# What constitutes "futile" fertility treatments? Are we pushing patients too early to use donor eggs?

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Futility has been defined as "The quality of having no useful result; uselessness." In medicine the bar for futility is usually set quite high. In decisions concerning patient mortality aggressive measures to save a patient are generally taken unless the chance of survival is less than 1%. The Ethics Committee of ACOG defined care as futile if it is ''incapable of producing a desired result'' or is unable ''to achieve a physiologic goal''. In 2012 the Ethics Committee of the ASRM echoed this opinion in saying "… ''futility'' refers to treatment that has a ≤1% chance of achieving a live birth; ''very poor prognosis'' refers to treatment for which the odds of achieving a live birth are very low but not nonexistent (>1% to % 5% per cycle)." ASRM went on to say that practitioners had no obligation to treat patients with outcome chances they considered inadequate. The Society, however, in such cases also recommended that patients be offered referrals to practitioners who do offer such treatments.

The modern medical profession has moved away from a paternalistic stance of "doctors' orders" to greater patient autonomy with transparent sharing of information upon which medical decisions are based so that patients can now participate in important medical decisions. For couples struggling with problems of fertility a decision to end their treatment is very difficult. For some couples in which medical intervention for fertility seems completely futile, the exercise of treatment is needed to assure that all paths to parenthood with their own gametes have been explored and allowing them to move on to other, more fruitful, treatments such as donor eggs.

Age alone is a powerful predictor but is not alone a sufficient indicator. In the United States, poor-prognosis patients with low functional ovarian reserve (LFOR) only rarely receive open access to IVF. This can be deduced from annual national Centers for Disease Control and Prevention (CDC) reports, which demonstrate that women above age 42 still represent only a minute fraction of IVF cycles. The U.S. 2013 CDC data reported that only 6.6% of fresh non-donor IVF cycles were performed in women >43 years and only 16.8% in women >41 years.

We recently reported outcomes for 483 patients, who under the Bologna criteria (three or fewer oocytes, >40 years of age, and/or antimullerian hormone [AMH] <1.1 ng/mL [2/3 criteria minimum]) were poor responders, 278 (381 fresh IVF cycles) qualified for the study because they had at least one embryo on day 3 for transfer. These women received androgen and CoQ10 supplementation and ovarian stimulation with daily gonadotropin dosages of 300–450 IU of FSH and 150 IU of hMG in microdose agonist cycles.

Ages did not differ between non-elective (ne) single ET (SET), ne2-ET, and neR3-ET cycles (41.3 ± 3.9, 41.7 ± 3.1, and 42.4 ± 2.1 years, respectively). Patients with neSETs demonstrated significantly lower AMH and higher FSH levels and required higher gonadotropin dosages than ne2-ET and neR3-ET patients. LBRs declined with age.

Of 68 women above age 42 who had at least three embryos transferred 5 (7.4%) achieved live birth. If women above age 42 had only two embryos available for transfer only 1/54 (1.8%) achieved live birth. No women above age 42 with only one embryo available for transfer achieved live birth (0/55). Above age 42, three or more embryos are required to achieve reasonable LBRs and two or more to avoid futility under American Society for Reproductive Medicine (ASRM) guidelines.

Very poor prognosis patients can still achieve acceptable pregnancy rates at least till their mid-40s if they reach ET. The degree to which egg donation is emphasized as the only treatment option in such patients, therefore, requires reconsideration. Above age 42, at least two, and preferably three embryos, are however required to exceed futility, as defined by ASRM.

**Translational relevance:** This presentation highlights the importance of a full informed consent process so patients can understand the odds of possible live birth and choose between proceeding with their own eggs or those of a donor. As physicians we are obligated to balance the goals of patient autonomy with our obligation of not exposing patients to fruitless expensive and potentially risky medical procedures. At the same time, we must continue to expand our efforts to improve the utility of the use of autologous oocytes for poor prognosis patients through better understanding of the early biology of gametogenesis and our attempts to improve that process.