



Reviews

Paying more for no better outcome: The add-on crisis in modern medicine – using infertility treatment as the primary example

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Introduction

Across many fields of medicine, expensive technologies have often been widely adopted based solely on biological plausibility and surrogate outcomes rather than validated outcome benefits. In reproductive medicine, in vitro fertilization (IVF) likely exemplifies this pattern more than any other medical practice. This is because IVF features among the lowest expected outcome success rates in medicine. Therefore, marketable interventions that demonstrate potential efficacy are in high demand by physicians and patients alike.

This commentary uses IVF as a case study to examine the “add-on phenotype” of contemporary medical innovation, exploring mechanisms that drive premature adoption of unvalidated technologies and outlining policy reforms to better align innovation with evidence, value, and equity.

Current State of the Field

Diagnostic and clinical add-ons have proliferated widely in routine IVF practice despite lacking any validation studies and, in some cases, despite showing strong evidence of no superiority or even inferiority. These add-ons include time-lapse incubation systems, preimplantation genetic testing for aneuploidy, routine blastocyst-stage culture, artificial intelligence-based embryo selection, and numerous additional unproven tests and clinical practices.

Analysis

The consequences of using these add-ons are serious. Despite the 2010 determination that chronological age is the primary predictor of IVF success, these add-ons have coincided with improvement failure or declining clinical pregnancy and live-birth rates in autologous fresh cycles nearly all around the world. This has occurred as treatment costs have steadily risen or skyrocketed in many countries, prompting governments and private insurers to provide less coverage and reduce access to treatment.

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Recommendations

Current IVF practices are in need of radical reforms at multiple levels. Critical peer reviews of published papers are designed to remove business interests from the IVF literature. Enhanced post-marketing surveillance should provide much more transparent communications with patients about evidence quality and costs. Reimbursement policies should reward demonstrated value. These steps promote a professional culture that balances innovation with restraint.

Conclusions

IVF is not alone, with similar patterns of new expensive interventions reportedly being widely used in orthopedics, aesthetic medicine, and other medical specialties without robust demonstration of benefit. Addressing this issue requires minimum evidentiary standards, especially for non-life-saving technologies and treatments, in which such abuses are more common than in life-saving medicine, where effectiveness is immediately apparent. Paradoxically, IVF, with its clear outcome metric of live-birth rates, can pioneer such an improved model of clinical practice and, in this fashion, set new standards for evidence-based innovation.

INTRODUCTION

Most private insurers pay for the initial infertility evaluation but not the costs of laboratory tests, imaging, and additional treatment. The median cost of IVF in the United States with medications is \$19,200.¹ This stunning cost has, over time, been “enriched” by the widespread use of time-lapse imaging, preimplantation genetic testing, artificial intelligence (AI)-based embryo selection and many other unvetted but costly add-ons.

However, a patient’s cumulative chance of bringing home a baby after an IVF cycle from all eggs generated in the cycle has, at best, remained the same as before these add-ons became prevalent. Even in large metropolitan areas, before add-ons were available, average costs were one-third to one-half of current costs.

Unfortunately, the economic costs of add-ons have been even more devastating if one looks at IVF cycle outcomes in autologous fresh IVF cycles, which have literally collapsed since 2010, declining year by year as add-on utilization expanded.²

This counterintuitive dynamic, that is, paying more for the same outcome, has become the defining feature of innovation in infertility practice and beyond, especially in non-life-saving medical fields. While technological innovations across numerous medical disciplines achieved substantial gains in survival and quality of life, a different pattern has emerged in non-life-saving medical practice areas, especially in fertility care, musculoskeletal dysfunction treatments, and aesthetic/cosmetic procedures. In all of these areas of medicine, expensive technologies have proliferated widely, often without any validated evidence that they indeed improve the treatment outcomes patients are primarily seeking.

IVF illustrates this pattern with profound clarity.³⁻⁷ Especially since chronological age was determined to be the single most critical predictor of IVF success,² the field of IVF has witnessed rapid, widespread adoption into routine IVF practice of add-ons such as time-lapse incubation systems, preimplantation genetic testing for aneuploidy (PGT-A), universal extended embryo culture to blastocyst stage,

all-freeze embryo cycles with delayed post-thaw transfers, AI-based embryo selection, etc., among major procedural changes. This list does not even take into consideration newly developed diagnostic tests, which, like PGT-A, are often responsible for many of these practice changes.

Understanding this “add-on phenotype” of innovation is essential for clinicians, patients, and policymakers who are seeking to improve value and equity in health care.⁸⁻¹¹ The following section details some of the add-ons and their issues.

CURRENT STATE OF THE FIELD

THE ADD-ON PHENOTYPE IN IVF

The last decade has witnessed a shift from relatively simple IVF laboratory workflows to highly technologically advanced environments. Clinics now commonly offer multiple add-ons layered onto standard cycles, each marketed as a tool to optimize cycle outcomes.

TIME-LAPSE IMAGING SYSTEMS

Time-lapse imaging incubators allow continuous embryo monitoring and generate morphokinetic data for selection. However, the largest multicenter randomized controlled trial (RCT) – a time-lapse imaging trial (TILT) of 1,575 participants – found no improvement in cumulative ongoing pregnancy or live-birth rates at 12 months compared with conventional incubation. Live births occurred in 33.7% of IVF cycles with time-lapse imaging versus 33.0% with standard care (adjusted odds ratio, 1.04; 97.5% CI, 0.73-1.47).³ Despite requiring substantial capital investment, often generating added-on per-cycle fees, these systems have been widely adopted. Initially adopted under now-disproven claims that they would improve clinical IVF outcomes and reduce costs, these systems are now marketed using the claim that they improve workflow efficiencies.

The high acquisition and maintenance costs of time-lapse incubators, along with additional expenses for disposables and software, are not offset by clinical outcome

improvements. Furthermore, the practice of charging patients extra for time-lapse monitoring cannot be justified in the absence of proven efficacy.^{3,12} Time-lapse annotation may also increase laboratory workload unless fully automated, which incurs additional operating costs.^{3,12} Therefore, current evidence supports the use of time-lapse incubators only for specific laboratory workflow or research purposes, not for routine clinical adoption on financial or operational grounds alone. The proposed advantages do not justify widespread implementation in IVF clinics without demonstrable clinical benefit.

ARTIFICIAL INTELLIGENCE-BASED EMBRYO SELECTION

AI-driven embryo-scoring algorithms, often integrated with time-lapse imaging systems, have been widely implemented in clinical practice. While retrospective studies have frequently claimed promising predictive accuracy for embryo assessments, randomized controlled trials have failed to confirm these findings. Initial randomized trials demonstrated only non-inferiority to standard morphology assessments, without showing superior clinical pregnancy rates.¹³⁻¹⁵ Systematic reviews emphasized that diagnostic accuracy in real-world practice does not automatically translate into improved cumulative live-birth rates.¹⁶ Nevertheless, AI platforms are increasingly deployed with additional licensing and per-cycle fees (Table 1).

That the commercial adoption of AI in IVF is dramatically outpacing its evidence base is well illustrated by recent survey data. A comparative analysis of two global surveys of IVF specialists and embryologists conducted in 2022 and 2025 documented that AI usage nearly doubled, from 24.8% to 53.2% of respondents, within just three years, with embryo selection remaining the dominant application.¹⁷ Strikingly, 83.6% of 2025 respondents reported intent to invest further in AI within 1 to 5 years, despite the absence of RCT-level evidence supporting improved live-birth rates. This pattern, rapidly accelerating adoption driven by commercial momentum rather than clinical proof, is the defining characteristic of the add-on crisis. Notably, the same survey identified cost as the primary barrier to adoption (38.0%) and flagged over-reliance on technology as a leading ethical concern (59.1%), underscoring that the field itself recognizes the risks even as adoption accelerates.¹⁷

PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY

The most financially and clinically wasteful add-on has likely been PGT-A, initially widely promoted to increase pregnancy and live-birth rates in IVF. When this benefit was disproven, proponents of PGT-A advertised miscarriage rate reduction and shortening the time to pregnancy. Both these claims were shown to be untrue in the September 2024 policy statement from the American Society for Reproductive Medicine (ASRM) and the Society for Assisted Reproductive Technology (SART) on PGT-A.⁷

Based on the most recently published data, one must conclude that PGT-A has not only failed to demonstrate any outcome benefits in general infertile patient populations in over 20 years, but, indeed, especially in women with low

egg or embryo counts, actually adversely affects all their IVF outcomes.

Indeed, a randomized trial of 1,212 women (aged 20-37 with ≥ 3 good-quality blastocysts) showed a cumulative live-birth rate of 77.2% in the PGT-A group versus 81.8% in the conventional IVF group (an absolute difference of -4.6 %; 95% CI, -9.2 to -0.0). Conventional IVF was not only non-inferior to PGT-A but was apparently clearly superior.⁴

Some observational studies reported reduced cumulative live-birth rates with PGT-A in first cycles, partly because cycles that yield no euploid embryos, of course, result in no transfer.^{5,6} In addition, it has become indisputable that PGT-A results in a large percentage of false-positive results, leading to non-use or even disposal of these embryos with still very good pregnancy and live birth chances. Therefore, these results, specifically the embryos not transferred, reduce the cumulative pregnancy chances for any embryo cohort in an IVF cycle.

Indeed, as noted above, recent practice guidance by ASRM/SART emphasized that any evidence of benefit or lack thereof is, of course, population-specific. Routine PGT-A for all IVF patients, as likely currently practiced by a majority of U.S. IVF clinics, is, therefore, absolutely nonsensical.⁷ And often, of course, PGT-A costs represent, at a minimum, 20% of total IVF cycle costs. However, for patients with IVF insurance coverage, PGT-A costs usually account for 100% of out-of-pocket expenses since not a single commercial medical insurance provider in the U.S. that covers IVF will cover PGT-A costs. In this case, insurance companies use the correct excuse that PGT-A is not a validated procedure.

BEYOND IVF: A SHARED PATTERN

The futile attempts to innovate IVF that are addressed here are not unique. Similar patterns can also be found across non-life-saving domains whenever patient distress is high, successful alternative treatments are limited, and the willingness to pay for an alleged benefit is substantial.

In orthopedics, arthroscopic procedures for degenerative meniscal tears and knee osteoarthritis expanded rapidly, based on imaging findings and short-term pain scores. Yet, high-quality trials demonstrated limited benefit over physical therapy or sham surgery in many patients.^{18,19} In aesthetic medicine/plastic surgery, successive generations of energy-based devices for skin rejuvenation and body contouring have gained acceptance in practice based largely on small, industry-sponsored studies using physician-rated scales rather than validated, long-term patient-reported outcomes.²⁰

These examples illustrate a recurring dynamic: in non-life-saving fields, based on surrogate outcomes, biological plausibility, and market forces, expensive technologies are rapidly and broadly adopted, often ahead of rigorous demonstration of benefits in patient-important endpoints.

Table 1. Major IVF Add-On Technologies: Costs and Evidence

Technology	Added Cost	Key RCT Finding
Time-lapse imaging	\$500-1,500/cycle	No improvement in live-birth rate (OR, 1.04; 95% CI, 0.73-1.47) ³
AI embryo selection	\$300-800/cycle	Non-inferior to experienced embryologists ¹⁵
PGT-A	\$3,000-6,000/cycle	Non-inferior to standard IVF (-4.6% live births, 95% CI, -9.2 to -0.0) ⁴

ANALYSIS

MECHANISMS DRIVING PREMATURE ADOPTION

RELIANCE ON SURROGATE ENDPOINTS

In IVF, embryo morphology, chromosomal status, and biochemical pregnancy are frequently substituted for cumulative live-birth rate per initiated cycle. Such surrogate endpoints often allow smaller, shorter trials that can show apparent benefit even when overall outcomes do not improve.

ASYMMETRIC REGULATION

Regulatory frameworks for devices and diagnostics are often less stringent than those for therapeutic drugs, enabling new technologies to be introduced into practice with limited pre-market evaluation.²¹ In IVF, many add-ons can be implemented as laboratory practice modifications without rigorous scrutiny.

Once again, PGT-A is likely the best example: Even though the U.S. Food and Drug Administration (FDA), which is responsible for the fate of hundreds of thousands of human embryos in IVF every year, has excluded PGT-A from its review, considering it a laboratory-developed test (LDT). Consequently, no FDA rules exist on how PGT-A should be performed, and therefore, practically every PGT-A laboratory does it differently. Considering that currently, this test determines the ultimate fate of a majority of embryos produced in the U.S. through IVF, this is astonishing.

COMMERCIAL PRESSURES

Intense emotional, social, and financial pressures often lower IVF tolerance for equipoise among all stakeholders in the IVF process – from patients to medical care providers, clinics, and other IVF-serving organizations.

A majority of IVF cycles are currently performed by IVF clinic networks, which are primarily owned by private equity firms. Physician-owned IVF clinics are quickly disappearing, being acquired by clinic networks owned by private equity firms and/or hospital systems. While it would be naïve to assume that under physician ownership, IVF clinics were not profit-driven, they most certainly were not as profit-driven as they are now under corporate ownership. Therefore, in an unsurprising example, clinic networks utilize more PGT than university-owned clinics, while physician-owned IVF clinics demonstrate the lowest PGT-A utilization.²²

Clinics compete with each other in many different ways, but, among the various ways of doing so, utilization of new, alleged “cutting-edge” technologies is, of course, very popular. Moreover, they produce healthy new revenue streams for clinics and the supporting industries, which in turn support the utilization of new add-ons through often highly effective “expert” marketing campaigns directed at physicians and, increasingly, directly targeting the public.

DIFFICULTIES OF DE-IMPLEMENTATION

Once technologies are embedded in protocols and marketed to patients, it is challenging, and often impossible, to deimplement them.

Once again, using PGT-A as an example, its utilization does not seem to have decreased after the September 2024 ASRM/SART policy statement that PGT-A does not improve IVF outcomes in general populations.⁷ Neutral or negative trial results are then frequently dismissed as biased, while positive surrogate outcomes, often lauded by financially incentivized “experts,” sustain demand, creating a “ratchet effect” in which costs rise but rarely fall.

CONSEQUENCES: COST, EQUITY, AND TRUST

The cumulative effects of this technology-driven cost inflation can be profound. As noted earlier with the PGT-A example, because many new non-life-saving technologies must be paid for out of pocket or are only partially reimbursed, their uncritical adoption can widen socioeconomic disparities in access. In fertility care, patients lacking financial resources may be unable to attempt IVF or may be forced to discontinue treatments prematurely, a problem that wealthier patients do not face.²³

Therefore, resources devoted to unvalidated add-ons could be more appropriately applied to support proven interventions. At the individual level, money spent on unproven add-ons represents forgone savings, while at the societal level, resources absorbed by expensive, unvalidated technologies reduce the public’s capacity for high-value care.

Moreover, as the PGT-A experience has begun to demonstrate in the U.S., overselling add-ons may have significant social consequences, reducing trust in medical “experts” and medicine in general. When patients discover that the costly technologies they purchased were oversold and lacked the evidence of real benefits (or may have even have harmed patients’ IVF chances), such a discovery not only undermines their trust in their physician, but makes them question the fabric of the broader health care system, with

long-term consequences for both patient-provider relationships and public confidence in medical innovation.²⁴

RECOMMENDATIONS

RAISING THE EVIDENCE BAR

Addressing the “add-on phenotype” requires fundamental shifts in how the medical field evaluates and adopts new technologies. Below are a few relevant points.

RIGOROUS PRE-ADOPTION EVALUATIONS

Expensive technologies intended to improve patient-important outcomes must undergo adequately powered validation studies before being integrated into standard IVF cycle protocols. This does not mean that all research must be a prospectively randomized study of thousands of patients; such a recommendation is unrealistic for IVF, which is completely excluded from U.S. federal funding.

But it means that every change to routine practice must be declared to the public and must be described as “experimental” until an authoritative body under widely accepted study criteria concluded one of the following: The new add-on should no longer be considered experimental (because studies of varying evidence levels have determined there is sufficient likelihood of specifically described outcome benefits), or the new practice did not produce expected outcome benefits after adequate time as an “experimental” procedure, and, should remain “experimental” or should no longer be used. After all, IVF itself was once an experimental procedure supervised by Institutional Review Boards. And only once IVF had achieved minimum expected results, did ASRM and other authoritative bodies declare the procedure no longer experimental. In short, the IVF field needs better regulation, preferably by its own professional organizations, such as ASRM, or, if they do not establish recommended practices, by the government, as is the case in the U.K.

Moreover, regulatory bodies and/or medical advisory societies should retroactively review every major clinical change introduced to IVF since 2010, when fresh embryo transfer rates in the U.S. plateaued, if their costs exceed a certain threshold. In addition, every new potential add-on should be prospectively evaluated before being put into clinical practice.

ENHANCED REGISTRIES

There currently exists no better tool for evaluating a country’s IVF performance than a well-designed national registry. Clearly, in this sense, the SART registry is the leading registry in the world; enhancing it with artificial intelligence (AI) will certainly make it even more powerful in the near future.

Access to these registries must be significantly eased because, at least for both the U.S. Centers for Disease Control (CDC) registry and the ASRM/SART registry, the bureaucratic hurdles are unacceptable. In addition, post-market-

ing surveillance should be mandatory for technologies introduced without pre-market RCT data.

TRANSPARENCY FOR PATIENTS

Professional societies could adopt a regulatory model similar to that of the Human Fertilisation and Embryology Authority (HFEA), which is charged with overseeing all IVF-related matters in the U.K. This approach would introduce an HFEA-like traffic-light rating system for interventions in which green = evidence of benefit, amber = uncertain, and red = evidence shows no benefit or the technology causes harm. Then, when a technology lacks sufficient evidence of benefit, IVF clinics should unequivocally disclose this to their patients and include it in informed consent documents.

VALUE-BASED REIMBURSEMENTS

It also seems reasonable to exclude unvalidated clinical services from mandated insurance coverage. This does not mean that experimental treatments should be categorically prohibited. On the contrary, well-informed patients should be entitled to choose unvalidated treatments if they so choose. But if properly informed, even wealthy patients will hesitate to waste their money, which could be put to much better use by funding an additional IVF cycle, if necessary.

CONCLUSIONS

Across IVF and other non-life-saving medical disciplines, the proliferation of costly add-on technologies has increased the cost of care without commensurate gains in outcomes that matter most to patients. IVF provides a vivid case study: While treatment costs have risen substantially, time-lapse incubators, PGT-A, AI-based embryo selection, and numerous adjuvants have proliferated widely despite limited evidence that they improve cumulative live-birth rates.

The fundamental question is not whether we should pursue innovation in these fields; we should, and we must; but how we should evaluate and adopt innovation is the question. The current model, in which expensive technologies are adopted based on surrogate endpoints, market forces, and biological plausibility before robust demonstration of benefit, serves neither patients nor the goal of creating a sustainable, equitable, and trustworthy health care system.

A better model would require that technologies prove their value in patient-important outcomes before they become routine, that costs and benefits be communicated transparently, and that reimbursement be tied to demonstrated gains in health and quality of life. IVF, with its clear outcome metric of live-birth rate and established infrastructure for outcome tracking, is ideally positioned to pioneer such a model. If fertility medicine cannot align innovation with evidence, what hope is there for the rest of healthcare?

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This review does not involve human participants or patient data; therefore, ethics approval by an institutional review board was not required.

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The datasets analyzed in this study are available from the corresponding author upon reasonable request. Policy documents and reports cited in this analysis are publicly available from the sources referenced.

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