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Mini-review

Developments in reproductive biology and medicine

New models of implantation: towards a whole better than the sum of parts

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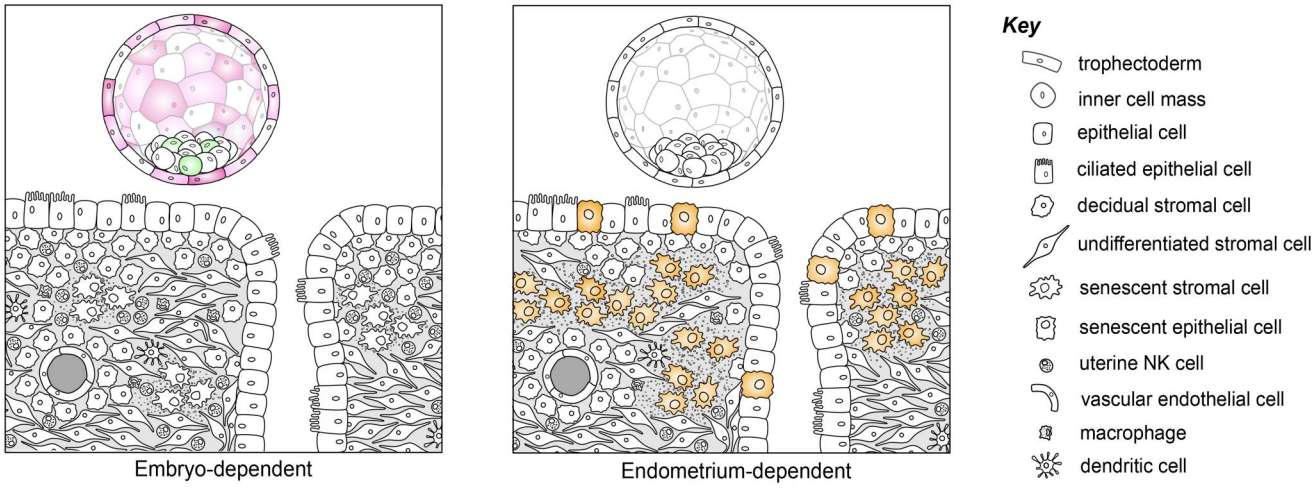
ABSTRACT

Recent advances in the development of stem-cell-based embryo models and endometrial assembloids have fuelled understanding of their respective biology. However, a faithful combined approach is required to truly advance our understanding of implantation processes. This mini-review considers the most recent developments in producing reliable *in vitro* models of the human endometrium and human embryo, and the next steps required to combine their respective potential. While the fundamental biology of implantation is the primary driver of *in vitro* model development, the combined effort of embryo and endometrial models to generate new models of implantation provides the opportunity to manipulate either compartment to further understand the aetiologies of reproductive dysfunction. Through combining both systems, their efforts are symbiotic, each extending the relevance and utility of their counterpart to generate a whole greater than the sum of its parts.

GRAPHICAL ABSTRACT



Combining blastoid and endometrial models to generate new models of implantation will provide insight into fundamental implantation processes and mechanisms of reproductive dysfunction, such as embryo mosaicism (left panel) and endometrial dysfunction (right panel).

Keywords: human endometrium / embryo / stem-cell-based embryo model / blastoid / implantation / early pregnancy / *in vitro* models

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Introduction

Recent developments in *in vitro* models of both the human embryo and endometrium have advanced our ability to understand these systems. In both cases, the availability of faithful *in vitro* models offers the opportunity to further our understanding of the fundamental biology of processes that are largely inaccessible in the human body, not to mention intractable.

The challenge ahead is to enhance the physiological relevance and reproducibility of both models and bring together their respective capabilities to construct an optimal combined system for understanding implantation and early pregnancy processes. Deeper biological insight is one key goal of these emerging models, but the potential for development of diagnostic and therapeutic approaches to treat reproductive dysfunction is certainly also on the horizon. Infertility and early pregnancy loss each affect between 10 and 18% of people of reproductive age (Quenby *et al.*, 2021; WHO, 2023); in approximately one third to one half of cases, the underlying causes are unexplained (Regan *et al.*, 2023; Romualdi *et al.*, 2023). Therefore, patient-specific models will also be extremely important. In this mini-review, we will discuss the most recent advances in both embryo and *endometrial in vitro* models and the next steps required to combine their respective potential.

Stem-cell-based embryo models

Access to human embryos is a major limitation in improving our understanding of the earliest steps in human development. Historical images provide some insight into fixed points in time during early implantation (Hertig *et al.*, 1956). Time-lapse data from IVF clinics (embryoscope) have afforded some insight into early preimplantation development. Donated embryos provide some scope for research. However, such embryos are generally provided after treatment cycles are complete and thus represent the lower quality unselected embryos from patients who have often encountered difficulties conceiving or sustaining a pregnancy. Availability is also geographically restricted by assisted reproduction practices and regulations. Embryos from animal models are more readily available; however, differences in early development and implantation limit their utility (Gerri *et al.*, 2020). Therefore, the development of models of the human embryo has been pursued with increasing effort in recent years.

Stem-cell-based models of the blastocyst-stage embryo (blastoids) are self-organized structures resembling the preimplantation blastocyst, which are derived from naïve pluripotent cells (Rivron *et al.*, 2018). Blastoid formation can be induced according to a range of approaches but each include a defined cocktail of growth factors and inhibitors (Fan *et al.*, 2021; Yanagida *et al.*, 2021; Yu *et al.*, 2021; Kagawa *et al.*, 2022). Blastoids can develop into structures resembling the gastrulating embryo—forming embryonic and extra-embryonic germ layers (De Santis *et al.*, 2024) including the appearance of a presumptive primitive streak along with trophoblast and amnion lineages, and are therefore presumed to be a good alternative to human or mouse embryos, although no amniotic or yolk sac cavitation is apparent.

The excitement created by the initial descriptions of blastoids (Rivron *et al.*, 2018; Li *et al.*, 2019; Sozen *et al.*, 2021) has resulted in a rapid output of studies describing continued development of the models, with considerable improvements in efficiency enabling higher throughput production of blastoids (Yu *et al.*, 2023; Martinez Arias *et al.*, 2024). Single cell RNA sequencing and signalling pathway comparisons demonstrate close alignment of lineage allocations and molecular features between blastoids and human blastocysts, although differences are apparent, confirming that these models are still not a perfect replica of the embryo (Yu *et al.*, 2023). However, a perfect model is not necessarily needed for the blastoids to be considered useful, with the key features of 'scalability, accessibility, modularity and amenability' already representing significant progress (Martinez Arias *et al.*, 2024). There remains scope to improve these models, but their very availability permits continued optimization and development experiments to be undertaken and research questions to be refined before potentially testing on true embryos (Yu *et al.*, 2023). Indeed, by reducing genetic heterogeneity between samples, the blastoid models have permitted a more reliable exploration of the mechanisms of early development (Yu *et al.*, 2023), including the identification of key molecules governing pluripotency regulation and cell fate decisions (Wong *et al.*, 2024; An *et al.*, 2025) as well as the interrogation of conserved pathways, such as the revelation that human blastoids can enter diapause (a state of developmental stasis seen in other mammalian species) through manipulation of the mTOR pathway (Iyer *et al.*, 2024). This consistency also advances the potential for these models to contribute to the development of novel strategies for drug screening (Niethammer *et al.*, 2022).

Achieving a consensus on hallmark features for standardization of the models is essential to underpin their relevance to the study of early development as well as to support their continued advancement (Martinez Arias *et al.*, 2024; Onfray *et al.*, 2024). This will enable benchmarking not only the cell types present within the structures but also the localization and interactions between cell types and molecules (Martinez Arias *et al.*, 2024). Combined with agreed standards on reporting, this will prevent overreliance on sub-optimal models which may lead to misleading or erroneous interpretations (Martinez Arias *et al.*, 2024) and permit direct comparisons between reports.

Despite the promise of the blastoid models, there are limitations to consider. The high efficiency of development does not accurately represent *in vivo* human development, where a high proportion of embryos are lost during the early peri-implantation period (Macklon *et al.*, 2002; Jarvis, 2016). Blastoid models showing formation and implantation efficiencies approaching 90%, while useful for experimental throughput, do not accurately represent normal developmental attrition and its underpinning processes, although the genetically identical nature of a cohort of blastoids from one stem cell line necessarily dictates the reproducibility in formation. Conversely, it could be argued that developing a high efficiency system offers the opportunity to control 'failure' and therefore more opportunity to understand the points of weakness in early human development. However, we should be cautious not to overinterpret findings from an excessively robust *in vitro* system.

Although some extended blastoid cultures have demonstrated milestones of post-implantation development in the absence of attachment or endometrial substrates (Weatherbee *et al.*, 2023), others have shown that *in vitro* attachment is required for and/or enhances the development of blastoids into post-implantation lineages. For example, De Santis *et al.* (2024) reported the ability of blastoids to recapitulate features of the gastrulating human embryo, but that identification of an appropriate substrate to support development of both embryonic and extraembryonic lineages is required (De Santis *et al.*, 2024). It is likely that the embryo needs the mechanical signals of attachment for continued

and appropriate development but that simple adherence to 2D plastic surfaces or simple substrates are not sufficient to truly recapitulate human embryonic development *in vitro* (Fig. 1).

Blastoid models also clearly lack the earlier stages of embryo development from fertilization to cleavage, during which critical cell fate decisions arise. Importantly, therefore, they also forgo

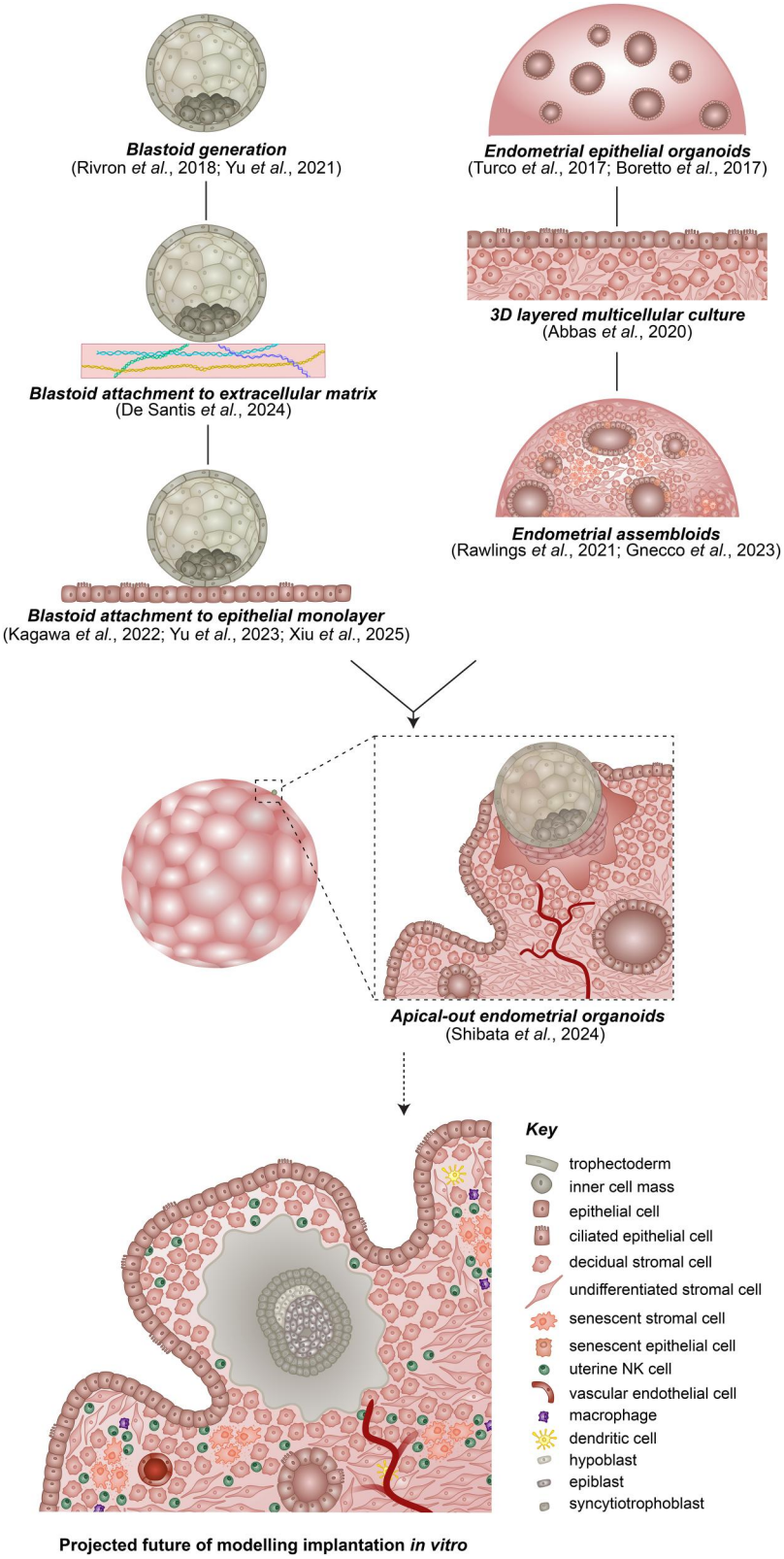

Figure 1. A schematic outlining recent progress towards an optimal model of implantation. From the initial development of blastoids through to simple attachment studies (left-hand side), and the description of endometrial organoids and increasing complexity first through improved layered models using organoid-derived epithelial cells, and then stromal-epithelial assembloids (right-hand side) to a combined model demonstrating syncytial formation. Future goals will be to enhance endometrial complexity and support ongoing embryonic development through post-implantation stages (bottom panel).

exposure to the environmental milieu of the fallopian tube and uterine lumen. While studies of *in vitro* fertilized embryos have demonstrated the ability of the laboratory environment to support successful development, questions still remain over the long-term impacts of the peri-implantation environment on lineage decisions and phenotypic changes (reviewed by Pinborg *et al.*, 2023). Consideration of the appropriate media and culture conditions to best mimic *in vivo* development is also required. Therefore, while the 'perfect' model may not be achievable on a short-term horizon, advancing the models to include the endometrial environment will support continued improvement and enhanced physiological resemblance (Yu *et al.*, 2023).

Endometrial models

The advent of organoid and, more recently, assembloid systems has supported increased complexity in *in vitro* endometrial modelling (Fig. 1), permitting the development of systems that closely mimic both the structural and functional characteristics of the native tissue (Boretto *et al.*, 2017; Turco *et al.*, 2017; Rawlings *et al.*, 2021a; Shibata *et al.*, 2024). However, these systems are still limited by their relative simplicity in terms of cellular composition and by both the requirements for complex and expensive culture media and the absence of optimal extracellular matrix (ECM) support. The availability of endometrial tissue also presents a barrier to widespread development and adoption of models, which will be key to continued progress. Here, we address recent steps towards tackling these obstacles and propose the essential actions to focus on for continued progress.

Advancing the cellular composition and structural features

The addition of an epithelial layer representing the luminal epithelium has been a particular challenge in modelling the endometrium. Early endometrial organoids were limited by the enclosure of the apical surface within the organoid lumen (Boretto *et al.*, 2017; Turco *et al.*, 2017). Recent adaptations have resulted in the formation of 'apical-out' endometrial epithelial systems. Tian *et al.* (2023) were able to promote the formation of a polarized luminal epithelium with functional cilia by using an air–liquid interface (ALI) culture. Ahmad *et al.* (2024) used suspension cultures to generate polarity-reversed endometrial epithelial organoids which better reflect the implantation environment than the original apical-in models, demonstrating successful attachment of mouse blastocysts. These approaches offer new insights into how hormonal and other cues impact on epithelial architecture, ECM components, and growth factor expression to influence endometrial function and embryo implantation and could be used to understand the mechanisms and develop treatments for disorders such as endometrial cancer, infection, and infertility (Tian *et al.*, 2023; Ahmad *et al.*, 2024; Zhang *et al.*, 2025).

Endometrial modelling has also been hindered by the absence of well-vascularized models, essential to further our understanding of early vascular remodelling during implantation which might impact on placental efficiency and the risk of obstetric complications, including pre-eclampsia. The incorporation of human umbilical vein endothelial cells (HUVECs) into an endometrium-on-a-chip model permitted the examination of *in vitro* trophoblast invasion into a multi-layered structure (Ahn *et al.*, 2021). Similarly, Shibata *et al.* (2024) introduced HUVECs to endometrial assembloids, established using apical-out epithelium and stromal cells, to develop an endothelial network; the model was then used to simulate the human embryo–endometrial interface, identifying key signalling pathways and ECM dynamics that mediate the process of embryo attachment and trophoblast invasion (Shibata *et al.*, 2024).

Future directions involve refining the system to integrate endometrial immune and vascular cell types for an even more comprehensive endometrial model (Fig. 1), with early work showing potential for incorporation of these cells (Tryfonos *et al.*, 2023; Van de Velde *et al.*, 2023).

Extracellular matrix support

Identifying the optimal matrix support and media conditions will be essential for continued development of 3D *in vitro* endometrial models. To date, most advanced 3D models of the endometrium have relied on hydrogel-based ECM formulations for structural support, which also promote essential cellular functions including cell-matrix adhesion, survival, migration, proliferation, and differentiation through endometrial cell interactions via integrins and other cell surface receptors (reviewed by Rawlings *et al.*, 2021b).

Endometrial epithelial organoids were first established in Matrigel, a murine sarcoma-derived basement membrane extract comprising a mixture of ECM proteins, growth factors, and other proteins (Boretto *et al.*, 2017; Turco *et al.*, 2017). The composition of this gel permits reliable polarization of epithelial cells within the organoids but does not represent the native stromal ECM well. The addition of a collagen-based gel seems to provide better support for endometrial organoid differentiation, including the increased expression of glycodelin (encoded by *PAEP*) upon hormone stimulation (Shibata *et al.*, 2024). Endometrial assembloid models also use a simple collagen-based hydrogel, which provides a more appropriate mimic but is still a relatively crude attempt to replicate the protein rich architecture of the endometrial stromal ECM (Aplin *et al.*, 1988; Aplin and Jones, 1989; Rawlings *et al.*, 2021b; Shibata *et al.*, 2024).

Jamaluddin *et al.* (2022) approached this problem by developing hydrogels based specifically on the endometrial ECM, using decellularized tissue to extract proteins for incorporation into gels. The resulting epithelial organoids exhibited improved similarity to native endometrium than those cultured in Matrigel. However, this approach is not likely to support large-scale studies but rather inform the requirements for developing customized approaches, including the proteomic analysis of the decellularized ECM (Jamaluddin *et al.*, 2022). Taking this one step further, a hybrid approach combining the rigidity of a synthetic hydrogel with the natural scaffold components and interactions of a decellularized endometrial ECM hydrogel has been shown not only to support organoid culture but also to enhance differentiation efficiency in comparison to Matrigel due to improved biochemical similarity with the native tissue (Gomez-Alvarez *et al.*, 2024). Improved duration of these gels in culture represents a further advantage over commercial alternatives (Gomez-Alvarez *et al.*, 2024).

Synthetic and semi-synthetic hydrogels offer the potential for bespoke matrix development: the mechanical properties of the system can be altered to suit different cell types or match tissue properties, along with functionalization of the gels to incorporate essential signals or specific molecules (Salisbury *et al.*, 2024). For example, gelatine methacryloyl (GelMA) hydrogels have been shown to support the growth and differentiation of human endometrial stromal cells and epithelial gland organoids (Salisbury *et al.*, 2024), while polyethylene glycol (PEG)-based hydrogel functionalized with a collagen-derived adhesion peptide (GFOGER) and a fibronectin-derived peptide (PHSRN-K-RGD) was sufficient to elicit characteristic morphological and molecular responses

from both stromal and epithelial cells in assembloid culture in response to hormone exposure (Gnecco *et al.*, 2023). Combining these approaches with a more developed understanding of the endometrial tissue ECM and physical properties of the endometrium to create a bespoke endometrial support certainly appears to be a very logical route to follow (Abbas *et al.*, 2019).

A further alternative is to remove the need for a scaffold completely, relying on endometrial stromal cells to synthesize sufficient ECM to support epithelial cell growth and organoid formation (Wiwatpanit *et al.*, 2020). Co-cultures of endometrial epithelial and stromal cells generated scaffold-free hormone-responsive endometrial organoids suitable for studying androgen-mediated changes in cellular differentiation, proliferation, and inflammatory signalling in PCOS endometrial samples. The scaffold-free system offers significant advantages, such as reduced interference from artificial matrices, making it particularly suitable for studying intrinsic cellular processes.

Media composition

Organoid culture requires a defined medium containing a combination of growth factors and inhibitors that mimics the tissue-specific *in vivo* local environment. Endometrial gland organoids rely on a chemically defined medium supplemented with several key components: nicotinamide, a PARP-1 inhibitor; R-spondin-1, which activates the WNT/β-catenin signalling pathway; A8301, a TGF-β signalling pathway inhibitor; the antioxidant N-acetyl-L-cysteine (NAC); and growth factors fibroblast growth factor 10 (FGF10), epidermal growth factor (EGF), and hepatocyte growth factor (HGF) (Boretto *et al.*, 2017; Turco *et al.*, 2017). A major challenge in organoid culture is the high cost, with R-spondin-1 being a significant contributor to the expenses in organoid research. R-spondin-1 is essential for organoid formation, with withdrawal coinciding with reduced formation efficiency and passaging (Boretto *et al.*, 2017). Activation of the Wnt/β-catenin signalling pathway is crucial for endometrial epithelial stem cells to maintain their stemness (Lien and Fuchs, 2014). The glycogen synthase kinase 3 (GSK-3α/β) inhibitor CHIR99021 is inexpensive and provides a similar efficiency to R-spondin-1 (Haider *et al.*, 2019). Furthermore, in the case of the endometrial assembloid, reliance on exogenous growth factors and pathway modulators for differentiation is reduced because of the presence of stromal cells within the culture. A minimal differentiation medium supplemented only with NAC, E2, 8-bromo-cAMP, and medroxyprogesterone acetate is sufficient for the efficient differentiation of endometrial assembloids (Rawlings *et al.*, 2021a).

Tissue availability

A major hurdle to establishing human organoid models in the lab is access to primary tissue. Only a handful of specialized clinics offer routine endometrial biopsy collection, hindering accessibility to researchers in the field. Despite being an outpatient procedure or adjunct to another procedure (e.g. laparoscopy or hysterectomy), endometrial biopsy is invasive and can be painful (Nastri *et al.*, 2013). Therefore, this procedure is usually restricted to patients experiencing gynaecological or fertility issues, potentially introducing bias into the resulting data. Recent demonstrations that endometrial epithelial organoids can be derived using cells isolated from menstrual flow present a novel alternative to combat this barrier (Cindrova-Davies *et al.*, 2021; Hewitt *et al.*, 2023). Similarly to other endometrial organoid models, these cultures exhibit key characteristics of the endometrial epithelium including hormone responsiveness and the morphological and transcriptomic changes reflective of *in vivo* menstrual cycle phases. Stromal cell cultures derived from menstrual fluid also exhibit the capacity for decidualization, mimicking critical processes during implantation (Hewitt *et al.*, 2023). The ability to isolate both epithelial and stromal cells highlights the potential for a non-invasive approach to establishing subject-matched assembloid cultures, and to recreate epithelial-stromal crosstalk, a critical process during embryo implantation.

A notable advantage of menstrual fluid samples is the accessibility and ease of sample collection. Not only would this provide the possibility for longitudinal studies in the same individuals but also permits scalability to enable high-throughput drug testing and disease modelling (Hewitt *et al.*, 2023). The potential for personalized medicine applications, particularly in diagnosing and treating conditions such as endometriosis and recurrent implantation failure, is clear (reviewed by Tindal *et al.*, 2024). Additionally, the method provides insights into the mechanisms of endometrial regeneration, given that cells in menstrual flow appear to include progenitor populations (Masuda *et al.*, 2021; Wyatt *et al.*, 2021). These studies emphasize the potential of menstrual fluid as an abundant, ethical, and non-invasive resource for advancing research in endometrial biology and gynaecological disorders. These approaches open avenues for studying endometrial regeneration, disease modeling, and personalized therapeutics. However, despite the potential of this cell source, the origin of the sample as being shed tissue necessitates caution with regards to the differing immune cell populations in the late secretory and menstrual phases, versus earlier in the cycle, and by association the excessive inflammatory and senescent status of the tissue and constituent cells characteristic of menstrual breakdown (Lucas *et al.*, 2020; Schwalie *et al.*, 2024; Tindal *et al.*, 2024).

Reproducibility

As mentioned above, reliance of endometrial models on patient biopsies results in potential bias towards an understanding of tissue dysfunction, rather than modelling normal endometrium. Although cell lines might confer the opportunity to standardize these models, available cell lines of the endometrium are unlikely to provide the optimal alternative: endometrial cell lines can adequately reflect undifferentiated and decidualized states of primary cells in some studies (Li *et al.*, 2022). However, the unwanted phenotypes introduced by transformation or cancerous origins mean these lines do not truly represent the biology of the normal cycling endometrium (Wenger *et al.*, 2004; Bloomfield and Duesberg, 2015; Li *et al.*, 2022).

Recent approaches to develop endometrial models overcome several issues that had been highlighted previously (reviewed by Rawlings *et al.*, 2021b). As yet, consensus on the best approach to endometrial modelling has not been achieved. The protocols remain expensive, technically/logistically complicated and lack consensus. As with the blastoids, standardization will be essential, including consideration not only of the matrix support but also media components and markers of differentiation and implantation responses (reviewed by Rawlings *et al.*, 2021b; Murphy *et al.*, 2022).

Modelling implantation

To realize the full potential of both embryo and endometrial models, not only in revealing the mechanisms underpinning development of either system but also in studying the maternal–foetal interface during implantation, progression to an optimal and robust combined model is clearly required.

Plating blastoids onto immortalized endometrial stromal cell monolayers revealed similar attachment dynamics and

outgrowth capability between blastocysts and blastoids (Yu *et al.*, 2023); indeed, co-culture with stromal monolayers facilitates blastoid outgrowth (Xie *et al.*, 2025). Furthermore, stromal monolayers appeared to prevent apoptotic activity that was seen when plating embryos or blastoids onto fibronectin coated surfaces (Yu *et al.*, 2023). Direct interaction with endometrial cells was superior to culture with conditioned media alone, promoting proliferation, inner cell mass expansion, and syncytialization (Yu *et al.*, 2023). These studies confirm that cell–cell interactions at the maternal–foetal interface are required for true replication of peri-implantation development and indeed that endometrial stromal cells have an essential role in the promotion of trophoblast invasion, migration, and ECM remodelling (Yu *et al.*, 2023; Xie *et al.*, 2025) consistent with previous reports using embryos (reviewed by Rawlings *et al.*, 2021b).

Moving to 3D systems, co-cultures comprising blastoids attached to an apical-out endometrial organoid model also confirmed the necessary contribution of the endometrial stromal cells to the promotion of trophoblast outgrowth and invasion (Shibata *et al.*, 2024), but also supports a role for the luminal epithelium as a barrier to implantation in a human model. Interestingly, in the absence of the epithelial layer, the orientation of the blastoids was disrupted and adhesion from the mural side was also observed, suggesting a role for the luminal epithelium in directing embryo placement for implantation (Shibata *et al.*, 2024). This model also revealed the formation of syncytial trophoblast incorporating the endometrial stromal cells, observed initially in the blastoid co-cultures and recapitulated with human embryos, confirming cell fusion as a mechanism for the implanting embryo to encroach into endometrial tissue (Shibata *et al.*, 2024). The application of blastoids in such a system permits a scale of analysis not possible (or responsible) with human embryos, but allows the optimization of the culture before validation studies on a limited number of embryos (Shibata *et al.*, 2024).

Although epigenetic profiles are remodelled to a certain extent during the establishment of embryonic stem cell and induced pluripotent stem cell lines, blastoid formation lacks the dynamic preimplantation epigenetic remodelling and re-establishment processes taking place in the embryo, including the re-establishment of allele-specific imprinting. This omission means that gene expression profiles and the associated cellular behaviours within the blastoid embryonic and trophoblast lineages lack the nuanced control required to truly model early differentiation events, especially if patient-specific characteristics might be lost (Lea *et al.*, 2025; Xie *et al.*, 2025). Recently, Xie *et al.* have demonstrated that the method of blastoid induction used influences the DNA methylome, with 4-CL (four chemicals plus leukaemia inhibitory factor (LIF))-derived blastoids appearing more similar to human blastocysts than either 5-iLA- (five kinase inhibitors, LIF and Activin A; Fischer *et al.*, 2022) or PXGL- (PD0325901, XAV939, Gö6983, and LIF; Bredenkamp *et al.*, 2019) derived blastoids, including at imprinted loci (Xie *et al.*, 2025).

Thus, moving toward blastoid co-culture studies with endometrial cells has improved the growth, differentiation, invasion, and longevity of the models than blastoid culture alone. Together, the whole is greater than the sum of its parts.

Future perspectives

Recent advances in the generation of models of the human embryo and endometrium offer the potential to transform our understanding of inaccessible processes taking place during the earliest stages of pregnancy. We propose that the essential focus of future work should be to bring these models together, to the benefit of both. However, technical barriers need to be overcome. Defining what constitutes a 'successful' implantation model remains an open question: which markers and timepoints should be prioritized, and are there specific extra-embryonic cell types, structural features, or endometrial fate divergences that will serve as hallmarks of an optimal model? Moreover, without direct *in vivo* comparators, how should benchmarks for implantation-like processes be established?

The goal is a physiologically relevant, tractable model of human implantation that provides otherwise unobtainable insights into early pregnancy. By systematically manipulating either the blastoid or the endometrium while constraining the other, future work could begin to parse the relative contributions of embryo- and endometrium-driven mechanisms within different reproductive disorders. For example, combining aneuploid or mosaic blastoids with healthy endometrial cells will help define embryo-dependent implantation failures or placentation defects; while the combination of euploid blastoids with dysfunctional endometrial cultures will delineate endometrial contributions. From an endometrial perspective, better representation of the tissue complexity is a necessity, moving from simple stromal-epithelial cultures to inclusion of functional vessels and the spectrum of immune cells, with a parallel focus on scale. In either case, the models address the unmet need for mechanistic discovery and pre-clinical studies in this critical window of development.

Looking ahead, addressing these questions will require not only overcoming technical barriers but also navigating broader challenges: weighing the unique benefits of integrated models against less ethically complex alternatives (e.g. cells, organoids, separate co-cultures), developing appropriate regulatory frameworks (Boiani and group, 2024; Martinez Arias *et al.*, 2024; Sturmey, 2024), and ensuring transparent, constructive engagement with the public (Sugarman *et al.*, 2023).

Data availability

No original data were generated in the production of this mini-review.

Authors' roles

E.S.L.: conceptualization, visualization, writing—original draft, writing—review and editing. T.M.R.: conceptualization, writing—original draft, writing—review and editing. S.A.G.: visualization, writing—review and editing.

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Conflict of interest

The authors have no conflicts to declare.

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