosis care, including diagnosis, treatment of endometriosis-associated pain, treatment of endometriosis-associated infertility and miscellaneous topics such as prevention, menopause and relationship with cancer. Of the 21 experts, 17 participated in at least one round while 16 (76.2%) participated in all 3 rounds.

LIMITATIONS, REASONS FOR CAUTION: The feasibility of the selected key recommendations was not assessed in this study. As not all panel members took part in all three rounds, some response bias may have occurred.

WIDER IMPLICATIONS OF THE FINDINGS: This set of key recommendations is the first step in the development of quality indicators for monitoring and improving endometriosis care. The set is generic and can be used in hospitals internationally. A practice test should be conducted to assess the feasibility of our key recommendations in clinical practice.

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Introduction

Endometriosis is defined as the presence of endometrial glands and stroma outside the uterus where it causes a chronic inflammatory reaction (Kennedy et al., 2005). It is one of the most common gynaecological disorders with an estimated prevalence of 2–10% within the world-wide female population (Eskenazi and Warner, 1997). However, the prevalence may go up to 50% in infertile women (Meuleman et al., 2009). Endometriosis can affect women of reproductive age, causing infertility and pain and can have a significant negative impact on different psychosocial aspects of a woman's life (Nnoaham et al., 2011; Culley et al., 2013; de Graaff et al., 2013; Moradi et al., 2014). Since there is currently no cure, treatment focuses on reducing endometriosis-associated pain and improving fertility.

Many medical professionals experience difficulties in the management of women with endometriosis, which is reflected in the wide variety of clinical practice among European countries (Johnson and Hummelshoj, 2013). As a result, many patients receive either delayed or suboptimal care (Kennedy et al., 2005; Ballard et al., 2006). The World Endometriosis Research Foundation's EndoCost study estimates the total costs arising from women with endometriosis as between 0.8 million and 12.5 billion euro per European country per year (Simoens et al., 2012). The total annual costs, including indirect costs of productivity loss related to endometriosis are estimated at €9872 (95% CI €7930–11 870) per patient, with costs of productivity loss representing 75% of total costs (Klein et al., 2014). The direct annual healthcare costs of €2238 (95% CI €1567–3240) per patient suffering from endometriosis are similar to those of diabetes mellitus (€2858) (von Ferber et al., 2006).

The ESHRE Guideline 'Management of Women with Endometriosis' (Dunselman et al., 2014) aimed to improve European endometriosis care by providing 83 recommendations based on literature evidence and good clinical practice. Unfortunately, guideline development is not automatically followed by healthcare improvement (Bero et al., 1998; Grol, 2001b). Several studies have identified barriers to guideline adherence (Cabana et al., 1999; Wensing et al., 2005; Carlsen et al., 2007; Lugtenberg et al., 2009). These barriers can be classified into patient-related barriers, physician-related barriers, guideline-related barriers and organizational barriers (Cabana et al., 1999). Implementation strategies tailored to these guideline-specific barriers are known to be the most effective in improving guideline adherence (Grol, 1997; Grimshaw et al., 2004). Hence, there is a need to gain insight into the application of the ESHRE guideline 'Management of Women with Endometriosis' in daily practice (i.e. the actual care) and the potential barriers to guideline adherence. By connecting guideline evidence to daily practice, 'quality indicators' are a suitable tool for measuring and monitoring the actual care and potential barriers (Grol et al., 2002). According to the ESHRE manual and additional literature (Mourad et al., 2007; Dancet et al., 2013; Luitjes et al., 2013), the first step in the development of quality indicators is to select a compact set of recommendations on which to focus, i.e. 'key recommendations'. Experts strongly recommend the involvement of both professionals and patients in this selection procedure, since patients and professionals conceivably have different views regarding the best quality of care (Krahn and Naglie, 2008; Uphoff et al., 2012; den Breejen et al., 2013; Kotter et al., 2013). When developed, these key recommendations can be translated and validated into quality indicators. Measuring and monitoring the actual care can help with better implementation of the ESHRE Guideline in European hospitals, thereby improving endometriosis care.

The aim of this study was 2-fold. The first aim was the selection of a compact set of key recommendations as a first step in the development of quality indicators. The second aim was to detect differences in perspectives between patients and professionals regarding essential endometriosis care.

Materials and Methods

Setting

A basic RAND Delphi procedure (Dalkey et al., 1969; Fitch et al., 2001; Boulkedid et al., 2011) was used to develop a set of key recommendations, suitable for transcription into quality indicators, and based on the ESHRE Guideline 'Management of Women with Endometriosis' (Dunselman et al., 2014). The Delphi procedure is an accepted methodology for the selection of key recommendations and development of quality indicators in healthcare (Campbell et al., 2003). In this systematic, stepwise method, evidence-based information is combined with the individual opinion of experts and aggregated into group consensus (Campbell et al., 2003; Boulkedid et al., 2011; Kotter et al., 2012; Diamond et al., 2014). In this study, two questionnaire rounds and one agreement round were performed to achieve panel consensus on the essential aspects of endometriosis care. Panel members were polled individually and anonymously. Opinions were swayed via repetitive feedback after each round, thus avoiding the negative social influences associated with face-to-face discussion (Fitch et al., 2001). Questionnaires were conducted with SurveyMonkey®. Possibilities to add comments on recommendations were provided in each questionnaire. Invitations and reminders were sent via SurveyMonkey®. All scores were listed in a database created with SPSS version 22.0. The consensus procedure took place between September 2015 and December 2015.

Composition of the expert panel

To enhance the acceptance of the key recommendations in clinical practice, the expert panel consisted of a representative diversity of international patients and professionals. Patients and professionals were selected for their expertise and knowledge of endometriosis and ability to communicate in English. Eligible experts were medical doctors with a longstanding experience in the management of women with endometriosis and member of the 'ESHRE Guideline Development Group', and endometriosis patients with a prominent role in a patient organization.

Thus, all European patient organizations ($n = 27$) and medical doctors of the 'ESHRE Guideline Development Group' ($n = 12$) were informed and invited to join this study by e-mail. A total number of 10 patients and 11 professionals from 9 different European countries gave consent for participate in this study, forming an international expert panel of 21 members. Of these, 17 members participated in at least one round of the questionnaires (Fig. 1).
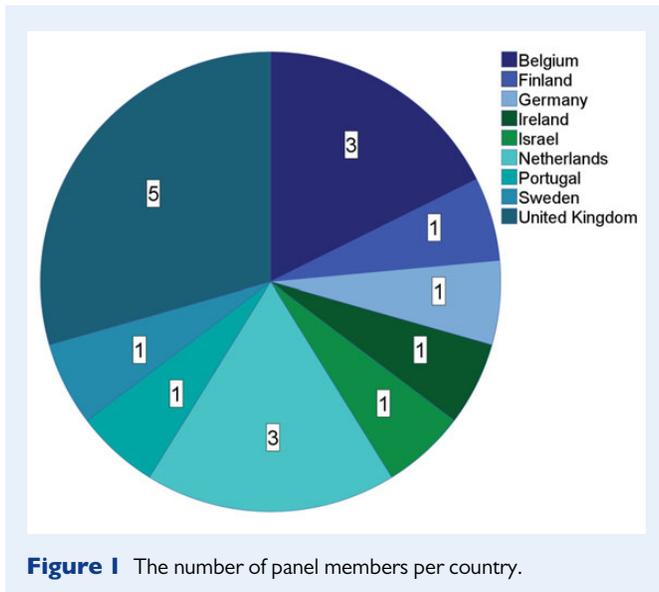
Figure 1 The number of panel members per country.

Selection of key recommendations

The selection of key recommendations consisted of six steps: (i) extraction and classification of recommendations, (ii) first questionnaire round, (iii) data analysis of the first round, (iv) second questionnaire round, (v) data analysis of the second round, and (vi) approval of selected recommendations. The steps taken in this Delphi method have been visualized in Fig. 2 and described below.

Step 1: extraction and classification of recommendations
Two authors (M.J.S. and N.V.) extracted 83 unique recommendations from the online version of ESHRE guideline 'Management of Women with Endometriosis', published September 2013. Subsequently, two authors (M.J.S. and W.L.D.M.N.) distributed these recommendations into four domains, based on guideline chapters: (i) diagnosis, (ii) treatment of endometriosis-associated pain, (iii) treatment of endometriosis-associated infertility (including treatment of endometriosis-associated infertility and medical-assisted reproduction) and (iv) miscellaneous topics (including menopause in women with endometriosis, asymptomatic endometriosis, prevention of endometriosis and endometriosis and cancer).

Step 2: first questionnaire round (Delphi round 1)
In the first round, all 83 recommendations were presented to the expert panel in an online questionnaire. Panel members were asked to assess all recommendations individually on relevance. Relevance was graded by the experts in response to the following question: 'to what extent is the following guideline recommendation an important determinant to ensure or improve the quality of endometriosis care in European hospitals' on a 9-point Likert scale ranging from 1 (extremely irrelevant) to 9 (extremely relevant). All participants had access to the ESHRE guideline and the patient version of this guideline for supporting evidence or background information during the rating process. An example of the score sheet is provided in online Supplementary data, Table SII.

Secondly, the experts were asked to provide for each domain a top-3 ranking of recommendations they considered to be the most relevant in the contribution to high quality of endometriosis care, in order to promote discrimination between recommendations with a high-Likert score.

Step 3: data analysis of the first round
The results of the first round were analysed using a priori defined consensus criteria based on Campbell's criteria (Campbell *et al.*, 2000). These criteria

include a median score of 8 or higher and panel agreement. Panel agreement was defined as in the case in which ≥75% of the individual scores was in the highest tertile of the scale (Likert score: 7–9) and the other 25% of the scores was divided over the remaining two tertiles (Likert score: 1–6). Previous studies (Mourad *et al.*, 2007; van den Boogaard *et al.*, 2010; Stienen *et al.*, 2011; Uphoff *et al.*, 2012; Dancet *et al.*, 2013; den Breejen *et al.*, 2013; Luitjes *et al.*, 2013; Woiski *et al.*, 2015) have shown that using these two criteria only, often does not provide enough discrimination. Therefore, a third criterion was added: recommendations should have at least 20% of the maximum top-3 score. Points were awarded to each top-3 ranking position, with number 1 position = 3 points, number 2 position = 2 points and number 3 position = 1 point. These points were converted into percentages based on the maximum top-3 score. The maximum top-3 score was defined as the number of participants multiplied by the points awarded to a number 1 position. The study investigator (M.J.S.) combined the three criteria as described above and converted them into three possible outcomes: 'selected', 'rejected' and 'no consensus'. Recommendations that met all three criteria were classified as 'selected', those that met none of the criteria were classified as 'rejected', and the remaining recommendations were classified as 'no consensus'. The 'no consensus' recommendations were the input for the second questionnaire round. Finally, a Mann–Whitney *U*-test was used to investigate potential different scoring behaviours between patients and professionals. An example of the consensus methodology is provided in online Supplementary data, Table SIII.

Step 4: second questionnaire round (Delphi round 2)
The second round started with an overview of the 11 selected recommendations and the 42 'no consensus' recommendations. The spread of opinions in the 42 remaining 'no consensus' recommendations was visualized in box-and-whisker plots, showing the differences in median scores and overall scores between patients and professionals. We conducted for each panel member a personal questionnaire with their individual scores of the first round visualized in the box-and-whisker plots, encouraging them to revise their opinion in light of the replies of the other panel members. An example of a personalized box-and-whisker plot is provided in online Supplementary data, Fig. S1. All panel members, including the non-responders of Step 2, were once again asked to assess the 42 'no consensus' recommendations on relevance on a 9-point Likert scale. Secondly, the experts were asked for their approval of the 11 preselected key recommendations. Moreover, each panel member had the possibility to add one extra 'no consensus' recommendation per domain or to agree with the current selection.
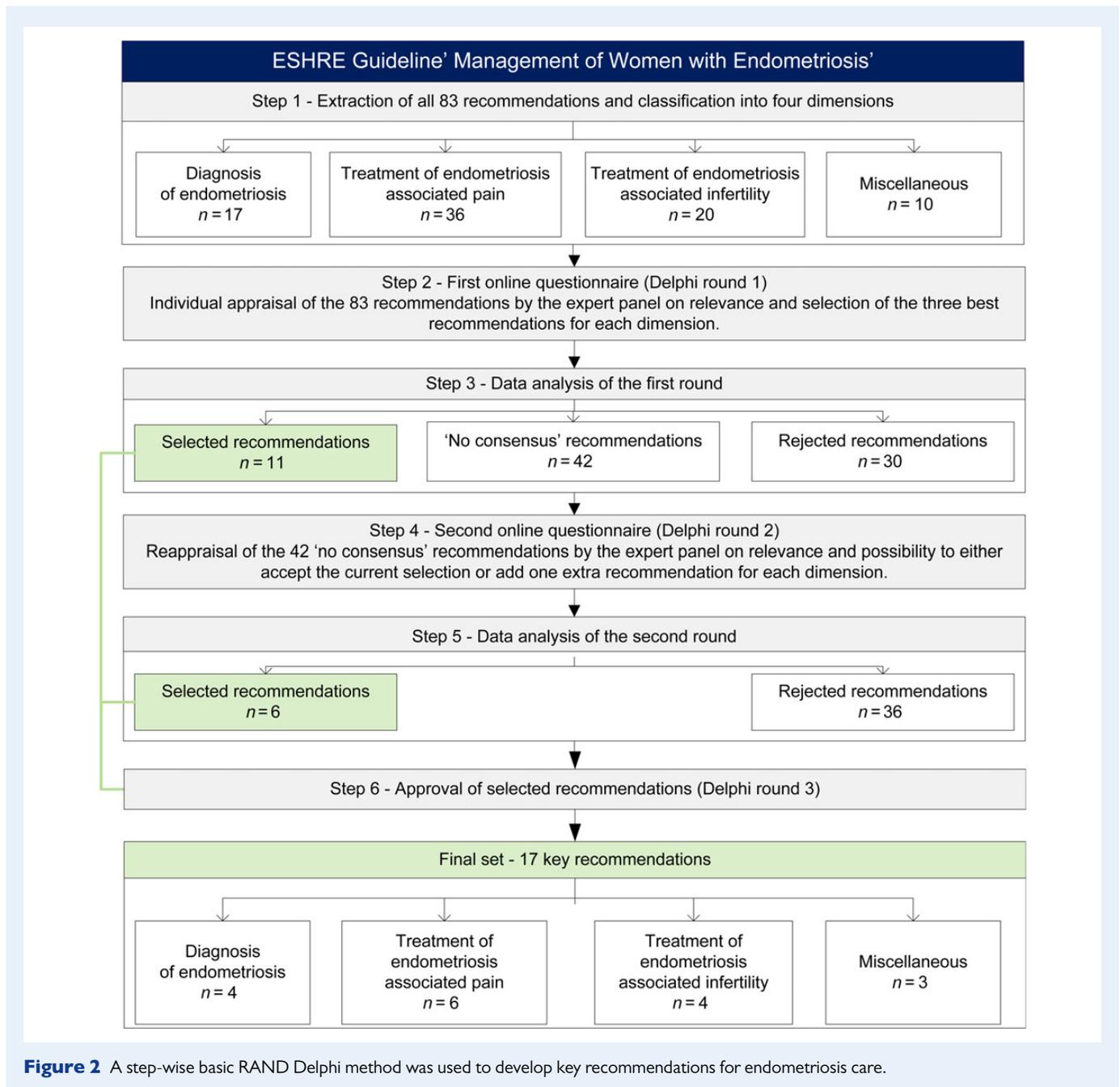
Step 5: data analysis of the second round
The two a priori defined consensus criteria as defined in Step 3 were used to analyze the results of the second questionnaire round. The selection of a recommendation by at least two experts was added as a third criterion. These three criteria were combined and converted into two possible outcomes: 'selected' or 'rejected'. Recommendations that met all criteria were classified as 'selected' and the remaining recommendations as 'rejected'. An example of the consensus methodology is provided in online Supplementary data, Table SIII.

As in the first round, a Mann–Whitney *U*-test was used to investigate differences in scoring behaviour between patients and professionals.

Step 6: approval of selected recommendations (Delphi round 3)
Finally, all 21 panel members, including those who did not participate in the selection rounds, received an overview of the selected recommendations by e-mail. Experts were asked to approve the final set and were provided with a last opportunity to make remarks. Comments were discussed by the authors.

Figure 2 A step-wise basic RAND Delphi method was used to develop key recommendations for endometriosis care.

Main outcome measures

The primary outcome measure was one set of key recommendations based on the ESHRE guideline and experts' opinion. To form the final set, the selected recommendations' of Step 2 were supplemented with the selected recommendations of Step 4 and approved by the expert panel in Step 6. The secondary outcome measure is the difference in perspective between patients and professionals according to the best quality of endometriosis care.

Ethical considerations

In this study, formal ethical approval from a medical ethical committee was not required, since we did not use any patient medical data. Because all participants were adults, chosen on their expertise and willingness to participate, they were not considered vulnerable. Patients and professionals were informed by e-mail

about the purpose and aim of this study, the procedures to be followed, the anticipated time commitment, and contact details for any questions. All participants gave consent before inclusion in this study. Withdrawal from the study was possible any time. One person (M.J.S.) collected all data to respect the privacy of the participants. Names of the participants were not linked to their responses in the questionnaire feedback. Responses were collected and analysed anonymously. Safe storage of all data was provided.

Results

Composition of the expert panel

The seven participating patients represented six different countries: Belgium ($n = 2$), Finland ($n = 1$), Ireland ($n = 1$), The Netherlands

($n = 1$), Sweden ($n = 1$) and the UK ($n = 1$). Most of the patients (57%) had been diagnosed with endometriosis more than 10 years ago. A majority (86%) had experienced a delay in diagnosis of at least 5 years. All seven patients had undergone surgery as a treatment; 86% of them received additional treatment for endometriosis-associated pain, and 43% received additional treatment for endometriosis-associated infertility.

The 11 participating professionals also represented 6 different countries: Belgium ($n = 1$), Germany ($n = 1$), Israel ($n = 1$) The Netherlands ($n = 3$), Portugal ($n = 1$) and the UK ($n = 4$). Most of the experts were gynaecologists specialized in endometriosis (91%) with a subspecialization in reproductive health (73%) or surgery (27%). One of the experts was a medical doctor and senior scientist specialized in reproductive health and indicator development.

Further characteristics of the panel members and descriptive data are provided in online Supplementary data, Table SI.

Step 1: extraction and classification of recommendations

Altogether, 83 recommendations were extracted from the ESHRE guideline and distributed into four domains: (i) diagnosis ($n = 17$), (ii) treatment of endometriosis-associated pain ($n = 36$), (iii) treatment of endometriosis-associated infertility ($n = 20$) and (iv) miscellaneous topics ($n = 10$).

Step 2: first questionnaire (Delphi round 1)

In the first Delphi round, 17 (81%) out of 21 experts who had given consent to participate, completed the first online questionnaire. The response rates were 70% ($n = 7$) for patients and 91% ($n = 10$) for professionals (Fig. 3). Reasons for not responding were time constraints among professionals and language restrictions among patients. Non-responders were sent a reminder after 2 and 3 weeks. Additional clarification about the aim of the study and time investment was provided to one professional. None of the participating patients needed additional clarification or information. One patient filled out the first questionnaire during the second round and could therefore not be included in the data analysis of the first round. The time needed for participants to fill out the first questionnaire was 0:33:59 h for professionals (0:13:21–0:58:11 h) and 0:56:29 h for patients (0:22:28–1:52:43 h).

Step 3: data analysis of the first round

Recommendations were selected as potential key recommendations if they matched all of the criteria described above. Data analysis resulted in the selection of 11 recommendations (13%) (Table I), and rejection of 30 recommendations (36%). For 42 recommendations (51%), consensus could not be reached. The Mann–Whitney *U*-test showed significant differences in the distribution of ratings between patients and professionals for in seven recommendations (Table II). All of these seven recommendations were rated more highly by patients than professionals. By using the consensus criteria, one of these seven recommendations was selected despite the inconsistency in ratings between patients and professionals, showing a prominent patients' interest in good communication.

Step 4: second questionnaire (Delphi round 2)

In the second Delphi round, 16 (76%) out of 21 experts, completed the second online questionnaire. The response rates were 60% ($n = 6$) for patients and 91% ($n = 10$) for professionals (Fig. 3). The expert panel consisted of the same experts as in the first round. Non-responders were sent a reminder after 2 and 3 weeks. The time needed for participants to fill out the second questionnaire was 0:21:15 h for professionals (0:10:26–0:45:33 h) and 0:51:36 h for patients (0:15:01–2:14:17 h).

Step 5: data analysis of the second round

Recommendations were selected as potential key recommendations if they matched the criteria described above. Data analysis resulted in the selection of 6 further recommendations (14%), and rejection of the remaining 36 recommendations (86%).

The Mann–Whitney *U*-test showed no difference in the distribution of ratings between patients and professionals, thus showing a shift towards consensus between both subgroups.

Step 6: approval of selected recommendations (Delphi round 3)

All 17 responding experts (81%) agreed with the final set of 17 selected recommendations for the management of women with endometriosis (Table I). Of the 17 key recommendations, 11 were selected in the first round and 6 were selected in the second round, representing 20% of the preliminary set of recommendations that were extracted from the ESHRE guideline. The 17 key recommendations were equally divided over the 4 domains: (i) diagnosis of endometriosis ($n = 4/17$, 24%), (ii) treatment of endometriosis-associated pain ($n = 6/36$, 17%), treatment of endometriosis-associated infertility ($n = 4/20$, 20%) and miscellaneous ($n = 3/10$, 30%). Most key recommendations ($n = 11$) were good practice points (expert opinion), while the remaining six were supported with Level A evidence (meta-analysis, systematic review or multiple randomized controlled trials).

Discussion

As a first step in the development of quality indicators, an international expert panel of patients and medical professionals extracted 17 key recommendations from the ESHRE guideline 'Management of Women with Endometriosis'. Differences between patients' perspective and professionals' perspective of essential endometriosis care were seen in the first Delphi round, but disappeared in the following two rounds when opinions were swayed. The set of key recommendations covers all fields of endometriosis care, including diagnosis, treatment of endometriosis-associated pain, treatment of endometriosis-associated infertility and miscellaneous topics such as prevention, menopause and the relationship between endometriosis and cancer.

To our knowledge, this is the first study to select key recommendations as a first step in the development of quality indicators for the management of women with endometriosis. Remarkably, it is one of the few studies where a combined panel of medical professionals as well as patients is involved in the selection procedure. It is well-known that patients have an invaluable merit when it comes to assessing the relevance or the weight of quality indicators (Dancet *et al.*, 2013; den Breejen *et al.*, 2013; Pohontsch *et al.*, 2015). Eventually, patients are the ultimate experts in patient-centeredness of care (Grol, 2001a;
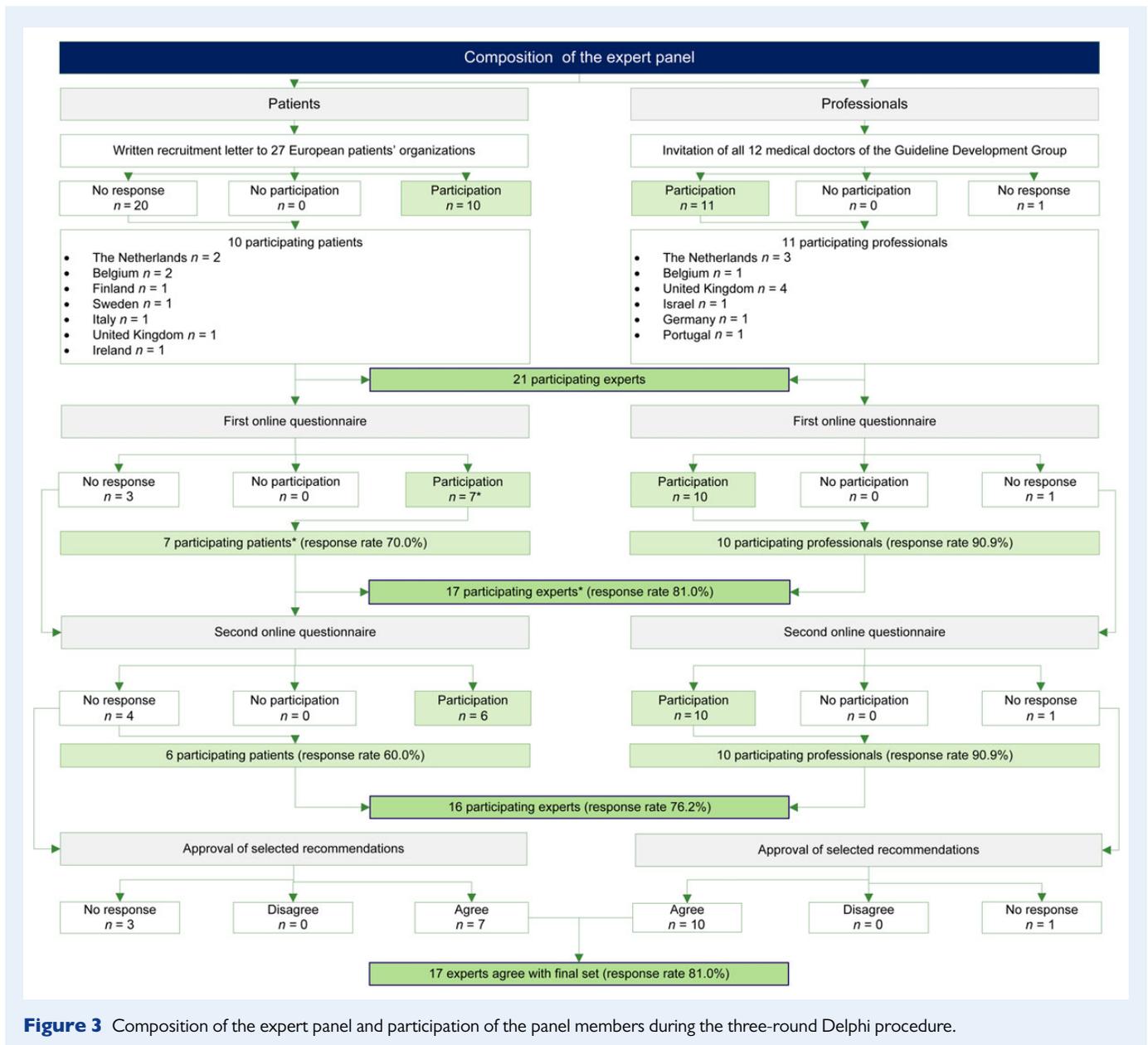
Figure 3 Composition of the expert panel and participation of the panel members during the three-round Delphi procedure.

Epstein and Street, 2011), which is one of core dimensions of quality of care (Institute of Medicine Committee on Quality of Health Care in America, 2001). The results of our study support the fact that there is a poor correlation between the patients' and professionals' initial perceptions regarding quality of care (Krahn and Naglie, 2008; Aarts et al., 2011; van Empel et al., 2011; Uphoff et al., 2012; den Breejen et al., 2013; Kotter et al., 2013). Hence, the set of key recommendations would have been different if only medical professionals were involved in the selection procedure. As an example, one of the key recommendations was selected by the patients despite a moderate popularity among the professionals, thereby overruling the opinion of the professionals. In this recommendation, medical professionals are advised to fully inform and counsel women about any incidental finding of endometriosis. This is in line with previous studies reporting that professionals underestimate the importance of 'softer' dimensions of healthcare

(e.g. respectful attitude and communication) and overestimate the importance of biomedical outcomes compared with patients (Laine et al., 1996; Rothwell et al., 1997; Mack et al., 2005; Wessels et al., 2010; van Empel et al., 2011). Furthermore, engagement of patients' perspective in healthcare not only leads to an higher patient-satisfaction, but is also proven to be effective clinically and economically (Coulter et al., 2008; Katz and Hawley, 2013; van Veenendaal et al., 2015). Several studies on shared-decision making show correlations with improved health outcomes, better communication, and reductions in costs and unwarranted variations in care (Stacey et al., 2011; Wennberg, 2011; Oshima Lee and Emanuel, 2013).

The final set of 17 key recommendations fits the need for process and structural indicators besides outcome indicators (Nelen et al., 2007). Quality indicators can assess structures, processes and outcomes of healthcare (Donabedian, 2005). Outcome indicators are mainly used

Table I The final set of key recommendations for the management of women with endometriosis in European hospitals.

Recommendations divided by chapter	Level of evidence	Selection round
Clinicans should, in all women with endometriosis		
Diagnosis of endometriosis		
I—Consider the diagnosis of endometriosis in the presence of gynecological symptoms such as: dysmenorrhea, non-cyclical pelvic pain, deep dyspareunia, infertility and fatigue in the presence of any of the above	GPP	1
II—Consider the diagnosis of endometriosis in women of reproductive age with non-gynecological cyclical symptoms (dyschezia, dysuria, hematuria, rectal bleeding and shoulder pain)	GPP	1
III—Perform transvaginal sonography to diagnose or to exclude an ovarian endometrioma (Moore *et al.*, 2002)	A	2
IV—Assess ureter, bladder and bowel involvement by additional imaging if there is a suspicion based on history or physical examination of deep endometriosis, in preparation for further management	GPP	2
Treatment of endometriosis-associated pain		
V—Counsel women with symptoms presumed to be due to endometriosis thoroughly, and empirically treat them with adequate analgesia, combined hormonal contraceptives or progestagens	GPP	1
VI—Prescribe hormonal treatment [hormonal contraceptives (Level B), progestagens (Level A), antiprogestagens (Level A) or GnRH agonists (Level A)] as one of the options, as it reduces endometriosis-associated pain (Vercellini *et al.*, 1993; Brown *et al.*, 2010, 2012)	A-B	2
VII—Take patient preferences, side effects, efficacy, costs and availability into consideration when choosing hormonal treatment for endometriosis-associated pain	GPP	1
VIII—Prescribe hormonal add-back therapy to coincide with the start of GnRH agonist therapy, to prevent bone loss and hypoestrogenic symptoms during treatment. This is not known to reduce the effect of treatment on pain relief (Mäkäräinen *et al.*, 1996; Bergqvist *et al.*, 1997; Taskin *et al.*, 1997; Moghissi *et al.*, 1998)	A	2
IX—Surgically treat endometriosis when identified at laparoscopy, i.e. 'see and treat', as this is effective for reducing endometriosis-associated pain (Jacobson *et al.*, 2009)	A	1
X—Refer women with suspected or diagnosed deep endometriosis to a centre of expertise that offers all available treatments in a multidisciplinary context	GPP	1
Treatment of endometriosis-associated infertility		
XI—Perform operative laparoscopy (excision or ablation of the endometriosis lesions) including adhesiolysis, rather than performing diagnostic laparoscopy only in infertile women with AFS/ASRM stage I/II endometriosis, to increase ongoing pregnancy rates (Nowroozi *et al.*, 1987; Jacobson *et al.*, 2010)	A	1
XII—Perform excision of the endometrioma capsule, instead of drainage and electro coagulation of the endometrioma wall in infertile women with ovarian endometrioma undergoing surgery, to increase spontaneous pregnancy rates (Hart *et al.*, 2008)	A	2
XIII—Counsel women with endometrioma regarding the risks of reduced ovarian function after surgery and the possible loss of the ovary. The decision to proceed with surgery should be considered carefully if the woman has had previous ovarian surgery	GPP	1
XIV—Use assisted reproductive technologies for infertility associated with endometriosis, especially if tubal function is compromised or if there is male factor infertility, and/or other treatments have failed	GPP	2
Miscellaneous topics		
XV—Continue to treat women with a history of endometriosis after surgical menopause with combined estrogen/progestagen or tibolone, at least up to the age of natural menopause	GPP	1
XVI—Fully inform and counsel women about any incidental finding of endometriosis.	GPP	1
XVII—Inform women with endometriosis, requesting information on their risk of developing cancer that (i) there is no evidence that endometriosis causes cancer, (ii) there is no increase in overall incidence of cancer in women with endometriosis and (iii) some cancers (ovarian cancer and non-Hodgkin's lymphoma) are slightly more common in women with endometriosis	GPP	1

ESHRE, European Society of Human Reproduction and Embryology; GPP, good practice points; GnRH, gonadotropin-releasing hormone; AFS/ASRM, American Fertility Society/American Society for Reproductive Medicine; Level A, meta-analysis, systematic review or multiple randomized controlled trials (high quality); Level B, meta-analysis, systematic review or multiple randomized controlled trials (moderate quality); Level C, single randomized controlled trial, large non-randomized trial, case-control or cohort studies (moderate quality); Level D, non-analytic studies, case reports or case series (high or moderate quality); GPP, expert opinion.

by health insurances to judge hospitals in clinical practice. However, good outcome measures do not necessarily stand for good quality of care, while the application of process and structural indicators in daily practice can lead to better outcome measures (Mant, 2001; Smith *et al.*, 2008). Therefore, process and structural indicators are more valuable in healthcare improvement than outcome indicators, because they reveal the barriers in healthcare and provide clear pathways for action (Mainz, 2004).

A key strength of this study is the combination of evidence and expert opinion, involving both patients and medical professionals from nine

Table II Recommendations with a significant difference between patients' opinion and professionals' opinion in the first questionnaire round.

Recommendations divided by chapter	Median score patients	Median score professionals	Mann–Whitney U-test	Conclusion
Clinicans should, in all women with endometriosis				
Diagnosis of endometriosis				
Consider the diagnosis of endometriosis in the presence of gynecological symptoms such as: dysmenorrhea, non-cyclical pelvic pain, deep dyspareunia, infertility, fatigue in the presence of any of the above	9	8	0.007[a]	No consensus
Be aware that the usefulness of 3D sonography to diagnose rectovaginal endometriosis is not well-established	9	5	0.007[a]	Rejected
Be aware that the usefulness of magnetic resonance imaging (MRI) to diagnose peritoneal endometriosis is not well-established	9	6	0.042[a]	Rejected
Treatment of endometriosis-associated pain				
Consider prescribing aromatase inhibitors in combination with oral contraceptive pills, progestagens, or GnRH analogues in women with pain from rectovaginal endometriosis refractory to other medical or surgical treatment, as they reduce endometriosis-associated pain	8	5	0.013[a]	Rejected
Be aware that presacral neurectomy (PSN) is effective as an additional procedure to conservative surgery to reduce endometriosis-associated midline pain, but it requires a high degree of skill and is a potentially hazardous procedure	8	7	0.040[a]	Rejected
Consider medical treatment of extragenital endometriosis when surgical treatment is difficult or impossible, to relieve symptoms	8	7	0.040[a]	No consensus
Miscellaneous				
Fully inform and counsel women about any incidental finding of endometriosis	9	7	0.008[a]	Selected

[a]$\alpha = 0.05$.

different countries. A second strength is the number of selected key recommendations. Although previous studies show an average number of 20–50 quality indicators per condition (Boulkedid et al., 2011), ideally the development of quality indicators results in a compact set of ≤5 indicators per clinical area (van Doorn-Klomberg et al., 2013). We expect the set to be reduced by 10–20% during the practice test (Wollersheim et al., 2007). Other strengths of our study are the satisfying response rates and the panel size. According to the RAND manual, a panel size of at least 7–15 experts is recommended in order to develop a reliable set of indicators (Fitch et al., 2001). The number of participants in this study is comparable with panels used in other Delphi studies (Fitch et al., 2001; Boulkedid et al., 2011; Kotter et al., 2012; Diamond et al., 2014). Furthermore, our expert panel represented a robust sample of the most important stakeholders to make sure that all aspects of endometriosis care could be discussed. All professionals were medical doctors specialized in endometriosis and involved in the development of the ESHRE guideline. Our study included both fertile- and non-fertile patients, who had all undergone surgical treatment for endometriosis and at least one other therapy for endometriosis-associated pain or infertility. The literature shows that diversity of experts panel members leads to better performance as this may allow the consideration of different perspectives (Murphy et al., 1998). This diversity provides a suitable set of key recommendations for endometriosis care and should support a broad acceptance in daily practice internationally. A fourth strength is our methodologically strong Delphi design based on the RAND-manual, which is a renowned method for the development of quality indicators.

Although the response rates were good, some response bias may have occurred as not all panel members took part in all three rounds (Sica, 2006) because of time constraints, complexity of the Delphi procedure or language problems, experienced especially by patients. Therefore, the final set might reflect the opinion of the most motivated panel members and higher educated patient representatives (Sica, 2006). Furthermore, the homogeneity of the patients included in this study (e.g. all had a prominent role in a patient organization, all underwent surgery, and most of them had a long delay in diagnosis) may have influenced their scoring behaviour. However, we consider the involved patients to be representative because of their diverse backgrounds and leadership in various international patient organizations (Hermens et al., 2006; Ouwens et al., 2010; Kesmodel and Jolving, 2011; Kotter et al., 2013). Another discussion point is the level of evidence of the selected recommendations. Quality indicators are more easily accepted in clinical practice if they are build on an high level of evidence (Mainz, 2004). Our final set included six recommendations based on Level A evidence. The remaining 11 recommendations were good practice points, formulated by members of the guideline development group. Although expert opinion is considered to be the lowest degree of evidence, the selection of these recommendations over recommendations with an higher level of evidence, shows their importance in daily practice (Eddy, 1998). Finally, the feasibility of the selected key recommendations was not assessed in this study.

Implications for practice and future research

In order to improve healthcare, quality indicators should be relevant, valid, reliable and feasible. All key recommendations in our final set are

facially valid and reliable because they are based on an evidence-based guideline and selected on strict criteria by a considerable expert panel. The next step in the development of quality indicators should be to assess the feasibility of the key recommendations in clinical practice (Campbell et al., 2003). We suggest a pilot study in one or two hospitals to establish the applicability and measurability of our set of our key recommendations.

In future, the final set of quality indicators should be available for all hospitals to measure and monitor the actual endometriosis care and potential barriers to guideline adherence internationally. A multifaceted implementation strategy tailored to guideline-specific barriers should facilitate further improvement of endometriosis care (Grol and Grimshaw, 2003). Future research has to establish whether this implementation strategy has a positive influence on guideline adherence and healthcare outcomes.

Conclusion

This study describes the systematic selection of key recommendations for endometriosis care by an international panel of patients and medical professionals as a first step in the development of quality indicators. The entire set of 17 key recommendations provides useful information on essential endometriosis care, regarding patients' and professionals' perspectives. In future, quality indicators can help to better implement the ESHRE guideline in hospitals by using strategies based on guideline-specific barriers, and thereby improve the quality of endometriosis care internationally.

Furthermore, our results reinforce the importance of involving patients in the development of guidelines and quality indicators.

Supplementary data

Supplementary data are available at http://humrep.oxfordjournals.org/.

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Authors' roles

M.J.S., W.L.D.M.N., G.A.J.D. and N.V. designed the research project. M.J.S. and N.V. composed the expert panel. M.J.S. conducted the surveys, led data collection, performed data analysis and wrote this manuscript. The EndoKey members filled out the surveys. W.L.D.M.N., G.A.J.D. and N.V. contributed substantially to data interpretation and manuscript revisions. All authors read and approved the final manuscript.

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Conflict of interest

The authors and members of the EndoKey study group declare that they have no conflict of interest in this procedure.

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