“Patient-centered fertility treatment”: what is required?

Reproductive medicine provides treatments of varying invasiveness, ranging from ovulation induction to assisted reproductive technology (ART) with preimplantation genetic diagnosis.

In daily practice, patients are insufficiently involved in choosing between treatment options [1], as treatment decisions are predominantly made by professionals based on their diagnosis of patients’ physical condition. Not only patients’ physical condition, but also patients’ treatment preferences, should be taken into account when choosing the right treatment option for an individual patient [2].

Similarly, clinical evaluation research primarily focuses on the effectiveness of treatments (secondarily on treatment safety and costs and less on burden) and conceptualizes outcomes from the viewpoint of professionals rather than patients. Increasing attention has been given to “patient-centered research”; this has, however, been restricted to patients’ perspectives on care (including system factors of care such as continuity and human factors such as emotional support) rather than treatment [3].

THE PROPOSED “FRAMEWORK FOR PATIENT-CENTERED FERTILITY TREATMENT”

This opinion paper proposes a “framework for patient-centered fertility treatment,” that gives patients a novel central position in daily practice treatment choices and in clinical evaluation research (Fig. 1).

The proposed framework looks at treatment through the patient’s rather than the professional’s eyes and simultaneously considers four treatment dimensions, namely: “burden,” “effectiveness,” “safety,” and (financial) “costs.” Giving patients this novel central position is crucial for simultaneously considering all treatment dimensions, which all influence patients directly. It should be noted that more treatment dimensions might be important to patients and might be added by future in-depth investigation of the patients’ perspective on fertility treatment.

Furthermore, the framework proposes that patients would be advised by professionals on effectiveness, safety, and costs (based on professionals’ education, clinical experience, scientific insights, and striving for beneficence), and that the results of systematic assessment of patients’ experiences should define advice on burden.

LITERATURE ON THE ELEMENTS OF THE FRAMEWORK

The proposed patient-centered fertility treatment framework is based on the results of discrete choice and trade-off experiments exploring subfertile patients’ hypothetical treatment choices starting from professionals’ conceptualizations of the four treatment dimensions [4]. To our knowledge, no studies have explored subfertile patients’ conceptualization and actual treatment choices.

The burden of treatment refers to a heavy workload and responsibility and the impact of treatment on patient functioning and well-being. Aspects considered by professionals to be burdensome for patients do not necessarily define patients’ preferences (e.g., number of medication injections). The importance of burden to patients’ hypothetical treatment choices differs between aspects of burden (e.g., medication side effects proved to be more important than cancellation stress).

Treatment effectiveness depends on the capability of producing a desired result in the real world of medical practice. Although patients agree with professionals that a live birth is desired, it is unclear which other results are desired (e.g., coping skills for potential childlessness?). Live birth rate (or its proxy, ongoing pregnancy rate) is the most important factor directing patients’ hypothetical treatment choices, but it is not fully dominant, because patients do not always choose the most effective treatment [4].

Treatment safety depends on avoiding all types (e.g., physical, psychologic) of non-desirable harm or injury. To date, most studies have been focused only on physical harm. More specifically, maternal safety risks (e.g., risk of ovarian hyperstimulation syndrome) affect patients’ hypothetical choices whether or not to start treatment rather than their choices between treatments [4]. The maternal and neonatal safety risks caused by multiple pregnancies are often accepted by patients, even if this would not result in higher pregnancy rates but only in more children per treatment. Furthermore, women waiting to undergo IVF value having a child with physical, cognitive, or visual impairment more than having no child at all.

The cost of treatment equals the money spent. Whereas no data are available on the influence of reimbursed and indirect costs (e.g., loss of work productivity), direct out-of-pocket costs are known to influence patients’ hypothetical treatment choices.

Studies on the influence of the six theoretically possible one-on-one trade-offs among the four treatment dimensions have shown that for patients’ hypothetical treatment choices, effectiveness is most important, followed equally by safety and financial costs, and then burden. Studies show that both the possibility to draw from other patients’ experience and the advice of professionals are important to patients and their treatment choices [3].

IMPLICATIONS OF THE FRAMEWORK FOR DAILY PRACTICE TREATMENT CHOICES

The patients’ central position in the patient-centered fertility treatment framework requires daily clinical practice to fully involve patients in treatment choices. This is only irrelevant in the exceptional circumstance where individual patients choose not to be involved. Nevertheless, shared decision making is required, because patients’ autonomy can not dismiss professionals’ autonomy and striving for beneficence.

Before sharing a decision, patients should be informed extensively on differences between treatments regarding all four treatment dimensions. Current evidence on the differences between treatments does not allow professionals to inform patients extensively. More specifically, there is a shortage of randomized controlled trials (RCTs) and
meta-analysis for “effectiveness,” large cohort studies for “safety,” cost-analysis for “costs,” and patients’ experience surveys for “burden.”

In their advice on treatment effectiveness and safety, professionals should take account of the following evidence from within the field of reproductive medicine: 1) provided risk information can be misunderstood as information on how to increase success rates; 2) awareness on risks does not necessarily result in concern about risks; and 3) stories from other patients increase consideration of safety. Furthermore, based on research from other fields, the following should be taken into account: professionals can encourage patients to value their overall long-term health, and patients have difficulties to correctly interpret risks owing to emotions and limited numeric skills.

Patients can potentially be informed extensively by using decision aids (DAs) [2], which are evidence-based tools allowing patient involvement in specific thought-out choices between treatment options. The only published DA for reproductive medicine guides patients’ choices between single- and double-embryo transfer and the study demonstrated that implementation of the DA led to an increased use of single-embryo transfer and limitation of cost, without increasing patients’ anxiety and depression [2].

In other fields, DAs have proven to offer several advantages. More specifically: for patients: 1) more knowledge; 2) reaching decisions that are in accordance with their values; and 3) less decisional conflict; and for professionals: beneficial for communication with patients. Furthermore, DAs can potentially decrease costs, the duration of consultations, and the number of patients seeking a second opinion (as a result of less decisional conflict). Moreover, the newest generation of DAs, option grids, promise to be easier to use than the older DAs because they are shorter (one A4 page) [2].

**IMPLICATIONS OF THE FRAMEWORK FOR RESEARCH**

Before full adaptation in daily practice, the patient-centered fertility treatment framework calls for more research. First, a truly patient-centered approach for fertility treatment requires research on patients’ conceptualization of treatment dimensions and actual treatment choices.

Second, DAs should be developed while adhering to the International Patient Decision Aids Standards. In reproductive medicine, DAs should provide patients with information on all treatment dimensions, tailored to the individual patient where possible (e.g., personalized success rates are valued by patients [3]). Furthermore, treatment options should always be compared with the option of trying to conceive naturally, which is safety-risk free, not burden free (i.e., not acting also results in burden), and low cost (i.e., ideally patient-centered care should be offered during the waiting time). Finally, information on rates should be tailored to patients’ ability to understand statistical and graphic information.

Third, to gather high-level evidence on differences between treatments, new multicenter RCTs should be set up comparing IVF, IUI, and trying to conceive naturally. In line with the proposed framework for patient-centered fertility treatment, patients should be given a more central role in these RCTs and all four treatment dimensions should be assessed. Patients should be involved in defining outcomes relevant to each of the four treatment dimensions, which goes further than using only “patient-reported outcomes” for the dimension burden. Based on the patients’ perspectives,
professionals can continue considering effectiveness as primary outcome. Furthermore, patients’ more central role in RCTs implies involving them as more than just study subjects (5). To our knowledge, no RCT has put patient involvement from its start (i.e., defining research questions), through its entire process (e.g., basing sample size calculations on the difference in effectiveness required for patients to change their preference), until its end (i.e., communicating results), to full practice. Finally, patients should also be involved in the decision on when to introduce new treatments into daily practice to make sure that all treatment dimensions important to them, rather than only safety and effectiveness, are taken into account.

CONCLUSION
The framework for patient-centered fertility treatment truly centrally concerns patients while simultaneously considering effectiveness, safety, costs, and burden of fertility treatments. This novel framework challenges the current approach of daily practice treatment decision making and calls for innovative research.

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