

## ARTICLE



# Identification of research priorities in infertility and assisted reproduction: an international, multicentre study



## BIOGRAPHY

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## KEY MESSAGE

Research into the efficacy and safety of fertility treatments is greatly valued by patients, but causes of infertility (environment, genetics, age), prevention (diet, lifestyle) and psychosocial aspects (how to cope with infertility) can be even more important than success rates of ART.

## ABSTRACT

**Research question:** What are the main research interests among patients of assisted reproductive technologies (ART)?

**Design:** Cross-sectional study consisting of an anonymous online survey sent to 2112 patients from eight centres in four countries in 2018. Patients were asked to identify research questions relevant to them in the field of infertility and ART. Answers were categorized into topics and ranked by frequency. A long list of the top 30 research topics was extracted from the aggregate results, from which a short list of the top 10 research topics was created. Ten research questions were finally formulated.

**Results:** A total of 945 responses were analysed. Main interests were side-effects, success rates, infertility prevention and emotional support. The 10 research questions were: 1. What are the side-effects of drugs used in ART treatments? (51.6%). 2. What are the most effective methods to cope with infertility from the psychological point of view? (35.7%). 3. What effects could diet have on fertility? (25.9%). 4. What are ART success rates per clinical profile? (24.8%). 5. Are there some habits and lifestyle factors that could prevent infertility? (20.0%). 6. What are the long-term risks associated with ART in mother and child? (18.5%). 7. Are alternative therapies such as acupuncture, yoga and meditation effective to treat/prevent infertility? (18.5%). 8. What is the impact of exercise on fertility? (15.4%). 9. How does oocyte quantity and quality affect fertility? (9.5%). 10. What are the genetic patterns or hereditary conditions causing/related to infertility? (9.5%).

**Conclusions:** Researchers and clinicians should keep in mind that, in addition to success rates and safety, patients greatly value research into causes, prevention and emotional aspects of infertility.

## KEYWORDS

ART treatments  
Fertility protection  
Healthy habits  
Infertility prevention  
Patient involvement  
Psychological effects

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## INTRODUCTION

In several medical fields and over the last decade, the involvement of patients and care-givers in setting research agendas has gathered significant momentum. Patient involvement in healthcare research offers a number of perceived benefits, including improved patient awareness and knowledge of their condition, and greater understanding of medical professionals about the implication of the condition on the patient's quality of life (Brett *et al.*, 2014). Moreover, setting a correct and relevant research agenda for patients has been proposed as an efficient way to reduce costs associated with redundant research activities (Chalmers *et al.*, 2014). The priority setting exercises carried out in several patient populations, for example by the James Lind Alliance (JLA) (<http://www.jla.nihr.ac.uk/>), have consistently reported significant differences in the perceived importance of research questions for researchers and academics compared with patients, which are ultimately the consumers of the research outcomes. The highest priorities are usually shared, for instance improving treatment to achieve a higher probability of cure, which is a high priority for all stakeholders. However, research into improving quality of life and lifestyle support is consistently given higher importance by patients and care-givers than by clinicians (Barnieh *et al.*, 2015).

Although priority setting partnerships have been used to identify specific research priorities for patients with several chronic diseases like Parkinson's (Deane *et al.*, 2014), spinal cord injury (van Middendorp *et al.*, 2016) or stroke survivors (Pollock *et al.*, 2014), such exercises have only recently started to appear in the general context of infertility, through the *Priority Setting Partnership for Infertility initiative* (2019). Nevertheless, infertility has been estimated to affect up to one in eight women and one in ten men attempting to conceive (Datta *et al.*, 2016); the ageing Western population and parenthood postponement (Schmidt *et al.*, 2012) indicate that the number of people needing treatment to conceive will increase in the future.

As it becomes more urgent to include infertile patients in the research agenda decision-making at both international and local level, the aim of this survey was to identify a list of patient needs in infertility and ART research.

## MATERIALS AND METHODS

This international, multicentre, cross-sectional study consisted of an anonymous online survey among people attending a fertility centre for ART consultation. The survey was sent to all patients having attended a visit with a physician in one of the eight participant centres in Spain (4), Denmark (1), Brazil (2) and Colombia (1) between January and December 2018. The survey was available in six languages (Danish, Spanish, Catalan, Italian, French and Portuguese) according to the patient's country of origin: Denmark, Spain, Italy, Spain, France, Brazil and Colombia. The study obtained all the approvals legally required in each country prior to study initiation; in Spain (approved 24 October 2017), Brazil (approved 10 October 2018, reference number 2.953.497) and Colombia (approved 3 September 2018) the approval was obtained from their local research ethics committees, while in Denmark surveys using questionnaires that do not involve human biological material do not require ethical clearance [section 14(2) of the Act on Research Ethics Review of Health Research Projects of the National Committee on Health Research Ethics of Denmark, <http://en.nvk.dk/how-to-notify/what-to-notify>].

An online survey was specifically designed for this study by two of the authors (RV, DG), taking into account the main areas of the infertility experience: infertility causes and prevention, fertility treatments (medication and ART) and the psychosocial aspects of infertility. Survey preparation took into account the JLA recommendations (<http://www.jla.nihr.ac.uk/>) and similar surveys developed for different diseases, such as spinal cord injury (van Middendorp *et al.*, 2016) or Parkinson's (Deane *et al.*, 2014). The survey was prepared through the platform 'Google Forms' and the expected completion time was about 20 min. The survey questions are listed in the **Supplementary Material**.

A pilot study was first performed to test the survey. Then, the main study was run and research priorities were gathered from the collected data. A long list of the top 30 main interest areas were identified, from which a short list of the top 10 interest areas was extracted. Finally, 10 research questions related to these main interest areas and

based on real patients' questions were constructed. These phases of the study are further described below.

### Pilot study

The pilot study was run to evaluate whether the proposed survey was an appropriate tool to identify research priorities in infertility, based on whether participants would answer by identifying questions, and the variability in their answers. For instance, because infertility does not usually represent a significant physical burden for the patient, it might be that all responses were centred on just one area of research, for instance success rates, narrowing the scope of the survey too much. The proposed survey was tested on a group of 100 individuals, randomly selected among all patients who attended a first visit in 2017 at one of the participating centres. The survey resulted in no modification following the analysis of the pilot study results. An initial categorization of patient answers by areas of interest was extracted, and the authors agreed with the categorization of possible answers for the main study.

### Main study

During this phase, the survey was sent to patients attending the participant centres in Spain, Denmark, Brazil and Colombia during the study period. Depending on the legal and ethical requirements of each participating country, patients were contacted retrospectively (Spain, Colombia) or prospectively (Spain, Denmark and Brazil). Patients attending the centre or planning a visit in 2018 at the time of sending the survey were invited to participate. When patients were in couples, the survey was open to both partners. When necessary, patients were informed about the study face to face or by telephone, prior to sending them the link to the survey by e-mail. Two reminders were sent to all the patients, 2 and 4 weeks after it was initially sent.

### Data analysis

Individual patient answers were collected, translated into English, analysed and classified according to the categories set up at pilot study by two authors at each study centre together with the first author. Categorized answers from each centre were aggregated by two of the authors (DG and SB). All identifiable research uncertainties in the survey were categorized according to their



theme and overall questions. Care was taken to strike a balance between over-binning (too much granularity) and under-binning (too few broad areas). The categorized answers were ranked according to their frequency per country and aggregated. A long list of the top 30 research topics was extracted and discussed among the authors to agree the top 10 topics of main interest per country and aggregated. To select the short list, some closely related items (e.g. general side-effects and long-term side-effects of drugs) were grouped, and their frequencies added. At the end, 10 research questions related to each of the top 10 research topics were constructed, based on the real answers

given by patients (similar structure and wording).

## RESULTS

### Study population

Overall, 2112 patients were contacted, and 945 surveys were completed (response rate 44.7%) and analysed. Female (845, 89.4%) and male (100, 10.6%) patients were included. At the time of the survey, mean age of patients was 37.8 (SD 17.4). Of 938 patients answering, 523 were childless (55.8%), 364 had children (38.8%), and 5 were pregnant (5/938 = 0.5%). Most of the patients (579/943, 61.4%) had undergone treatment with their own gametes, 304/943 (32.2%) had resorted to gamete

donation, and 60/943 (6.4%) had not yet started treatment.

Regarding the distribution of answers per the patient's origin and mean age, 342 (36.2%) were Danish (35.6 years), 170 (18.0%) Italian (40.9 years), 159 (16.8%) Spanish (37.7 years), 122 (12.9%) French (38.6 years), 108 (11.4%) Brazilian (36.5 years) and 44 (4.7%) Colombian (37.4 years).

### Long list of research priorities

The general long list of research priorities with the top 30 main topics highlighted by participants is displayed in TABLE 1.

Overall, the main interests were related to protection of fertility, prevention of infertility and improvement of treatment safety and success rates. For instance, participants were concerned about the effects that modifiable habits and lifestyle (diet, exercise) may have. Some examples of real answers given by patients regarding these aspects are: 'Is there a diet that can improve fertility/sperm quality, or are there any dietary supplement we should take?', 'Can nutrition help improve sperm quantity?', 'Are there any foods or vitamins that help in prevention?', 'Do pineapple and coconut water actually help the embryo in the uterus?', 'How much exercise am I allowed to do and what type, and can exercise improve fertility?'. These interests were even more important than success rates and safety of ART.

Regarding success rates, patients were interested in absolute values of ART results for different clinical profiles: 'How high a percentage of a specific age group becomes pregnant', 'Percentage of completed pregnancies dependent on the techniques used'. With regard to safety, concerns about the side-effects of drugs and the risks associated with ART, in mother and child, were common: 'How safe is the medication for the mother and the child?', 'Which pathologies are related to fertilization treatments?', 'Does the biopsy cause any problems for the embryo?', 'What are the risks for my child, and are ART children more likely to suffer from some diseases/conditions?'. The main concern was the risk of cancer in the future: 'Can the drugs for ovarian hyperstimulation lead to future cancer?', 'I would like to know the actual risks of getting cancer because of the treatment and if people with a family history of cancer are more likely to get the disease if they undergo

**TABLE 1 LONG LIST OF RESEARCH PRIORITIES (30 ITEMS)**

Topics	Frequency (%)
Impact of diet on fertility and ART success	25.9
Success rates of ART	24.8
Long-term side-effects of drugs (including cancer)	21.6
How to cope with infertility (general)	20.1
Healthy habits (general)	20.0
General side-effects of drugs (including short-term)	19.9
Alternative therapies	18.5
Risks associated with ART	18.5
Impact of exercise on fertility and ART success	15.4
General psychological support	12.1
Safety of treatments (general)	10.1
Individual psychological support	9.6
Genetic or hereditary causes	9.5
Oocyte quality, ovarian reserve	9.5
Impact of nervousness, stress, anxiety	9.4
Implantation failures (miscarriages)	8.8
Early infertility diagnosis	8.4
Male factor infertility reasons	7.7
Treatment personalization	7.5
Idiopathic infertility (not identifiable) reasons	6.8
Woman's age	6.7
Diseases (not STD) related to infertility	6.6
Composition, action mode of drugs used in ART	6.5
Efficacy of drugs used in ART	5.1
Impact of environmental pollution on fertility	5.0
Cancer risk in the future due to drugs used in ART	4.4
Group psychological support	4.2
How to cope with the couple relationship	4.2
How to cope with infertility in society	4.1
Availability of diagnostic tests (infertility, ovarian reserve)	4.0

ART = assisted reproductive technology; STD = sexually transmitted disease.

IVF. Evidence for alternative therapies was often queried: 'Does acupuncture help?', 'It would be interesting to be informed about the value of acupuncture, osteopathy, homeopathy, etc... following ART (with supporting studies)'.

The emotional aspects of infertility and its treatment were important to participants too, for example, one patient wrote: 'I wonder if the medication used during treatment affects the emotional side. I feel that I become more emotional and less patient, but I often believe this is due to the unwelcome anxiety that the treatment generates. Is there any evidence of mood swings with the use of these medications?' Patients also requested more skills to cope with infertility and more emotional support (individual or couple support and group therapy), for example: 'What is the best therapeutic approach in psychology to treat aspects of infertility?', 'We would like to know more about techniques to avoid depression/anxiety during treatment', 'How can you talk to your partner about it, and what should you talk about before starting treatment?'.

Participants wondered about the causes of infertility, especially genetic or hereditary causes: 'Is infertility hereditary?', 'Is infertility a process that you develop or is it already defined by our DNA?', ovarian reserve: 'Why are my eggs not fertile?', male factor: 'I'd like more research on DNA fragmentation and its effect on fertility', effect of stress on fertility: 'How can anxiety affect treatment (does the release of hormones such as cortisol change the response to IVF medications)?', the origin of miscarriages: 'I wonder whether anxiety

and panic disorder can affect pregnancy establishment or cause miscarriage', 'Why does implantation failure happen?', accurate impact of female age: 'More knowledge and information about how female age influences infertility', 'At what age should we think about prevention? When we have the first menstruation or when we initiate sexual life?', 'It would be interesting to know in a personalized way the consecutive phases of the fertility decrease with time in a given person', concomitant diseases: 'I have hypothyroidism and I don't know whether this will further affect my infertility?', 'Does celiac disease affect male fertility?'.

Importantly, participants' answers throughout the survey indicate a need for more efforts on treatment personalization (personalized success rates, therapies adapted to individual patients), for instance: 'Which is the most effective treatment for infertility and the best adapted to my situation?', 'What are the actual success rates of a treatment taking into account the particular case?', 'Which treatment is best for us, and is it possible to customize the dose of medication by measuring parameters in blood?' Finally, participants would like a broader range of diagnostic tests to be available (infertility tests, ovarian reserve tests): 'Which tests should be requested by professionals so that infertility could be diagnosed earlier?', 'Is there any embryonic analysis that can detect whether the embryo will have infertility problems in the future?'.

#### Short list of research priorities and research questions

The general short list of research priorities with the top 10 main topics

extracted from the initial long list of 30 items and their frequencies are displayed in TABLE 2. After adding the topics related to side-effects of drugs (general, long-term and short-term) to the topic 'safety of treatments (general)', this became the number one research topic (51.6%). Similarly, topics related to psychological support (general, individual, group) and specific tools to cope (with the couple's relationship and with society) were grouped in a broader topic 'coping with infertility' and ranked at number 2 (35.7%). Numbers 3 and 4 were 'impact of diet on fertility and ART success' (25.9%) and 'success rates of ART' (24.8%), respectively.

Regarding similarities and differences in the answers of patients from different countries, all agreed on ranking 'safety of treatments', 'success rates of ART', 'coping with infertility' and 'diet' among their top 10 topics. 'Safety of treatments' was the top priority for all except Danish patients, who ranked it as second, after 'coping with infertility'. Danish patients also included 'treatment personalization' within their top 10 priorities. Other topics agreed by at least half of the countries were 'alternative therapies', 'exercise', 'general healthy habits' and 'genetic or hereditary causes'. In contrast, 'implantation failure and miscarriage' was a priority for Spanish and Italian patients, while Colombians were particularly concerned about 'male factor infertility', 'gametes and embryo selection' and 'woman's age'. French patients were also especially concerned about 'woman's age' (TABLE 3).

Finally, the general 10 research priority questions formulated with the short list of research priorities were: 1. What are the side-effects of drugs used in ART treatments? 2. What are the most effective methods to cope with infertility from the psychological point of view? 3. What effects could diet have on fertility? 4. What are ART success rates per clinical profile? 5. Are there some habits and lifestyle factors that could prevent infertility? 6. What are the long-term risks associated with ART in mother and child? 7. Are alternative therapies such as acupuncture, yoga and meditation effective to treat/prevent infertility? 8. What is the impact of exercise on fertility? 9. How does oocyte quantity and quality affect fertility? 10. What are the genetic patterns or hereditary conditions causing/related to infertility?

**TABLE 2 SHORT LIST OF RESEARCH PRIORITIES (10 ITEMS)**

Topic	Frequency (%)
Safety of treatments (side-effects)	51.6
Coping with infertility	35.7
Impact of diet on fertility and ART success	25.9
Success rates of ART	24.8
Healthy habits (general)	20.0
Risks associated with ART	18.5
Alternative therapies	18.5
Impact of exercise on fertility and ART success	15.4
Oocyte quality, ovarian reserve	9.5
Genetic or hereditary causes	9.5

ART = assisted reproductive technology.

**TABLE 3** SHORT LIST OF RESEARCH PRIORITIES (10 ITEMS) PER PATIENT'S ORIGIN

Order	Danish (n = 342)	Italian (n = 170)	Spanish (n = 159)	French (n = 122)	Brazilian (n = 108)	Colombian (n = 44)
1	Coping with infertility	Safety of treatments (side-effects)	Safety of treatments (side-effects)	Safety of treatments (side-effects)	Safety of treatments (side-effects)	Safety of treatments (side-effects)
2	Safety of treatments (side-effects)	Coping with infertility	Coping with infertility	Success rates of ART	Coping with infertility	Healthy habits (general)
3	Impact of diet on fertility and ART success	Impact of diet on fertility and ART success	Success rates of ART	Coping with infertility	Risks associated with ART	Success rates of ART
4	Healthy habits (general)	Oocyte quality, ovarian reserve	Impact of diet on fertility and ART success	Alternative therapies	Success rates of ART	Coping with infertility
5	Impact of exercise on fertility and ART success	Success rates of ART	Risks associated with ART	Impact of nervousness, stress, anxiety	Impact of diet on fertility and ART success	Gametes / embryo selection
6	Alternative therapies	Alternative therapies	Alternative therapies	Woman's age	Healthy habits (general)	Diseases (not STD) related to infertility
7	Success rates of ART	Implantation failures (miscarriages)	Early infertility diagnosis	Impact of diet on fertility and ART success	Alternative therapies	Male factor infertility reasons
8	Treatment personalization	Early infertility diagnosis	Implantation failures (miscarriages)	Genetic or hereditary causes	Impact of exercise on fertility and ART success	Early infertility diagnosis
9	Risks associated with ART	Risks associated with ART	Healthy habits (general)	Risks associated with ART	Oocyte quality, ovarian reserve	Woman's age
10	Impact of nervousness, stress, anxiety	Genetic or hereditary causes	Genetic or hereditary causes	Impact of exercise on fertility and ART success	Genetic or hereditary causes	Impact of diet on fertility and ART success

ART = assisted reproductive technology; STD = sexually transmitted disease.

## DISCUSSION

Priorities in infertility research according to the views of ART patients have gained importance in recent years, and several international groups are currently working through collaborative engagement, such as the Priority Setting Partnership for Infertility initiative. This study presents, in the form of 10 relevant research questions, a preliminary work on the aspects of reproductive research that patients wish to see investigated, based on their actual answers.

Unsurprisingly, the main concern of patients is the safety of ART (overall and within countries), including short-term and long-term side-effects of drugs, and risks for the mother and the child associated with techniques. Essentially, side-effects of fertility drugs are a common concern to patients in general, as they appear in similar studies performed in diseases like asthma (Elwyn *et al.*, 2010), epilepsy (Thomas *et al.*, 2010) or Parkinson's (Deane *et al.*, 2014). It might be expected that success rates of ART would be ranked at number two, next to safety; however, safety and efficacy are not always together and in this study success rates of ART is ranked at number four

(overall; it was between rank two and seven in the per country analysis). There are some other aspects of treatment that appear to be more important to patients than success rates, in line with previous studies showing that success rates were relatively more important to physicians than to patients (van Empel *et al.*, 2010). In particular, patients are more concerned with how to cope with infertility and its treatment; this concern ranked first among Danish patients, and second for all other groups. Clearly, both infertility and its treatment can generate high levels of distress (Massarotti *et al.*, 2019), especially in patients with multiple treatment failures (Verhaak *et al.*, 2007) or poor ovarian response (Gonda *et al.*, 2018). It is important to remember that some infertile patients in this study had already undergone several previous failed treatments. As shown by previous collaborative research, conditions around reproductive medicine like miscarriage (Prior *et al.*, 2017), stillbirth (Heazell *et al.*, 2015) and preterm birth (Duley *et al.*, 2014) require effective emotional support to be investigated. Similarly, another study among women with endometriosis (Horne *et al.*, 2017) draws attention to improving the quality of life of patients.

While counselling has been judged by ART patients to be useful prior to treatment (Dancet *et al.*, 2010) and necessary during treatment (van Empel *et al.*, 2010), more research into the effectiveness of alternative therapies aimed at reducing distress around treatment is needed (ranked priority number seven overall). A systematic review of complementary therapies (mainly acupuncture, mind-body and cognitive techniques) showed the effectiveness of these techniques in decreasing anxiety in women undergoing IVF, indicating they might help women to cope with distress (LoGiudice and Massaro, 2018). However, reproductive outcomes after acupuncture were found to be increased when compared with no adjunctive treatment controls, but no significant differences were identified when compared with sham controls (Smith *et al.*, 2019). Similarly, elevated levels of negative emotions have been associated with using complementary and alternative medicines (Bardawell *et al.*, 2013). These medicines can be viewed as natural, enhancing or low-cost treatments, but their efficacy and safety are inconclusive (Porat-Katz *et al.*, 2015). More research (and dissemination of research results) is needed in order to make clear to patients and professionals



which habits and complementary/alternative medicines and therapies may help (or not) in preventing infertility and add to fertility treatments.

Prevention of infertility is an important issue raised by ART patients, specifically through concerns about the nature of a healthy lifestyle. This is reflected in the questions in this study, with a special interest in the impact of diet on infertility and its treatment (ranked at number three overall). Although recent published studies about diet and fertility (Chiu *et al.*, 2018, Nassan *et al.*, 2018) and different diet patterns and IVF outcomes (Karayiannis *et al.*, 2018, Sugawa *et al.*, 2018) indicate a keen interest in this topic, in this survey the relative importance of diet appears to be unexpectedly high. This could be due to the relatively low difficulty in modifying this factor, for example by introducing food supplements or so called 'superfoods', in comparison to other lifestyle changes that are more difficult to maintain, such as changing unhealthy habits or introducing regular physical activity into one's routine.

In addition to research into the aspects commented on above, there is still room for research into the causes of infertility. For instance, Spanish and Italian patients were particularly concerned by implantation failure and miscarriage, possibly because participants from these countries were amongst the oldest and these conditions are associated with a woman's age. Genetic and hereditary causes were a main interest for 1 in 10 patients overall, who wondered whether or not they could have done something to prevent infertility, and more importantly, whether infertility could be transmitted to their offspring. Although not related to treatment safety, this aspect is related to the ever-present preoccupation about the health of the future child. Among other possible infertility causes, causes related to ovarian reserve and oocyte quality were the most frequently interrogated, while interest in male factor was probably underrepresented because only 10.6% of respondents were men, in addition to a historical lack of focus on male factor diagnosis and treatment.

This study does have some limitations. First, although all respondents had attended a fertility centre, not all had

already started treatment at the time of response, while a few were pregnant; priorities for research in different groups of participants might have been influenced by their infertility journey. Second, participants were recruited in private fertility centres, and areas of research interest may vary in different public settings (for instance, patients in a private setting might feel more confident that pregnancy rates are already as high as possible in the clinic environment, and thus focus their questions on other areas of treatment). Third, the survey was mainly sent to women, so male patients are present, but underrepresented. Lastly, all patients attended a first visit in one of the participating centres, but not all of them were diagnosed with infertility (for instance single women or women in a same-sex relationship). Therefore, some participants might not have answered the survey because they did not consider themselves concerned with infertility, lowering the response rate of the study, or skewing some of the answers towards questions related to techniques and drugs, rather than, for instance, infertility causes.

The topics indicated by patients in this research are also reflected in the report by the Priority Setting Partnership for Infertility. This report differentiates between uncertainties in four main areas (male infertility; female and unexplained infertility; medically assisted reproduction; and ethics, access and organization of care research) and includes some questions that can be considered aligned to these results, for instance: 'What are the causes of implantation failure?', 'Can age-related infertility be prevented?', 'Are nutraceuticals useful in improving male reproductive potential?', 'What is the optimal method of embryo selection during IVF cycles?' and 'What are the emotional and psychological impacts of repeated fertility treatment failure?'.

Following the current study, the next step in setting the research agenda for infertility research should be to establish which questions need further research to be answered, and which ones are in fact already answered. Patients cannot be expected to possess sufficient knowledge of the field to know which questions can and cannot be answered on the basis of research already published. Therefore, researchers and care-givers should ensure that evidence gathered

from biomedical research is effectively transmitted to patients. Once this sorting has been performed, the results can be translated to all stakeholders, who are more and more interested in addressing the needs of patients in research. In line with this, the European Medicines Agency (EMA) has recently published a booklet about the European procedure for human medicines authorization (EMA, 2019), which highlights how patients participate together with healthcare professionals in scientific advisory groups (one in five groups in 2017 involved patients). In these groups, patients are involved as experts, giving their views on whether a medicine can address their needs, describing their experience and their personal balance of the risk/benefit ratio for a given treatment (93% of procedures in 2017 were adapted on the advice of patients).

In conclusion, researchers and clinicians should keep in mind that, in addition to improvements in treatment success rates and side-effects of fertility treatments, patients greatly value research into causes, prevention and emotional aspects of infertility. As their views might differ from those of medical professionals, patients' voices should be incorporated when setting infertility research priorities. This study should be considered as a preliminary work on the involvement of ART patients in assessing relevant outcomes for clinical research.

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## SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.rbmo.2019.10.012.

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