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Artificial Wombs As A Solution For Premature Birth: Current Innovations And Future Implications For Neonatal Health

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Abstract
Objective: *Artificial womb technology (AWT) offers a groundbreaking solution to the challenges of premature birth, aiming to replicate the natural uterine environment and support fetal development. This study explores the potential of AWT to transform neonatal care by addressing technological, biological, and ethical challenges.*
Method: *A comprehensive review of current advancements in AWT was conducted, focusing on preclinical studies, technological innovations, and ethical considerations. The study analyzed existing research on artificial placentas, vascular engineering, and neonatal developmental outcomes while drawing comparisons to*

traditional neonatal intensive care methods.
Findings: *AWT demonstrates significant potential to improve survival rates and long-term outcomes for extremely premature infants. Key advancements include the development of bioengineered systems that mimic placental functions and provide controlled environments for fetal growth. However, critical challenges remain, such as ensuring vascular integration, managing immunological responses, and addressing long-term developmental impacts. Ethical concerns, including equitable access and implications for parent-child relationships, highlight the need for multidisciplinary collaboration.*
Conclusion: *AWT represents a transformative innovation in neonatal health, offering hope for improved outcomes in preterm birth management. The technology's successful implementation will require continued research, ethical deliberation, and interdisciplinary efforts to overcome existing barriers. With robust clinical protocols and public acceptance, AWT has the potential to redefine neonatal care and advance our understanding of human development.*

Keywords: ***Artificial womb technology, neonatal care, premature birth, fetal development, bioengineering, ethical considerations***

1. Introduction

Preterm birth is a pervasive global health challenge, affecting between 5% and 18% of pregnancies annually and accounting for over 15 million premature births worldwide (Novac et al., 2022; Tong & Abrahams, 2019). It is the leading cause of neonatal mortality, contributing to 75% of neonatal deaths globally, and is associated with significant morbidity, including long-term developmental, cardiovascular, and metabolic disorders (Pusdekar et al., 2020; Jańczewska et al., 2023). For many preterm infants, survival is accompanied by the likelihood of enduring complications that impact their quality of life, underscoring the urgent need for innovative solutions in neonatal care.

Advances in neonatal care have improved survival rates for extremely preterm infants, particularly those born at the threshold of viability. However, these gains come with trade-offs. Survivors face increased risks of long-term health sequelae, including neurodevelopmental disorders and chronic respiratory conditions such as bronchopulmonary dysplasia (BPD). Notably, data from the EPICure2 study revealed stagnation in reducing the incidence of BPD and other major morbidities among extremely preterm infants over the last few decades (Rodgers & Singh, 2020). This highlights the limitations of traditional neonatal intensive care unit (NICU) interventions, even in the face of technological and medical advancements.

Furthermore, the NICU environment itself can exacerbate challenges for preterm infants. Beyond their medical fragility, extremely preterm infants are subjected to numerous painful and invasive procedures. These interventions, while essential for survival, often have negative developmental consequences, including neurodevelopmental impairments later in life (Fulkoski et al., 2023). The disruption of parent-infant bonding within the NICU setting compounds these difficulties, affecting mental health outcomes for both parents and children (Ettenberger et al., 2021; Givrad et al., 2020).

In light of these challenges, artificial womb technology has emerged as a potential game-changer in the field of neonatal care. This innovative approach aims to mimic the natural uterine environment, offering preterm infants a controlled setting to support their continued development outside the mother's womb. By addressing the limitations of NICUs and reducing the risks associated with traditional interventions, artificial wombs hold the promise of revolutionizing care for preterm infants. This paper explores the current state of artificial womb technology, its potential to mitigate complications of preterm birth, and its broader implications for neonatal health and healthcare systems worldwide.

2. Understanding Premature Birth and Its Challenges

Premature birth, defined as birth before 37 weeks of gestation, affects approximately 10% of newborns globally,

leading to over 15 million preterm births each year (Morniroli et al., 2023).
The degree of prematurity is often classified into three categories based on gestational age:

Gestational Age	Category	Description
<28 weeks	Extremely Preterm	High mortality and morbidity risks
28 to <32 weeks	Very Preterm	Significant health complications
32 to <37 weeks	Moderate to Late Preterm	Lower but still notable risks

Prematurity carries numerous risks for newborns, with preterm infants experiencing a higher likelihood of serious health complications. Preterm birth is the leading cause of infant mortality and morbidity, contributing significantly to the global neonatal death toll (Morniroli et al., 2023). Preterm infants face challenges such as respiratory distress syndrome (RDS), cerebral palsy, developmental delays, and other organ immaturities, which can have profound long-term effects on their health (Morniroli et al., 2023; Cassiano et al., 2016).
The risks associated with prematurity extend well beyond infancy, with studies showing that preterm birth is linked to a higher prevalence of chronic conditions in adulthood, including cardiovascular diseases, diabetes, and hypertension. The interference with organ system development during the in-utero and perinatal periods plays a significant role in these long-term health problems (Morniroli et al., 2023). Additionally, emotional and behavioral issues, such as anxiety and depression, are more prevalent in children born prematurely, with the degree of prematurity and low birth weight being strong predictors (Cassiano et al., 2016).

Table 1: Risks and Complications in Preterm Birth

Complication	Associated Risk Factors	Potential Long-Term Effects
Respiratory distress syndrome (RDS)	Surfactant deficiency, immature lungs	Chronic respiratory issues, long-term ventilation needs
Cerebral palsy	Premature brain development	Motor impairment, cognitive delays
Developmental delays	Inadequate growth, premature birth	Learning disabilities, speech delay
Chronic conditions (Cardiovascular, Diabetes)	Immature organ development, birth weight	Increased risk of adult diseases

As highlighted in the table above, the most immediate complications for preterm infants often revolve around respiratory distress. Respiratory distress syndrome (RDS) is one of the most common and severe conditions, primarily due to surfactant deficiency and underdeveloped lungs, which hinders the infant's ability to breathe adequately after birth. This often results in tachypnea, chest wall retractions, and cyanosis, and in severe cases, requires mechanical ventilation and long-term respiratory support (Çekinmez et al., 2013; Hermansen & Lorah, 2008).
Interestingly, RDS is not the only respiratory challenge faced by preterm infants. Transient tachypnea of the newborn, which results from excess lung fluid, and meconium aspiration syndrome, caused by the inhalation of meconium in utero, are also significant contributors to neonatal respiratory distress (Hermansen & Lorah, 2008).
While advances in perinatal care, such as the use of antenatal corticosteroids and exogenous surfactant therapies,

have significantly improved survival rates for preterm infants, these therapies are not without limitations and complications (Fraser et al., 2004).

In addition to respiratory challenges, preterm infants are vulnerable to other health risks related to their organ immaturity. Early-onset sepsis, vascular pathologies, and gastrointestinal complications, such as necrotizing enterocolitis, are common concerns in this vulnerable population (Safranow et al., 2012; Jakiel et al., 2015). Furthermore, recent studies indicate that preterm birth may negatively impact the development of the gut microbiome, potentially leading to growth disturbances and other health issues (Zeng et al., 2022).

Another critical challenge for preterm infants is the development of bronchopulmonary dysplasia (BPD), a chronic lung disease caused by abnormal lung development following prolonged mechanical ventilation and oxygen therapy. BPD is associated with significant morbidity and can lead to lifelong respiratory issues, including the need for continuous oxygen therapy in some cases (Rodgers & Singh, 2020).

Table 2: Common Health Complications in Preterm Infants

Health Issue	**Cause**	**Long-Term Impact**
Respiratory distress syndrome (RDS)	Surfactant deficiency, immature lungs	Ongoing lung issues, need for ventilation
Bronchopulmonary dysplasia (BPD)	Abnormal lung development, oxygen therapy	Chronic lung disease, risk of long-term complications
Early-onset sepsis	Immune system immaturity, infection exposure	Increased risk of neurodevelopmental delays
Necrotizing enterocolitis (NEC)	Premature gastrointestinal development	Potential for long-term gut issues

As the table illustrates, the complications stemming from prematurity are diverse and have long-lasting effects on both the infant's immediate survival and their long-term development. With such a complex range of health issues, preterm infants require advanced and multifaceted medical interventions. While current neonatal intensive care unit (NICU) practices, such as mechanical ventilation, surfactant replacement, and intravenous nutrition, have saved countless lives, they are not without limitations. NICU interventions often fail to address the root cause of premature birth: the premature and incomplete development of vital organs.

Despite substantial advances in neonatal care, NICUs remain under pressure to improve outcomes for extremely preterm infants. One significant limitation is the inability of current technologies to fully replicate the conditions of the womb. This gap in care creates ongoing risks for preterm infants, such as exposure to invasive procedures, pain, and stress, which can negatively affect neurodevelopmental outcomes (Fulkoski et al., 2023). Furthermore, the lack of a natural environment for bonding between parents and infants, compounded by restrictions like those experienced during the COVID-19 pandemic, hinders essential parent-infant connections (Ettenberger et al., 2021; Kelleher et al., 2022).

In conclusion, preterm birth poses a significant challenge, not only in terms of immediate health concerns but also with respect to long-term developmental outcomes. As current NICU approaches fall short in addressing these challenges comprehensively, exploring new technologies—such as artificial wombs—may offer a promising solution to mitigate the risks associated with premature birth and improve the health outcomes for preterm infants.

3. **Artificial Womb Technology: An Overview**

Artificial womb technology (AWT), also referred to as Artificial Placenta and Artificial Womb (APAW) or ectogenesis, represents a groundbreaking advancement in neonatal care and reproductive medicine. It aims to replicate the natural environment of the uterus, offering critical support for extremely premature infants while opening new avenues in human gestation research (Haren et al., 2024; Sailis et al., 2023). The development of AWT is built upon decades of research, technological innovations, and ethical discussions.

- **Concept and Components of Artificial Womb Technology**

Artificial womb systems are designed to mimic the natural conditions of a mother's womb. Key components include:

1. Fluid-filled incubator: A chamber replicating the amniotic environment, providing a liquid medium for fetal development (Haren et al., 2024).
2. Oxygenator: A device connected to umbilical vessels to supply oxygen and nutrients while facilitating waste removal, emulating placental functions (Haren et al., 2024).
3. Umbilical-like blood exchange: Systems utilizing arteriovenous (AV) or veno-venous (VV) extracorporeal life support (ECLS) for gas exchange and circulation (Fallon & Mychaliska, 2021).
4. Temperature regulation: Maintaining optimal conditions to support growth, taking into account the role of maternal-fetal heat exchange (Kasiteropoulou et al., 2020).

Two distinct approaches to artificial womb systems have emerged:

- ❖ AV-ECLS approach: Utilizes only umbilical vessels for cannulation, requiring immediate transfer to a fluid-filled environment after birth.
- ❖ VV-ECLS approach: Can be initiated after birth for infants who fail conventional medical interventions (Fallon & Mychaliska, 2021).

The ultimate goal of AWT is to enhance survival rates and improve health outcomes for extremely premature infants. However, the technology raises ethical, legal, and societal concerns that must be addressed before clinical implementation (Horn & Romanis, 2020).

- **History and Development of Artificial Womb Technology**

The journey toward AWT has spanned several decades, with significant milestones contributing to its evolution:

- 1950s: Early human studies on artificial placenta technology.
- 1960s: Foundational animal studies explored sustained fetal development outside the uterus.
- 1990s: Extended use of artificial placenta technology with innovations in fetal pulmonary resuscitation.
- 2000s: Development of systems powered by the fetal heart.
- 2010s: Adaptation of artificial placenta systems for extremely preterm fetuses (Usuda et al., 2022).

The introduction of in vitro fertilization in the 1980s catalyzed discussions on artificial gestation, highlighting the potential of ectogenesis and sparking debates on its ethical implications (Bie et al., 2022). Notably, advances in artificial intelligence, virology, and other fields have accelerated progress in artificial womb research (Guerrero, 2023; Salam et al., 2024).

However, challenges persist, including reconciling complex ethical dilemmas, addressing societal concerns, and navigating anti-abortion rhetoric that often overshadows broader implications of the technology (Horn, 2020).

Animal studies have demonstrated the feasibility of AWT, with notable breakthroughs in lamb studies. In 2017, researchers successfully sustained lamb fetuses in an artificial womb system resembling uterine conditions, allowing them to develop from an equivalent of 22–24 weeks' human gestation to term. The lambs were born in good health, marking a significant step forward in ectogenesis research (Horn, 2020).

Table 3 illustrates key prototypes and their findings:

Prototype	**Species Tested**	**Developmental Stage Supported**	**Findings**	**Challenges**
Advanced Incubator	Lambs	22–24 weeks (human	Healthy development to	Translation to human use,

(2017)		equivalent)	term.	ethical concerns.
Fluid-filled system	Animal models	Preterm fetuses	Effective oxygenation and nutrient delivery.	Risk of developmental abnormalities.

While promising, the translation of these prototypes to human neonates presents ethical and technical challenges. Full-term ectogenesis in humans remains speculative, with current research focusing on partial ectogenesis for supporting preterm infants. Rigorous clinical trials and interdisciplinary discussions will be critical to addressing safety, efficacy, and ethical considerations (Romanis, 2019).
Artificial womb technology has the potential to revolutionize neonatal care and reproductive medicine by providing a controlled environment for fetal development outside the human body. While significant progress has been made in animal models, the path to clinical application in humans involves addressing ethical, legal, and social challenges. Continued research, coupled with robust regulatory frameworks, will determine the role of AWT in shaping the future of healthcare for preterm infants.

4. Current Innovations in Artificial Womb Technology

Artificial womb technology (AWT) represents a groundbreaking advancement in reproductive and neonatal care, focusing on mimicking the natural uterine environment to support fetal development. Recent innovations have centered on refining the design and functionality of AWT systems, enhancing support for organ development, and improving the simulation of intrauterine conditions. These strides aim to address the needs of extremely premature neonates and open avenues for alternative approaches to gestation (Kukora et al., 2023; Singh et al., 2022).

➢ **Design and Functionality**

The design of artificial womb systems has evolved to incorporate cutting-edge engineering and biomedical principles. These systems typically consist of:

1. Artificial Placenta (AP): Replicates placental functions by providing oxygenation, nutrient exchange, and waste removal through an extracorporeal life support (ECLS) system (Kukora et al., 2023).
2. Fluid-filled Chambers: Mimic the amniotic environment, providing the fetus with a liquid medium for growth and protection against external pressures (Sailis et al., 2023).
3. Temperature Regulation: Maintains optimal thermal conditions, crucial for cellular and physiological development (Rodger & Blackshaw, 2024).

Advanced designs integrate ***Multicellular Engineered Living Systems (M-CELS),*** which utilize principles from genetic engineering, microfluidics, and systems biology to create bioengineered tissues that closely simulate natural gestational environments (Aydin et al., 2022). Despite significant progress, no prototypes have yet been developed for human application, with current focus limited to animal models and laboratory simulations (Singh et al., 2022).

➢ **Support for Organ Development**

Artificial womb systems aim to replicate conditions that promote the proper growth of critical fetal organs, particularly the lungs and brain.

- **Lung Development**

Innovations in lung organoid technologies have contributed significantly to understanding fetal pulmonary growth:
Mechanobiology and Biophysical Cues: Lung organoids now incorporate mechanical stretching to mimic respiratory movements, aiding alveolar development (Najrana et al., 2020).
Branching and Co-alignment: Research on airway-vascular interactions has highlighted the importance of

synchronized lung tissue growth and vascular patterning for functional development (Kina et al., 2021).

- **Brain Development**

Brain organoid advancements have enhanced modeling of neurological growth and disease mechanisms:
Three-dimensional Brain Organoids: Generated from stem cells, these structures exhibit complex architectures that mimic fetal brain development (Fan et al., 2021).
Integration with Synthetic Biomaterials: Technologies such as microfluidic systems enhance nutrient delivery and waste removal, improving organoid functionality (Adlakha, 2023).
These developments provide invaluable insights into the physiological processes underpinning fetal organ growth, offering a foundation for therapeutic applications and advancing the capabilities of artificial womb systems.

➢ **Simulation of Intrauterine Environment**

Accurately replicating the uterine environment requires innovations in fluid dynamics, oxygenation, and temperature regulation.

- **Fluid Dynamics**

The design of blood-mimicking fluids plays a pivotal role in simulating amniotic and vascular conditions:
Viscosity Adjustments: Recent research has optimized the preparation of synthetic fluids, ensuring consistency in flow properties and tactile feedback (Dong et al., 2022).

- **Oxygenation**

Advances in oxygenation systems have enabled more precise replication of placental gas exchange:
Microdevice Innovations: Multifunctional microdevices simulate oxygen gradients and flow dynamics, capturing the interplay of red blood cell (RBC) concentration and oxygen saturation (Nakshatrala, 2023).

- **Temperature Control**

Sophisticated thermal regulation systems mimic maternal-fetal heat exchange:
Microvascular Composites: These systems provide fine-tuned temperature control through fluid circulation, ensuring stability in fetal development conditions (Nakshatrala, 2023). The integration of these technologies into comprehensive simulation platforms offers a closer approximation of the natural uterine environment, enhancing the feasibility of AWT.

Table 1: Summary of Key Innovations in Artificial Womb Technology

ponent	vation	tionality
cial Placenta	corporeal life support (ECLS)	cates placental oxygenation, nutrient exchange, and waste removal (Kukora et al., 2023).
-filled Chamber	nced amniotic fluid simulation	des a protective liquid medium for fetal development, mimicking the natural uterine environment (Sailis et al., 2023).
Organoids	anobiological stimuli	tates lung development through respiratory-like mechanical stretching (Najrana et al., 2020).
Organoids	ration with biomaterials and microfluidics	orts brain development by ensuring nutrient delivery and mimicking neurological architecture (Adlakha, 2023).
erature Control	ovascular thermal regulation systems	tains stable intrauterine temperature conditions, critical for fetal growth

		(Nakshatrala, 2023).
enation Devices	functional microdevices	late oxygen gradients and flow, replicating placental gas exchange dynamics (Dong et al., 2022).

The ongoing evolution of artificial womb technology reflects the intersection of biomedical innovation and clinical need. Advances in design, organ support, and environmental simulation have brought AWT closer to potential application in neonatal care. However, significant challenges remain, particularly regarding ethical considerations and translational research for human use. Future efforts must prioritize multidisciplinary collaboration to refine these systems and address societal implications.

5. Future Directions and Research Needs

Animal models have been indispensable in preclinical research, serving as a critical step in the development of innovative medical technologies. However, transitioning findings from animal models to human trials presents inherent challenges, particularly in the field of artificial womb technology (AWT). One of the primary obstacles is the physiological and biological differences between species. These disparities often result in poor predictive outcomes when translating animal research to human applications, a common issue across various biomedical fields (Loewa et al., 2023).

While rodent models are commonly used for initial studies due to their accessibility and cost-effectiveness, they lack the anatomical and physiological relevance needed for scaling AWT to human trials. Large animal models such as sheep and non-human primates offer closer parallels in organ development and fetal physiology, making them valuable for bridging this gap (West & Kaiser, 2020). For example, sheep have been widely utilized in artificial placenta studies to assess oxygenation and nutrient transfer mechanisms, which are critical for sustaining fetal growth in an artificial environment (Hicks et al., 2021).

Despite their advantages, large animal models are not without limitations. Ethical considerations, high costs, and differences in immune responses remain significant barriers. Dose conversion and physiological scaling also require rigorous scientific justification to avoid errors in extrapolation to human trials (Shekunova et al., 2020). To enhance the translational validity, researchers are exploring co-clinical trials, which integrate preclinical and clinical data to refine study designs and improve outcomes (Palmer et al., 2021). These approaches may help bridge the translational gap, paving the way for human trials of AWT.

Advancing AWT involves addressing numerous technological and medical challenges. One critical area is vascular tissue engineering, where creating a reliable vascular connection between the artificial womb and the developing fetus remains a complex task. Current biofabrication technologies, such as 3D bioprinting, have made strides in producing autologous blood vessels. However, these technologies still struggle to replicate the structural and functional integrity of native vascular systems (Devillard & Marquette, 2021). Another significant hurdle lies in immunological considerations. The fetal immune system, though underdeveloped, interacts with maternal and external factors during pregnancy. Replicating this delicate immunological balance in AWT systems is essential to prevent complications such as graft rejection or inflammatory responses (Zor et al., 2019). Research into biomaterials that can mimic immune-privileged environments is ongoing, aiming to reduce the risk of adverse immune reactions while supporting normal fetal development.

Additionally, technological innovations such as implantable sensors and bioreactors are being explored to monitor and optimize conditions within the artificial womb. While promising, these technologies face challenges related to long-term performance, biocompatibility, and integration into clinical workflows (Yogev et al., 2023). Addressing these issues through interdisciplinary research will be critical for the safe and effective implementation of AWT.

The long-term developmental outcomes of infants born through AWT remain one of the most pressing concerns as this technology advances. While AWT aims to replicate the natural uterine environment, subtle deviations from physiological norms may impact fetal development in ways that are not immediately apparent at birth. Long-term studies are essential to assess these impacts comprehensively. Existing research on premature infants provides valuable insights into potential challenges. For instance, conditions such as intraventricular hemorrhages and prolonged oxygen exposure have been linked to chronic developmental delays and neurodevelopmental disorders (Safina & Volyanyuk, 2020). Similar risks may apply to infants supported by AWT, emphasizing the need for systematic follow-up studies.

Evidence from assisted reproductive technologies (ART) further underscores the importance of long-term monitoring. Although early developmental delays observed in ART-conceived infants often resolve by 24 months, the initial disparities highlight the necessity of tracking growth and development over time (Acharyya & Acharyya, 2022). For AWT, such monitoring should extend beyond physical growth to include cognitive, social, and emotional outcomes. Ethical concerns also play a significant role in shaping the scope of long-term studies. Ensuring informed consent, addressing potential societal biases, and safeguarding the rights of AWT-born individuals are critical for the responsible implementation of this technology (Werner & Mercurio, 2021). Comprehensive follow-up protocols will not only provide data on the safety and efficacy of AWT but also help address ethical and societal concerns, ultimately guiding its clinical and regulatory adoption.

Transitioning from animal studies to human trials, addressing technological and medical hurdles, and ensuring thorough long-term follow-up represent the next critical steps in the development of AWT. By investing in translational research, fostering interdisciplinary collaboration, and prioritizing ethical considerations, researchers can advance AWT toward safe and effective clinical use. These efforts will not only improve neonatal care but also contribute to the broader understanding of human development and medical innovation.

6. Conclusion

Artificial womb technology (AWT) represents a groundbreaking innovation poised to address one of the most significant challenges in neonatal health: premature births. Premature delivery remains a leading cause of neonatal mortality and long-term health complications, including respiratory issues, neurodevelopmental delays, and chronic diseases. By simulating the natural uterine environment, AWT offers a transformative solution, potentially bridging the gap between extreme prematurity and full-term birth. This promising technology aims to reduce the mortality and morbidity associated with preterm births while providing a controlled environment to support optimal fetal development.

The potential impact of AWT extends beyond immediate neonatal outcomes. The artificial womb could revolutionize perinatal care, ensuring that even the most vulnerable preterm infants receive the support they need to thrive. By replacing or supplementing traditional neonatal intensive care units (NICUs), AWT might significantly improve survival rates and reduce long-term complications. Moreover, it provides a platform for studying fetal development in ways previously unimaginable, potentially unveiling new insights into human growth and physiology.

The transformative potential of AWT for neonatal health cannot be overstated. For infants born at the edge of viability—those delivered before 24 weeks of gestation—the current survival rates are dishearteningly low, and those who survive often face lifelong health challenges. AWT has the potential to redefine this viability threshold by creating a safe and supportive environment for these fragile lives. By closely mimicking the conditions of a natural womb, AWT can support organ development, reduce stress on immature systems, and minimize complications such as intraventricular hemorrhage and bronchopulmonary dysplasia.

In addition to improving individual outcomes, the widespread adoption of AWT could alleviate the economic burden associated with preterm births. Prematurity currently imposes significant healthcare costs, both in terms of acute medical care in NICUs and long-term management of associated disabilities. AWT could reduce these expenses by decreasing the need for intensive care interventions and improving the overall health trajectory of preterm infants.

Despite these promising outcomes, the road ahead is complex and multifaceted. Extensive research is still required to address the technological, biological, and ethical challenges associated with AWT. For instance, ensuring the safety and efficacy of AWT in humans will require rigorous preclinical studies followed by carefully designed clinical trials. Additionally, the development of personalized approaches to AWT—tailored to meet the specific needs of individual infants—will be crucial for optimizing outcomes.

Another critical consideration is the long-term impact of AWT on children's health and development. While short-term survival is an essential goal, the broader objective must include ensuring that children born through AWT achieve normal physical, cognitive, and emotional development. This requires comprehensive follow-up studies to monitor growth, assess potential risks, and refine the technology as needed.

The successful implementation of AWT will depend on sustained collaboration among medical professionals, scientists, ethicists, and policymakers. Interdisciplinary teamwork is essential to address the diverse challenges associated with this technology, from its biological intricacies to its societal implications. For instance, engineers and biologists must work together to refine AWT systems, while ethicists and regulators must ensure that its use aligns with societal values and ethical principles.

Ethical considerations will play a central role in shaping the future of AWT. Questions about parental consent, the rights of AWT-born individuals, and potential societal implications must be addressed proactively. Additionally, ensuring equitable access to AWT will be critical to prevent disparities in neonatal care. Policymakers must work to ensure that this transformative technology benefits all segments of society, particularly those who are most vulnerable.

Another important aspect is public awareness and acceptance. As with any groundbreaking innovation, the introduction of AWT is likely to raise questions and concerns among the general public. Transparent communication about the benefits, risks, and ethical considerations of AWT will be essential for building trust and fostering informed discussions.

Looking ahead, the promise of AWT lies not only in its ability to save lives but also in its potential to advance our understanding of human development. By enabling researchers to study fetal physiology in unprecedented detail, AWT could pave the way for new discoveries in medicine and developmental biology. These insights could inform a wide range of applications, from improving maternal-fetal health to developing novel therapies for congenital disorders.

In conclusion, artificial womb technology has the potential to transform neonatal care, addressing the challenges of prematurity and advancing our understanding of human development. While the journey toward clinical implementation is fraught with challenges, the rewards are immense. Continued investment in research, ethical deliberation, and interdisciplinary collaboration will be crucial for realizing the full potential of this revolutionary technology. As we navigate the complexities of developing and deploying AWT, it is imperative to prioritize the well-being of the infants and families it aims to serve, ensuring that this innovation fulfills its promise of creating a brighter future for neonatal health.

Reference

1. Tong, M., & Abrahams, V. M. (2019). Neutrophils in preterm birth: Friend or foe? Placenta, 102, 17–20. https://doi.org/10.1016/j.placenta.2019.12.010
2. Jańczewska, I., Jańczewska, A., Wierzba, J., Szczurek-Gierczak, M., & Domżalska-Popadiuk, I. (2023). Prematurity and Low Birth Weight and Their Impact on Childhood Growth Patterns and the Risk of Long-Term Cardiovascular Sequelae. Children, 10(10), 1599. https://doi.org/10.3390/children10101599
3. Novac, O., Dima, V., Paduraru, L., Hincu, M. A., Avasilcai, A.-I., & Zonda, G. I. (2022). Facing the outcome of prematurity – opinions from the general practitioner. Romanian Journal of Medical Practice, 17(4), 160–163. https://doi.org/10.37897/rjmp.2022.4.2

4. Pusdekar, Y., Kurhe, K., Bose, C., Goldenberg, R. L., Garcés, A., Carlo, W. A., Goudar, S., Bauserman, M., Chomba, E., Liechty, E. A., Bhargav, S., Esamai, F., Thorsten, V., Saleem, S., Derman, R., Patel, A., Krebs, N. F., Koso-Thomas, M., Mcclure, E., … Hibberd, P. L. (2020). Rates and risk factors for preterm birth and low birthweight in the global network sites in six low- and low middle-income countries. Reproductive Health, 17(Suppl 3). https://doi.org/10.1186/s12978-020-01029-z
5. Rodgers, A., & Singh, C. (2020). Specialist neonatal respiratory care for babies born preterm (NICE guideline 124): a review. Archives of Disease in Childhood - Education & Practice Edition, 105(6), 355–357. https://doi.org/10.1136/archdischild-2019-317461
6. Givrad, S., Dowtin, L. L., Scala, M., & Hall, S. L. (2020). Recognizing and mitigating infant distress in Neonatal Intensive Care Unit (NICU). Journal of Neonatal Nursing, 27(1), 14–20. https://doi.org/10.1016/j.jnn.2020.09.009
7. Fulkoski, N., Kecskes, Z., & Chaudhari, T. (2023). Minor painful procedures in extremely preterm infants admitted to a tertiary neonatal intensive care unit: Opportunities to improve pain mitigation. Journal of Paediatrics and Child Health, 59(3), 542–547. https://doi.org/10.1111/jpc.16352
8. Ettenberger, M., Bieleninik, Ł., Elefant, C., & Epstein, S. (2021). Defining Attachment and Bonding: Overlaps, Differences and Implications for Music Therapy Clinical Practice and Research in the Neonatal Intensive Care Unit (NICU). International Journal of Environmental Research and Public Health, 18(4), 1733. https://doi.org/10.3390/ijerph18041733
9. You, S. Y., & Kim, A. R. (2020). South Korean nurses' lived experiences supporting maternal postpartum bonding in the neonatal intensive care unit. International Journal of Qualitative Studies on Health and Well-Being, 15(1), 1831221. https://doi.org/10.1080/17482631.2020.1831221
10. Kelleher, J., Paul, J. J., Dempsey, J., Dempsey, A. G., Takamatsu, S., & Kent, E. (2022). Adaptation of infant mental health services to preterm infants and their families receiving neonatal intensive care unit services during the COVID-19 pandemic. Infant Mental Health Journal, 43(1), 100–110. https://doi.org/10.1002/imhj.21961
11. Morniroli, D., Tiraferri, V., De Rose, D. U., Maiocco, G., Giannì, M. L., Coscia, A., Mosca, F., & Cresi, F. (2023). Beyond survival: the lasting effects of premature birth. Frontiers in Pediatrics, 11. https://doi.org/10.3389/fped.2023.1213243
12. Cassiano, R. G. M., Linhares, M. B. M., & Gaspardo, C. M. (2016). PREMATURITY, NEONATAL HEALTH STATUS, AND LATER CHILD BEHAVIORAL/EMOTIONAL PROBLEMS: A SYSTEMATIC REVIEW. Infant Mental Health Journal, 37(3), 274–288. https://doi.org/10.1002/imhj.21563
13. Çekinmez, E., Yapıcıoğlu, H., & Özlü, F. (2013). Respiratuar Distres Sendromu ve Komplikasyonları. Arsiv Kaynak Tarama Dergisi, 22(4), 615–630. https://doi.org/10.17827/aktd.53140
14. Hermansen, C., & Lorah, K. (2008). Respiratory Distress in the Newborn. 17–25. https://doi.org/10.1002/9781444300109.ch4
15. Fraser, J., Walls, M., & Mcguire, W. (2005). ABC of preterm birth: Respiratory complications of preterm birth. BMJ, 331(Suppl S1), 0507278. https://doi.org/10.1136/sbmj.0507278
16. Jakiel, G., Bińkowska, M., Kowal, A., Rumowska, S., Ciebiera, M., & Wilińska, M. (2015). Late preterm infants – impact of perinatal factors on neonatal results. A clinical study. Annals of Agricultural and Environmental Medicine, 22(3), 536–541. https://doi.org/10.5604/12321966.1167730
17. Mihaylova, A., Ivanov, K., Karaslavova, E., Sandeva, M., Parahuleva, N., Ivanova, S., Uchicova, E., Gueorguieva, E. P., & Gueorguiev, S. (2018). Frequency of hyaline membrane disease in preterm infants after prenatal corticosteroid prophylaxis. Biomedical Research, 29(6). https://doi.org/10.4066/biomedicalresearch.29-17-3642
18. Safranow, K., Machaliński, B., Kotowski, M., Celewicz, Z., Lewandowska, J., Dziedziejko, V., Machalińska, A., Czajka, R., & Rudnicki, J. (2012). Circulating endothelial progenitor cells in

premature infants: is there an association with premature birth complications? Journal of Perinatal Medicine, 40(4), 455–462. https://doi.org/10.1515/jpm-2011-0199
19. Fraser, J., Mcguire, W., & Walls, M. (2004). Respiratory complications of preterm birth. BMJ, 329(7472), 962–965. https://doi.org/10.1136/bmj.329.7472.962
20. Dassios, T. (2023). Critical functional lung volumes in neonatal intensive care: evidence and clinical applications. Pediatric Research, 94(1), 82–88. https://doi.org/10.1038/s41390-022-02450-9
21. Chen, I.-L., & Chen, H.-L. (2022). New developments in neonatal respiratory management. Pediatrics & Neonatology, 63(4), 341–347. https://doi.org/10.1016/j.pedneo.2022.02.002
22. Zeng, S., Li, S., Qu, Y., Ying, J., Wang, S., & Mu, D. (2022). First 1000 Days and Beyond After Birth: Gut Microbiota and Necrotizing Enterocolitis in Preterm Infants. Frontiers in Microbiology, 13. https://doi.org/10.3389/fmicb.2022.905380
23. Kapadia, V., & Oei, J. L. (2020). Optimizing oxygen therapy for preterm infants at birth: Are we there yet? Seminars in Fetal and Neonatal Medicine, 25(2), 101081. https://doi.org/10.1016/j.siny.2020.101081
24. Dyke, J. P., Grimm, R., Blatt, L. K., Voskrebenzev, A., Vogel-Claussen, J., Worgall, S., Kovanlikaya, A., & Perlman, J. M. (2023). Assessment of lung ventilation of premature infants with bronchopulmonary dysplasia at 1.5 Tesla using phase-resolved functional lung magnetic resonance imaging. Pediatric Radiology, 53(6), 1076–1084. https://doi.org/10.1007/s00247-023-05598-6
25. Rodgers, A., & Singh, C. (2020). Specialist neonatal respiratory care for babies born preterm (NICE guideline 124): a review. Archives of Disease in Childhood - Education & Practice Edition, 105(6), 355–357. https://doi.org/10.1136/archdischild-2019-317461
26. Morniroli, D., Tiraferri, V., De Rose, D. U., Maiocco, G., Giannì, M. L., Coscia, A., Mosca, F., & Cresi, F. (2023). Beyond survival: the lasting effects of premature birth. Frontiers in Pediatrics, 11. https://doi.org/10.3389/fped.2023.1213243
27. Baldassarre, M. E., Laforgia, N., Pensa, M., Schettini, F., Quercia, M., Marazzato, M., Lombardi, F., & Loverro, M. T. (2023). SLAB51 Multi-Strain Probiotic Formula Increases Oxygenation in Oxygen-Treated Preterm Infants. Nutrients, 15(17), 3685. https://doi.org/10.3390/nu15173685
28. Van Haren, J. S., Schoberer, M., Delbressine, F. L. M., Te Pas, A. B., Oei, S. G., Van Laar, J. O. E. H., & Van Der Hout-Van Der Jagt, M. B. (2024). Transferring an extremely premature infant to an extra-uterine life support system: a prospective view on the obstetric procedure. Frontiers in Pediatrics, 12. https://doi.org/10.3389/fped.2024.1360111
29. Singh, S. K., Dey, A., Putatunda, S., & Singh, M. K. (2022). Artificial Womb Technology: A Roadmap to a changing Medico-Legal Landscape. Journal of Experimental Biology and Agricultural Sciences, 10(1), 201–210. https://doi.org/10.18006/2022.10(1).201.210
30. Horn, C., & Romanis, E. C. (2020). Establishing Boundaries for Speculation About Artificial Wombs, Ectogenesis, Gender, and the Gestating Body (pp. 227–254). springer. https://doi.org/10.1007/978-3-030-42200-4_10
31. Kasiteropoulou, D., Downe, S., & Topalidou, A. (2020). A computational fluid dynamics modelling of maternal-fetal heat exchange and blood flow in the umbilical cord. PLOS ONE, 15(7), e0231997. https://doi.org/10.1371/journal.pone.0231997
32. Horn, C. (2021). Abortion Rights after Artificial Wombs: Why Decriminalisation is Needed Ahead of Ectogenesis. Medical Law Review, 29(1), 80–105. https://doi.org/10.1093/medlaw/fwaa042
33. Sailis, G., Shaholli, D., Perna, C., Moretti, L., Bongiovanni, A., Ricci, E., Vezza, F., Colaprico, C., Manai, M. V., Barletta, V. I., & La Torre, G. (2023). Bioetics Issues of Artificial Placenta and Artificial Womb Technology. La Clinica Terapeutica, 174(Suppl 2(6)), 33–41. https://doi.org/10.7417/ct.2023.2494

34. Fallon, B. P., & Mychaliska, G. B. (2021). Development of an artificial placenta for support of premature infants: narrative review of the history, recent milestones, and future innovation. Translational Pediatrics, 10(5), 1470–1485. https://doi.org/10.21037/tp-20-136
35. Muhsin, S. M., Chin, A. H. B., & Padela, A. I. (2023). An Ethico-Legal Analysis of Artificial Womb Technology and Extracorporeal Gestation Based on Islamic Legal Maxims. The New Bioethics, 30(1), 1–13. https://doi.org/10.1080/20502877.2023.2269638
36. De Bie, F. R., Kim, S. D., Bose, S. K., Nathanson, P., Partridge, E. A., Flake, A. W., & Feudtner, C. (2022). Ethics Considerations Regarding Artificial Womb Technology for the Fetonate. The American Journal of Bioethics, 23(5), 67–78. https://doi.org/10.1080/15265161.2022.2048738
37. Usuda, H., Watanabe, S., T, H., Saito, M., Sato, S., Ikeda, H., Kumagai, Y., Choolani, M. C., & Kemp, M. W. (2022). Artificial placenta technology: History, potential and perception. Placenta, 141, 10–17. https://doi.org/10.1016/j.placenta.2022.10.003
38. Horn, C. (2020). Ectogenesis is for Feminists. Catalyst: Feminism, Theory, Technoscience, 6(1). https://doi.org/10.28968/cftt.v6i1.33065
39. Singh, S. K., Dey, A., Putatunda, S., & Singh, M. K. (2022). Artificial Womb Technology: A Roadmap to a changing Medico-Legal Landscape. Journal of Experimental Biology and Agricultural Sciences, 10(1), 201–210. https://doi.org/10.18006/2022.10(1).201.210
40. Aydin, O., Dar, R. D., Tordoff, J., Spellicy, S. E., Zartman, J., Weinberg, R. P., Sample, M., Kamm, R. D., Bashir, R., Montserrat, N., Saif, M. T. A., Weiss, R., Passaro, A. P., Truskey, G. A., Wang, J., Raman, R., & Palacios, S. (2022). Principles for the design of multicellular engineered living systems. APL Bioengineering, 6(1), 010903. https://doi.org/10.1063/5.0076635
41. Kukora, S. K., Mychaliska, G. B., & Weiss, E. M. (2023). Ethical challenges in first-in-human trials of the artificial placenta and artificial womb: not all technologies are created equally, ethically. Journal of Perinatology, 43(11), 1337–1342. https://doi.org/10.1038/s41372-023-01713-5
42. Sailis, G., Shaholli, D., Perna, C., Moretti, L., Bongiovanni, A., Ricci, E., Vezza, F., Colaprico, C., Manai, M. V., Barletta, V. I., & La Torre, G. (2023). Bioetics Issues of Artificial Placenta and Artificial Womb Technology. La Clinica Terapeutica, 174(Suppl 2(6)), 33–41. https://doi.org/10.7417/ct.2023.2494
43. Rodger, D., & Blackshaw, B. P. (2024). Detached From Humanity: Artificial Gestation and the Christian Dilemma. Christian Bioethics: Non-Ecumenical Studies in Medical Morality, 30(2), 85–95. https://doi.org/10.1093/cb/cbae002
44. Romanis, E. C. (2019). Artificial womb technology and clinical translation: Innovative treatment or medical research? Bioethics, 34(4), 392–402. https://doi.org/10.1111/bioe.12701
45. Shao, Z., Michielin, F., & De Coppi, P. (2023). Leveraging mechanobiology and biophysical cues in lung organoids for studying lung development and disease. Frontiers in Chemical Engineering, 5. https://doi.org/10.3389/fceng.2023.1255783
46. Kina, Y. P., El Agha, E., Seeger, W., & Khadim, A. (2021). The Lung Vasculature: A Driver or Passenger in Lung Branching Morphogenesis? Frontiers in Cell and Developmental Biology, 8. https://doi.org/10.3389/fcell.2020.623868
47. Fan, W., Christian, K. M., Song, H., & Ming, G.-L. (2021). Applications of Brain Organoids for Infectious Diseases. Journal of Molecular Biology, 434(3), 167243. https://doi.org/10.1016/j.jmb.2021.167243
48. Najrana, T., Schulte, V., Mahadeo, A., Quesenberry, P., Uzun, A., Sanchez-Esteban, J., Schorl, C., Kreienberg, E., Goldberg, L., & Abu-Eid, R. (2020). Mechanical stretch regulates the expression of specific miRNA in extracellular vesicles released from lung epithelial cells. Journal of Cellular Physiology, 235(11), 8210–8223. https://doi.org/10.1002/jcp.29476

49. Zhang, D. Y., Song, H., & Ming, G.-L. (2020). Modeling neurological disorders using brain organoids. Seminars in Cell & Developmental Biology, 111, 4–14. https://doi.org/10.1016/j.semcdb.2020.05.026
50. Adlakha, Y. K. (2023). Human 3D brain organoids: steering the demolecularization of brain and neurological diseases. Cell Death Discovery, 9(1). https://doi.org/10.1038/s41420-023-01523-w
51. Dong, R., Yang, Y., Li, Y., Chen, C., Liu, S., Tao, L., Qian, Z., & Li, W. (2022). On-chip spectroscopic monitoring of erythrocyte oxygenation under hematocrit and oxygen gradients. Journal of Science: Advanced Materials and Devices, 7(4), 100515. https://doi.org/10.1016/j.jsamd.2022.100515
52. Kalyana B Nakshatrala, K. B. N. (2023). Modeling Thermal Regulation in Thin Vascular Systems: A Mathematical Analysis. Communications in Computational Physics, 33(4), 1035–1068. https://doi.org/10.4208/cicp.oa-2022-0240
53. Storey, J., Olzinski, A., Gobbetti, T., & Berridge, B. R. (2021). A Structured Approach to Optimizing Animal Model Selection for Human Translation: The Animal Model Quality Assessment. ILAR Journal, 62(1–2), 66–76. https://doi.org/10.1093/ilar/ilac004
54. Hicks, W. H., Haider, A. S., Cohen-Gadol, A. A., Bentley, R. T., Aoun, S. G., Bachoo, R. M., El Ahmadieh, T. Y., Dobariya, A., Pascual, J. M., Bird, C. E., Mickey, B. E., Pernik, M. N., & Abdullah, K. G. (2021). Large Animal Models of Glioma: Current Status and Future Prospects. Anticancer Research, 41(11), 5343–5353. https://doi.org/10.21873/anticanres.15347
55. Loewa, A., Feng, J. J., & Hedtrich, S. (2023). Human disease models in drug development. Nature Reviews Bioengineering, 1(8), 545–559. https://doi.org/10.1038/s44222-023-00063-3
56. Palmer, D., Dumont, J. R., Dexter, T. D., Prado, M. A. M., Finger, E., Bussey, T. J., & Saksida, L. M. (2021). Touchscreen cognitive testing: Cross-species translation and co-clinical trials in neurodegenerative and neuropsychiatric disease. Neurobiology of Learning and Memory, 182, 107443. https://doi.org/10.1016/j.nlm.2021.107443
57. West, F., & Kaiser, E. (2020). Large animal ischemic stroke models: replicating human stroke pathophysiology. Neural Regeneration Research, 15(8), 1377. https://doi.org/10.4103/1673-5374.274324
58. Shekunova, E. V., Kovaleva, M. A., Makarova, M. N., & Makarov, V. G. (2020). Dose Selection in Preclinical Studies: Cross-Species Dose Conversion. The Bulletin of the Scientific Centre for Expert Evaluation of Medicinal Products, 10(1), 19–28. https://doi.org/10.30895/1991-2919-2020-10-1-19-28
59. Peehl, D. M., Ding, L., Li, S., Talpaz, M., Kurhanewicz, J., Sriram, R., Roudi, R., Zhou, R., Luker, G. D., Kinahan, P. E., Chenevert, T. L., Ross, B. D., Rosen, M., Wahl, R. L., Dobrolecki, L. E., Mowery, Y. M., Manning, H. C., Ma, C., Daldrup-Link, H., … Lewis, M. T. (2023). Animal Models and Their Role in Imaging-Assisted Co-Clinical Trials. Tomography (Ann Arbor, Mich.), 9(2), 657–680. https://doi.org/10.3390/tomography9020053
60. Shukla, A., Vallamkonda, N., Maria, A., & Bandyopadhyay, T. (2020). Long-Term Neurodevelopmental Outcomes of Neonatal Chikungunya: Follow-Up of a Series of Cases Till 1 Year. Journal of Tropical Pediatrics, 67(3). https://doi.org/10.1093/tropej/fmaa053
61. Safina, A. I., & Volyanyuk, E. V. (2020). Long-term neuropsychiatric outcomes of deeply premature infants, prospects for diagnosis and correction. Rossiyskiy Vestnik Perinatologii i Pediatrii (Russian Bulletin of Perinatology and Pediatrics), 65(5), 227–231. https://doi.org/10.21508/1027-4065-2020-65-5-227-231
62. De Bie, F. R., Deprest, J., Flake, A. W., Davey, M. G., & Larson, A. C. (2020). Artificial placenta and womb technology: Past, current, and future challenges towards clinical translation. Prenatal Diagnosis, 41(1), 145–158. https://doi.org/10.1002/pd.5821
63. Werner, K. M., & Mercurio, M. R. (2021). Ethical considerations in the use of artificial womb/placenta technology. Seminars in Perinatology, 46(3), 151521. https://doi.org/10.1016/j.semperi.2021.151521

64. Acharyya, S., & Acharyya, K. (2022). A Cohort Study Comparing the Growth and Neurodevelopmental Outcome of Babies Conceived by Assisted Reproductive Technology with Those of Naturally Conceived Babies from Birth till 24 Months. Indian Journal of Pediatrics, 90(1), 16–21. https://doi.org/10.1007/s12098-021-04065-0