

Correspondence

Response to: Paying more for no better outcome: The add-on crisis in modern medicine

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The authors raise important concerns regarding the proliferation of adjunctive technologies in assisted reproduction. Rigorous evaluation of emerging interventions is essential. However, the interpretation of time-lapse imaging, preimplantation genetic testing for aneuploidy (PGT-A), and artificial intelligence (AI)-based embryo selection warrants further nuance.

TIME-LAPSE IMAGING

Randomised controlled trials, including the large multicentre TILT trial, have not demonstrated improved live-birth rates following first embryo transfer with time-lapse incubation compared with conventional culture.¹ However, live birth per first transfer does not capture the full clinical contribution of this technology. Time-lapse systems have fundamentally altered embryology practice by allowing continuous monitoring, improved detection of abnormal cleavage patterns, and confirmation of fertilisation events that might otherwise go unrecognised. Studies have demonstrated that embryos arising from atypical fertilisation patterns, including those in which pronuclear formation is not observed, can result in live births when appropriately selected.²⁻⁴ Without continuous imaging, such embryos may be discarded unnecessarily. Thus, time-lapse imaging may increase the pool of embryos considered viable rather than directly improving implantation rates per embryo.

Additionally, TILT evaluated live birth following first transfer rather than cumulative live-birth rate across a treatment cycle.¹ Given that IVF success is commonly defined cumulatively, this distinction is clinically relevant. The study also permitted heterogeneous morphokinetic algorithms across centres, potentially diluting benefits associated with specific validated models. Earlier trials have most focussed on algorithms using early cleavage parameters while it is blastocyst morphokinetics work most associated with live birth.^{5,6}

PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY

The role of PGT-A remains complex and patient-specific. While randomised trials have not demonstrated improved cumulative live-birth rates in unselected populations.⁷ PGT-A is not designed to improve cumulative live birth or the absolute number of embryos capable of producing a live birth, but to improve selection. Arguably therefore, RCTs on cumulative live birth may not be the most effective way of investigating the utility of PGT-A. Non-selection studies on the other hand have demonstrated that the transfer of aneuploid embryos didn't result in a live birth in any cases, giving us confidence in the genetic results.⁸ Furthermore, observational studies consistently demonstrate higher live birth rates per transfer following euploid embryo transfer.⁴ The UK Human Fertilisation and Embryology Authority acknowledges that PGT-A reduces miscarriage risk, an experience and outcome that cannot be ignored for patients undertaking assisted conception since miscarriage carries substantial psychological burden.⁹

ARTIFICIAL INTELLIGENCE

AI-based embryo selection is frequently integrated within existing laboratory platforms rather than marketed as a distinct premium intervention by most clinics. While superiority in live-birth outcomes remains unproven, deep learning models have demonstrated promising predictive performance and reduced inter-observer variability.^{10,11} Laboratory standardisation is central to IVF success, and technologies that enhance reproducibility may confer indirect benefit. Whether associated costs should be passed to patients is a separate policy question.

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ECONOMIC CONTEXT AND CONCLUSION

Rising IVF costs cannot be attributed solely to add-on technologies. Increased expenditure on consumables, staffing, regulatory compliance, and infrastructure has significantly raised operational costs.¹² A balanced appraisal of emerging technologies should therefore acknowledge both their evidentiary limitations and their evolving clinical contri-

butions, while continuing to demand high-quality data to guide responsible adoption.

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