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Commentary on “Dropout rate and cumulative birth outcomes in couples undergoing In Vitro Fertilization (IVF) within a funded and actively managed system of care in New Zealand.”

**Title:** It is beneficial to support young, good prognosis patients, who strongly desire a biological child, through multiple cycles of treatment.

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It is well known that IVF/ICSI per cycle live birth rates are low (25%-30%) but that patients can increase their chances of achieving parenthood by undergoing repeated cycles. Women under 40 with good prognosis, in particular, have a 62.6% chance of achieving pregnancy with 3 cycles of treatment, and this goes up to 80.3% if they do 6 cycles (1).

Researchers have strived to understand to which degree IVF/ICSI treatment dropout is a problem and why some patients discontinue, but results have been highly heterogeneous. In 2012 myself and colleagues from the UK and The Netherlands conducted the first systematic review and meta-analysis of compliance rates with IVF/ICSI treatment, bringing together data from 10 studies and 14,810 patients (2). Our study showed that around 4 in every 5 patients who start IVF/ICSI treatment (i.e., 78.2%) either get pregnant or undergo at least three cycles of treatment. Nonetheless, dropout increases as patients repeat cycles, from 21.8% to 28.5% after the 1<sup>st</sup> and 2<sup>nd</sup> cycle, respectively.

Miller and colleagues (3) reported a lower dropout rate after the 1<sup>st</sup> cycle, of 10.4%, in a group of 974 young good prognosis couples who accessed funded fertility treatment in New Zealand and were actively managed through their treatment pathway. The authors explained patients were managed by treatment coordinators, who kept in touch with them and organized each step of treatment. They also had regular free contact with their fertility team, from whom they received written and in person information about treatment, and were encouraged to access counselling if in need. Finally, they had a review consultation with their doctor at the end of a failed complete cycle or when the cycle had an unexpected outcome (e.g., cancelled due to low response to ovarian stimulation). The cumulative birth rate for two complete cycles (totality of funded treatment in New Zealand) was 59.3% and higher than optimal estimates reported in the literature (50.6%, 1). The authors argue that it pays off to support young good prognosis patients through funded fertility treatment in order to prevent dropout and achieve high cumulative live birth rates.

To prevent dropout one has to understand why it happens. In Miller's study (3), consistently with current understanding, even though only 1 in 10 couples dropped out, the majority (63.8%) did it because of the psychological burden of treatment. Indeed, recent studies show that patients start treatment with strong intentions to achieve their goal of parenthood but these are eroded by the multiple challenges they experience during treatment, in particular the experience of an unsuccessful cycle. Patients tend to finish an IVF/ICSI cycle in a negative motivational state that is paired with depressive symptoms and low hopefulness of future success, and these compromise their ability to reengage with treatment despite sustained desire for parenthood (4). Results reported by Miller and colleagues (3) seem to indicate that actively managing patients by keeping in contact with them, and in particular after failure, can help to address erosion of initial treatment intentions. Recently we suggested that preparing patients in advance for the challenges of treatment and what to do if cycle(s) fail could help them normalize this experience and rebuild hope after failure (4). Harrison et al. (5) showed that the majority of patients (56%) value the opportunity to plan in advance to do multiple cycles of treatment. While they acknowledge the challenges of doing so (e.g., the ability to afford multiple cycles, the emotional impact of treatment), they feel able to do it and perceive multiple benefits, from better preparing for the full cost and time investment of treatment, to increasing their chances of success, but also, if all treatment is unsuccessful, having peace of mind of having tried everything they set themselves up to.

Overall, the work done by Miller and colleagues (3) further supports the idea that it is beneficial to support young, good prognosis patients, who have a strong desire to be biological parents, through multiple cycles of treatment. Such support could entail planning from the start for multiple cycles and providing the necessary information that allows patients to prepare in advance for how to cope with all challenges they may come to face. Furthermore, in the aftermath of a failed cycle, and as suggested by Miller et al. (3), clinics could be proactive in reaching out to their patients, with the goal of supporting them in revisiting their initial treatment plan and expressed values underlying such plan, while also boosting back hope of success. Active management of patients with low prognosis or who do not want to plan for multiple cycles would likely differ from the one specified.

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