Research Article

ENDOMETRIAL MICROBIOME AND RECURRENT IMPLANTATION FAILURE AFTER TRANSFER OF PGT-A EUPLOID EMBRYOS: IS THERE A MISSING LINK?

***ANA AIVAZOVA**, MD, PhD Candidate* [1]

[1] *Georgian-German Reproduction Center, Tbilisi, Georgia*

ABSTRACT

Background: Recurrent implantation failure (RIF) remains a challenging problem in assisted reproductive technology (ART). The increasing use of preimplantation genetic testing for aneuploidy (PGT-A) has reduced the contribution of embryo aneuploidy to implantation failure after transfer of euploid blastocysts, increasing interest in maternal endometrial factors. Among these, endometrial receptivity, chronic endometritis, immune regulation, and the endometrial microbiome have received considerable attention. Molecular assays including Endometrial Receptivity Analysis (ERA), Endometrial Microbiome Metagenomic Analysis (EMMA), and Analysis of Infectious Chronic Endometritis (ALICE) have been proposed as tools for individualized evaluation, although their clinical utility remains uncertain.

Methods: A narrative review was conducted using evidence from peer-reviewed studies, systematic reviews, meta-analyses, randomized controlled trials, and contemporary recommendations from the European Society of Human Reproduction and Embryology (ESHRE) and the American Society for Reproductive Medicine (ASRM). Particular attention was given to evidence concerning endometrial microbiota, chronic endometritis, endometrial receptivity, and outcomes following euploid embryo transfer.

Results: The endometrial microbiome is biologically plausible as a component of the implantation environment. Still, current evidence is heterogeneous and limited by low microbial biomass, sampling-related contamination, inconsistent sequencing methodologies, and the absence of standardized definitions of dysbiosis. Although associations between microbial composition and reproductive outcomes have been reported, causality has not been established. Randomized evidence does not support routine ERA-guided embryo transfer, and evidence for EMMA – or ALICE-guided treatment remains insufficient. Patients with repeated implantation failure following euploid embryo transfer represent an important under-studied population.

Conclusion

Current evidence does not support routine microbiome or receptivity testing in IVF. However, after comprehensive evaluation for established causes of implantation failure, selected pa-

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tients with repeated failure after PGT-A-confirmed euploid embryo transfer may be considered for individualized endometrial assessment, with appropriate counseling that the clinical utility of ERA, EMMA, and ALICE remains unproven. Prospective studies specifically enrolling this population are required.

Keywords: recurrent implantation failure; PGT-A; euploid embryo; endometrial microbiome; chronic endometritis; endometrial receptivity; embryo implantation

Introduction

Embryo implantation is a highly coordinated biological process requiring temporal and functional synchrony between embryonic development and the maternal endometrium. Despite major advances in ovarian stimulation, embryo culture, blastocyst selection, vitrification, and genetic testing, implantation remains an inefficient step of human reproduction. Successful implantation depends not only on embryonic developmental competence but also on endometrial decidualization, progesterone responsiveness, vascular remodeling, immune regulation, epithelial function, and embryo-endometrial communication.[1,2]

Historically, embryo quality was considered one of the principal determinants of implantation. Embryonic aneuploidy is indeed strongly associated with implantation failure and early pregnancy loss, particularly with increasing maternal age. PGT-A has enabled the preferential selection of blastocysts without detected whole-chromosome aneuploidy, thereby changing the clinical interpretation of repeated implantation failure.[3,4]

However, a euploid embryo is not synonymous with a universally competent embryo, and euploid embryo transfer does not guarantee implantation. Developmental competence may also be influenced by factors not assessed by conventional PGT-A, including mitochondrial function, epigenetic regulation, cellular metabolism, trophoblast competence, and biological limitations of embryo biopsy and chromosome testing.[5,6] Consequently, implantation failure after repeated transfer of euploid embryos cannot be attributed exclusively to the embryo and raises important questions concerning maternal and endometrial factors.

The endometrium is a dynamic tissue that undergoes profound cyclic changes under endocrine regulation. Decidualization, extracellular matrix remodeling, vascular adaptation, epithelial transformation, immune cell recruitment, and molecular signaling create a transient environment that supports embryo attachment and invasion.[7,8] The possibility that microorganisms may also participate in this environment has generated substantial interest.

The concept of an endometrial microbiome remains controversial. Molecular techniques, particularly 16S ribosomal RNA sequencing and metagenomic approaches, have detected bacterial DNA in endometrial samples. However, the endometrial environment is characterized by extremely low microbial biomass, making results particularly vulnerable to contamination and methodological differences.[9,10]

Early studies suggested that a Lactobacillus-dominant microbial profile might be associated with improved reproductive outcomes, generating interest in microbiome-based diagnostics. 11-13 Subsequent studies, however, have produced inconsistent results, and the biological significance of bacterial DNA detected in the uterine cavity remains incompletely defined.

This uncertainty has contributed to the development and clinical use of molecular assays such as ERA, EMMA, and ALICE. ERA evaluates transcriptomic markers associated with endometrial receptivity; EMMA characterizes microbial composition; and ALICE was developed to detect microorganisms associated with chronic endometritis.

The central question is therefore not whether these biological phenomena exist, but whether their assessment and treatment improve clinically meaningful reproductive outcomes.

This distinction is particularly relevant in patients with repeated implantation failure after transfer of PGT-A-confirmed euploid embryos. These patients represent a highly selected population in whom one major contributor to implantation failure–embryonic aneuploidy–has been substantially reduced, although not eliminated. Yet this population remains underrepresented in clinical trials of molecular endometrial diagnostics.

The objective of this review is to critically evaluate the evidence linking the endometrial microbiome with RIF after euploid embryo transfer, examine the clinical evidence for ERA, EMMA, and ALICE, and consider whether integrated endometrial assessment may have a role in carefully selected patients.

Recurrent Implantation Failure After Euploid Embryo Transfer

There is no universally accepted definition of RIF. ESHRE has emphasized that RIF should be interpreted individually, taking into account the patient's probability of implantation rather than relying solely on a fixed number of failed transfers.[1] The recently published ASRM committee opinion similarly emphasizes individualized assessment of patients with repeated unsuccessful embryo transfers.[14]

This distinction is important because the probability of implantation varies according to maternal age, embryo quality, embryo developmental stage, number of embryos transferred, laboratory performance, and other clinical factors.

Transfer of a PGT-A-confirmed euploid embryo reduces the probability that whole-chromosome aneuploidy is responsible for a failed transfer. However, PGT-A does not measure all components of embryonic competence. Mosaicism, limitations of trophectoderm biopsy, mitochondrial function, epigenetic regulation, and developmental competence remain relevant biological variables.[5,6]

Consequently, repeated failure after euploid embryo transfer should not automatically be interpreted as evidence of an endometrial abnormality. Nevertheless, when several good-quality euploid embryos fail to implant, systematic reassessment of both embryo-related and maternal factors becomes increasingly reasonable.

The first step should remain evaluation of established causes of implantation failure. These include uterine cavity abnormalities, untreated hydrosalpinx, clinically significant adenomyosis or endometriosis when relevant, endocrine disorders, and other patient-specific factors.[1,14]

Only after such factors have been considered should less well-validated molecular or microbiological investigations be discussed.

The Endometrial Microbiome: Biological Plausibility and Methodological Challenges

The discovery of bacterial DNA in endometrial samples challenged the traditional concept of a sterile uterine cavity. However, the presence of microbial DNA does not necessarily demonstrate the presence of a stable, metabolically active microbial community.

The endometrium is a low-biomass environment. This creates a methodological problem that is considerably less pronounced in high-biomass environments such as the vagina or gastrointestinal tract. During transcervical sampling, bacterial DNA from the vagina, cervix, instruments, reagents, extraction kits, or laboratory environment may influence sequencing results.[9,10]

Therefore, interpretation of endometrial microbiome studies requires particular attention to negative controls, sampling methodology, sequencing platforms, bioinformatic pipelines, and the distinction between true biological signals and contamination.

Early studies proposed that Lactobacillus-dominant endometrial communities were associated with improved implantation and pregnancy outcomes.[11] However, subsequent investigations have not consistently reproduced this association. ESHRE specifically notes that studies examining the relationship between Lactobacillus abundance and implantation have produced conflicting findings and that the clinical relevance of uterine and vaginal microbiome profiling remains uncertain.[1] This inconsistency suggests that microbial composition alone may be an insufficient measure of endometrial health.

The functional characteristics of microbial communities may be more relevant than the relative abundance of individual taxa. Microbial metabolites, host-microbe interactions, immune signaling, epithelial integrity, and local inflammatory responses may all influence the biological environment in which implantation occurs.

At present, however, evidence supporting these mechanisms remains predominantly observational or experimental. The critical unanswered question is whether a particular microbial abnormality causes implantation failure or simply reflects another underlying alteration of the endometrium.

This distinction has direct clinical implications. If dysbiosis is causal, correcting it could theoretically improve implantation. If dysbiosis is instead a consequence of, or a marker for, another endometrial disorder, microbial manipulation alone may not improve reproductive outcomes. Therefore, detection of bacterial DNA should not automatically be equated with active infection or with an indication for antibiotic treatment.

Endometrial Microbiome and Implantation Biology

The biological hypothesis linking the microbiome to implantation is nevertheless compelling. Microorganisms and microbial products may interact with epithelial and immune cells through pattern-recognition receptors, including Toll-like receptors and nucleotide-binding oligomerization domain-like receptors. These pathways participate in the regulation of cytokines, chemokines, antimicrobial peptides, and other mediators of mucosal immunity.[15,16]

The implantation process itself requires a carefully controlled inflammatory environment. Local immune activation is necessary for tissue remodeling and implantation, while excessive or persistent inflammation may interfere with decidualization and trophoblast invasion.[7,8]

Microbial communities could theoretically influence this balance through direct interactions with epithelial, immune, or stromal cells and through the production of metabolites. Lactate and other microbial metabolites may have biological effects on local cellular metabolism and immune signaling.

However, much of this mechanistic evidence does not specifically demonstrate a causal relationship between endometrial dysbiosis and implantation failure in humans.

Furthermore, the microbiome is not independent of the hormonal and anatomical environment. Progesterone exposure, estrogenic stimulation, menstruation, antibiotic use, sexual activity, uterine instrumentation, and the local inflammatory environment may all influence microbial composition.

Therefore, the microbiome may represent one component of a broader endometrial ecosystem rather than an isolated pathological entity.

ERA: Biological Rationale Versus Clinical Utility

Endometrial Receptivity Analysis was developed on the premise that the timing of endometrial receptivity may vary among women and that a displaced implantation window could contribute to implantation failure.

ERA uses transcriptomic analysis of endometrial tissue to classify the endometrium's molecular state and potentially personalize the timing of embryo transfer.[17,18] The biological hypothesis is attractive: if a patient's endometrium is not synchronized with embryo development, adjustment of progesterone exposure could theoretically improve implantation.

Initial observational studies generated considerable interest. However, subsequent randomized evidence has not demonstrated a consistent improvement in live birth with ERA-guided embryo transfer.

A major randomized clinical trial published in JAMA compared endometrial receptivity testing-guided timing with standard timing of frozen embryo transfer and found no significant improvement in live birth.[19]

More recent evidence, therefore, does not support the routine use of ERA as a universal diagnostic test.

The negative randomized evidence should not be interpreted as proof that transcriptomic receptivity has no biological significance. Rather, it demonstrates that identifying a transcriptomic state and modifying transfer timing based on it has not consistently been shown to improve live birth.

Several explanations are possible. Endometrial receptivity is not a single molecular event but a complex and dynamic process. A single biopsy may not completely represent biological variation between cycles, and transcriptomic signatures may capture only one component of implantation competence.

Importantly, most ERA trials have not been specifically designed around patients with repeated failure following transfer of multiple PGT-A-confirmed euploid embryos. Therefore, whether a highly selected euploid-RIF population could derive a different degree of benefit remains uncertain.

Current ASRM guidance recognizes the conflicting evidence surrounding ERA and does not support routine endometrial receptivity testing as standard care for RIF.[14]

Accordingly, ERA should currently be regarded as an investigational or selectively considered assessment rather than a validated intervention capable of improving live birth in routine IVF.

EMMA and ALICE: What Do They Actually Tell Us?

EMMA and ALICE address different biological questions and should not be interpreted as interchangeable tests.

EMMA is intended to characterize the microbial composition of the endometrial cavity. Its clinical premise is that a particular microbial profile, especially one dominated by Lactobacillus species, may be associated with a more favorable implantation environment.

ALICE is intended to identify microorganisms associated with chronic endometritis.

This distinction is clinically important because microbiome composition and chronic endometritis are not synonymous.

A patient may have bacterial DNA detected without histological evidence of chronic endometrial inflammation. Conversely, chronic endometritis may be diagnosed by the identification of plasma cells, despite uncertainty about the specific microbial cause.

The principal limitation of EMMA is the absence of a universally validated definition of a `normal~ endometrial microbiome. A fixed threshold of Lactobacillus abundance should therefore not be interpreted as an established biological cutoff capable of predicting implantation or live birth.

Similarly, a positive ALICE result should not automatically be interpreted as proof of clinically significant infection requiring antimicrobial treatment.

Molecular assays detect nucleic acids. They do not necessarily establish bacterial viability, tissue invasion, or causality.

ESHRE currently states that uterine and vaginal microbiome profiling is not routinely recommended in RIF because important questions regarding sampling, reproducibility, spontaneous changes in the microbiota, and treatment efficacy remain unanswered.[1]

This is an important distinction from the question of whether microbiome research should continue. The evidence is insufficient for routine clinical implementation, but the hypothesis remains scientifically relevant.

Chronic Endometritis: A Different Clinical Question

Chronic endometritis warrants separate consideration, as it is not equivalent to microbiome profiling.

Chronic endometritis is generally characterized by the presence of endometrial stromal plasma cells and may be assessed using histological examination with or without CD138 immunohistochemistry. However, diagnostic thresholds remain inconsistent between studies.[14,20]

The prevalence of chronic endometritis varies substantially depending on the population studied and the diagnostic method used.

Some observational studies have reported improved reproductive outcomes following treatment of chronic endometritis, particularly when eradication is documented. However, these studies are predominantly observational and are affected by heterogeneous diagnostic criteria, antibiotic regimens, and patient populations.[21,22]

A 2022 systematic review and meta-analysis reported better reproductive outcomes among patients in whom chronic endometritis was considered cured compared with those with persistent disease. Still, they emphasized important limitations of the available evidence.[23]

The recently published 2026 ASRM RIF committee opinion recognizes chronic endometritis as a potentially relevant consideration in RIF while emphasizing the lack of standardized diagnostic criteria and the limitations of the evidence.[14]

Therefore, in a patient with repeated implantation failure after euploid embryo transfer, evaluation for chronic endometritis may be clinically reasonable when appropriately indicated. Still, it should not be equated with routine microbiome testing.

Importantly, treatment decisions should be based on a clinically meaningful diagnosis rather than solely on detection of bacterial DNA.

Should ERA, EMMA, and ALICE Be Tested in Patients With Repeated Euploid Implantation Failure?

This question requires a distinction between routine testing and selective investigation.

Current evidence does not support routine ERA, EMMA, or ALICE testing for all IVF patients. ESHRE explicitly recommends against routine uterine and vaginal microbiome profiling in RIF, and ASRM's 2026 RIF guidance remains cautious regarding endometrial receptivity testing and microbiome-based diagnostics.[1,14]

However, the population of women experiencing repeated implantation failure after transfer of multiple PGT-A-confirmed euploid embryos has not been adequately studied.

This creates an important evidence gap.

A patient with one failed euploid embryo transfer should not automatically be considered to have an endometrial disorder. Even a euploid embryo can fail to implant for biological reasons that remain incompletely understood.

In contrast, after repeated failures with several good-quality euploid embryos, a clinician may reasonably reconsider whether additional maternal factors warrant investigation.
In such a patient, I would consider the following hierarchy:

1. Reassess embryo-related factors and the limitations of PGT-A.
2. Reassess uterine anatomy and cavity pathology.
3. Review endocrine and systemic factors.
4. Review the frozen embryo transfer protocol and luteal support.
5. Consider clinically indicated assessment for chronic endometritis.
6. Only after comprehensive evaluation, discuss the potential role of molecular endometrial tests such as ERA, EMMA, or ALICE.
7. Provide explicit counseling that the clinical benefit of these tests remains unproven.

This approach avoids both extremes: indiscriminate testing of all IVF patients and complete dismissal of potentially informative investigations in exceptionally selected cases.
The critical principle is that testing should not automatically lead to treatment.
An abnormal EMMA or ALICE result should not, by itself, mandate antibiotics or probiotics. Similarly, an ERA result should not automatically be assumed to identify the correct timing of embryo transfer in a way that improves live birth.

From Individual Biomarkers to Integrated Endometrial Assessment

The limitations of individual tests may reflect the biological complexity of implantation itself. ERA evaluates transcriptomic receptivity. EMMA evaluates microbial composition. ALICE attempts to identify microorganisms associated with chronic endometritis. Histopathology evaluates inflammatory cellular changes. Ultrasound and hysteroscopy assess anatomical factors. Each test interrogates a different component of the endometrium.
Implantation, however, is an integrated process.
A useful conceptual framework would therefore combine four domains:

1. Endometrial receptivity

This includes progesterone-dependent transcriptomic maturation and synchronization between embryo development and the endometrial cycle.

2. Microbial homeostasis

This includes microbial composition, diversity, functional activity, and the methodological reliability of microbial detection.

3. Inflammatory and immune status

This includes chronic endometritis, local inflammatory pathways, and clinically meaningful immune abnormalities.

4. Clinical and embryological context

This includes maternal age, infertility diagnosis, uterine anatomy, embryo morphology and developmental kinetics, PGT-A results, previous transfer outcomes, endocrine status, and treatment protocol.

The concept of integrated functional endometrial assessment is therefore biologically attractive. However, it is important to emphasize that this is a research framework, not a validated clinical algorithm.
No randomized controlled trial has yet demonstrated that combining ERA, EMMA, ALICE, histopathological assessment, and individualized treatment improves live birth in women with repeated implantation failure after transfer of euploid embryos.
Consequently, this framework should not be presented as an established standard of care.

Current Evidence From Professional Societies

The recommendations of professional societies are particularly important because commercial availability of a diagnostic test does not constitute evidence of clinical validity.

ESHRE's 2023 good-practice recommendations emphasize that RIF is heterogeneous and that many investigations used in clinical practice lack sufficient evidence of benefit. Specifically, uterine and vaginal microbiome profiling is currently not recommended because the clinical relevance, optimal sampling methodology, stability of microbiome profiles, and effectiveness of interventions remain uncertain.[1]

The 2026 ASRM committee opinion similarly takes a cautious approach. It discusses the conflicting evidence for ERA and emphasizes that additional evidence is required before routine screening and treatment based on microbiome findings can be recommended.[14]

These recommendations should not be interpreted as a rejection of the underlying biology.

Rather, they illustrate an essential principle of evidence-based medicine: a plausible biological mechanism is not sufficient to establish clinical utility.

The appropriate question is whether a diagnostic test followed by a specific intervention improves outcomes that matter to patients, particularly live birth.

Discussion

The endometrial microbiome represents one of the most intriguing potential contributors to implantation biology, but the current evidence does not justify describing it as an established cause of RIF.

Several observations support continued investigation. Microbial DNA can be detected in endometrial samples; microorganisms and microbial products can interact with host immune and epithelial pathways; and associations between microbial profiles and reproductive outcomes have been reported.[9-13]

At the same time, important limitations remain.

The endometrium is a low-biomass environment, and contamination can substantially affect sequencing results. Different studies use different sampling methods, sequencing technologies, bioinformatic approaches, and definitions of dysbiosis. Furthermore, the presence of bacterial DNA does not establish viability or pathogenicity.

The concept of Lactobacillus dominance is similarly more complex than initially proposed. Although Lactobacillus species have an established role in the vaginal microbiome, a specific Lactobacillus threshold cannot currently be regarded as a validated predictor of implantation or live birth in the endometrium.[1]

The euploid-RIF population is particularly interesting because embryonic aneuploidy has been substantially reduced as an explanation for repeated failed transfers. Nevertheless, this does not establish that endometrial abnormalities are responsible.

This distinction is crucial.

It is scientifically reasonable to hypothesize that maternal factors may contribute more strongly when repeated euploid embryo transfers fail. It is not scientifically justified to conclude that a positive microbiome test identifies the cause of implantation failure.

The same reasoning applies to ERA. Transcriptomic differences are biologically meaningful, but randomized evidence does not demonstrate that changing embryo transfer timing according to ERA improves live birth.[19]

Therefore, the most defensible position is neither enthusiastic adoption nor complete dismissal.

In routine IVF practice, current evidence does not support universal testing for ERA, EMMA, or ALICE.

For carefully selected patients with repeated implantation failure after multiple PGT-A-confirmed euploid embryo transfers, however, discussion of these investigations may be reasonable once conventional evaluation is complete and the patient understands that their clinical utility remains uncertain.

This is particularly true for chronic endometritis, where contemporary evidence and ASRM guidance provide a stronger clinical rationale for consideration of diagnostic evaluation than for microbiome profiling itself.[14,23]

The distinction between testing and treatment is also fundamental.

A molecular abnormality should not automatically result in antibiotic therapy, probiotic administration, or alteration of progesterone exposure. Such interventions require their own evidence base.

The ultimate objective should therefore not be to identify the largest number of molecular abnormalities. It should be to identify abnormalities that are reproducible, biologically meaningful, causally related to implantation failure, and therapeutically modifiable.

Limitations

This review has several limitations.

First, it is a narrative review rather than a systematic review or meta-analysis and may therefore be affected by selection of literature.

Second, the available evidence concerning the endometrial microbiome is heterogeneous, particularly with respect to sampling techniques, microbial biomass, sequencing methodology, and diagnostic definitions.

Third, randomized trials specifically investigating patients with repeated implantation failure after transfer of PGT-A-confirmed euploid embryos remain limited.

Fourth, many studies examining ERA, EMMA, ALICE, and chronic endometritis include heterogeneous IVF populations, making direct extrapolation to euploid-RIF patients uncertain.

Finally, the proposed concept of integrated endometrial assessment remains hypothetical and should not be interpreted as a validated clinical pathway.

Future Research Priorities

Future studies should specifically enroll patients with repeated implantation failure after transfer of PGT-A-confirmed euploid embryos rather than combining them with heterogeneous IVF populations.

Research priorities should include:

1. **Standardization of microbiome sampling,** including rigorous contamination controls and reproducible laboratory protocols.
2. **Functional microbiome characterization,** moving beyond simple taxonomic abundance toward metagenomics, meta-transcriptomics, metabolomics, and strain-level analysis.
3. **Standardized definitions of chronic endometritis,** including reproducible histological and immunohistochemical criteria.
4. **Prospective evaluation of ERA,** specifically in patients with repeated euploid embryo-transfer failure.
5. **Prospective evaluation of EMMA and ALICE,** with predefined diagnostic thresholds and clinically meaningful treatment algorithms.
6. **Randomized controlled trials of test-directed treatment,** rather than observational studies reporting outcomes after treatment.

7. **Integration of molecular and clinical phenotypes,** including transcriptomics, microbiome data, immune profiling, progesterone responsiveness, decidualization, and embryo characteristics.
8. **Use of cumulative live birth as the principal endpoint,** rather than implantation rate or biochemical pregnancy alone.

The most important future study would be a prospective, multicenter randomized trial enrolling women with repeated implantation failure after transfer of PGT-A-confirmed euploid embryos and comparing standard evaluation with a predefined integrated endometrial diagnostic and treatment strategy.
Such a study could determine whether molecular endometrial testing has clinical value in the population in which its biological rationale is strongest.

Conclusion

The endometrial microbiome is a biologically plausible component of the maternal environment in which implantation occurs. However, current evidence does not establish endometrial dysbiosis as an independent, causal, and therapeutically modifiable cause of recurrent implantation failure.
PGT-A has reduced, but not eliminated, the contribution of embryonic chromosomal abnormalities to implantation failure. Repeated failure after transfer of multiple PGT-A-confirmed euploid embryos therefore represents an important clinical scenario in which maternal factors deserve careful reassessment.
Current evidence does not support routine use of ERA, EMMA, or ALICE in IVF. Randomized evidence has not demonstrated consistent improvement in live birth with ERA-guided embryo transfer, while evidence supporting microbiome-guided interventions remains insufficient.[1,14,19]
Nevertheless, the absence of evidence for routine use should not be interpreted as proof that these technologies have no value in every patient. Women with repeated implantation failure after multiple euploid embryo transfers remain underrepresented in clinical trials and may represent a biologically distinct population.
After comprehensive assessment of established anatomical, endocrine, embryological, and systemic factors, selective evaluation of the endometrium may be considered in carefully counseled patients. Evaluation for chronic endometritis currently has a stronger clinical rationale than routine microbiome profiling. In contrast, ERA, EMMA, and ALICE should be regarded as complementary or investigational tools whose ability to improve live birth has not been proven.
The future of reproductive medicine is unlikely to depend on a single biomarker. The more promising direction is an integrated understanding of endometrial receptivity, microbial ecology, inflammation, immune regulation, endocrine responsiveness, decidualization, and embryonic competence.
The endometrial microbiome may ultimately prove to be part of the missing link in recurrent implantation failure after euploid embryo transfer. At present, however, it should be regarded as a promising biological hypothesis rather than an established clinical diagnosis.

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Ethical Approval

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Author Contributions

Ana Aivazova was responsible for the manuscript conception, literature review, interpretation of the evidence, drafting, critical revision, and final approval of the submitted version.

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