

Letter to the Editor

IVF Add-ons: The case for individualized application

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Keywords: IVF add-ons

<https://doi.org/10.46989/001c.166488>

Journal of IVF-Worldwide

Vol. 4, Issue 3, 2026

To the Editor:

I read with interest the recent exchange on IVF add-ons published in the *Journal of IVF-Worldwide*.¹⁻³ While I agree that the indiscriminate use of add-ons may increase costs without improving outcomes, a generalized dismissal risks oversimplifying a clinically complex and highly individualized field.

Drawing on more than three decades of clinical experience and over 22,000 IVF cycles, I have observed that outcomes are influenced by a multifactorial interplay of laboratory performance, embryo competence, endometrial receptivity, and patient-specific biological characteristics that are not always adequately captured in large, unselected studies. For this reason, the clinical value of certain add-ons may emerge primarily in carefully selected subgroups rather than in the general IVF population. Their use should therefore not be routine, but individualized, evidence-informed, and supported by transparent counselling.⁴

One example is time-lapse embryo monitoring. Beyond embryo selection, time-lapse systems may provide clinically relevant information in selected cases of recurrent implantation failure by identifying abnormal developmental events that may be missed during conventional fixed-point embryo assessment, including direct cleavage patterns, delayed or failed extrusion of the second polar body, and transient abnormal pronuclear configurations such as temporarily visible 3PN embryos.⁵ Although these findings are not independently diagnostic, they may contribute to a broader prognostic evaluation in selected clinical scenarios.

Similarly, in patients with recurrent implantation failure or recurrent pregnancy loss, individualized adjunctive approaches may include endometrial receptivity assessment, evaluation of chronic endometrial inflammatory conditions, carefully selected immunological investigations and treatments, and procedures such as endometrial scratching.^{6,7} While the evidence remains heterogeneous and these interventions should not be routinely proposed, some clinicians consider them reasonable in highly selected patients after repeated failure despite transfer of good-quality embryos.

Preimplantation genetic testing for aneuploidy (PGT-A) remains one of the most debated IVF add-ons. Large ran-

domized studies, including the trial by Yan and colleagues, have questioned its routine use in unselected patient populations.⁸ However, the recent committee opinion of the American Society for Reproductive Medicine and the Society for Assisted Reproductive Technology acknowledges that a potential role may still exist in selected groups, particularly in patients of advanced maternal age or in those with recurrent implantation failure or recurrent pregnancy loss.⁹ Observational studies have also suggested possible benefit in carefully selected populations.¹⁰ Therefore, while PGT-A should not be routinely recommended to all IVF patients, its selective and individualized application may still be clinically reasonable in specific contexts.

Recurrent IVF failure and miscarriage carry a substantial emotional and psychological burden for patients. Acknowledging this burden does not justify the indiscriminate use of unproven add-ons. Rather, it highlights the importance of transparent counselling, shared decision-making, and individualized discussion of potential adjunctive options, including their uncertain benefit, possible risks, and financial implications.^{4,11} Selective use of IVF add-ons is ethically justifiable when patients are fully informed about the quality of the evidence, the expected costs, and the possibility that additional expenditure may not improve live birth rates.^{1,4} In some cases, resources directed toward adjunctive interventions could be more appropriately invested in further treatment cycles with established benefit; individualized application must therefore always be accompanied by careful cost-benefit discussion and realistic counselling.

Current ESHRE recommendations emphasize transparent communication regarding the level of evidence supporting IVF add-ons, individualized counselling, and shared decision-making between clinicians and patients.⁴ These principles are particularly important in reproductive medicine, where biological variability and repeated treatment failure often complicate rigid protocol-based approaches.

In conclusion, the evidence-informed use of IVF add-ons in carefully selected patients remains compatible with individualized reproductive medicine and responsible counselling.

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Sincerely,
Domenico Ranieri, MD

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FUNDING

No financial support was received for this work.

CONFLICTS OF INTEREST

The author declares no conflict of interest.

ETHICAL APPROVAL

Not required for this correspondence.

DECLARATION OF AI USE

AI-assisted language editing tools were used exclusively for grammatical refinement and language improvement. All scientific content, interpretations, and clinical opinions are those of the author.

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Not available.

Submitted: July 15, 2026 CDT. Accepted: August 06, 2026 CDT.

Published: August 12, 2026 CDT.



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