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Voices of experience in periviable decision-making and artificial placenta technology

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Part II

The artificial amnion and placenta technology as potential treatment for extremely premature infants

Chapter 5

Navigating the ethical landscape of the artificial placenta: a systematic review

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Prenatal diagnosis, 2025

Abstract

This systematic review aims at presenting the ethical debate on the artificial placenta (AP) by identifying, distinguishing, and organizing the different ethical arguments described in the literature. Articles were selected based on predefined inclusion criteria: discussing ethical arguments, on AP, written in English. QUAGOL methodology was used for analysis. Forty-five articles were included. We identified three themes. First, foundational-ethical issues. There is disagreement on whether the AP subject should be considered an infant or a new moral entity. While physiologically it stays a foetus, it sits outside the womb. Second, reproductive ethics issues. Few authors believed that the AP would increase reproductive choices. The majority warned that the AP could limit reproductive choices by creating pressure to use it in healthy pregnancies or as an alternative to abortion. Third, research ethics issues. Publications mostly focused on selection of the in-human trial participants. We concluded that AP ethical literature focuses mostly on the potential use of AP as an alternative to abortion or healthy pregnancies rather than on the intended use as treatment after extremely premature birth. We conclude, therefore, that the current ethical literature on AP is imbalanced: it leans more towards science fiction than actual clinical and technological reality.

Introduction

The artificial placenta (AP)[1] is being developed to improve survival and quality of life of extremely premature infants (EPIs) between 22 and 28 weeks of gestation. Currently, EPIs experience high mortality and morbidity,[1,2] with the latter being partially iatrogenic.[1,3,4] By mimicking the function of the placenta, the AP aims to preserve a physiological fetal state, and therefore prevent severe complications of extreme prematurity.[5]

Reflecting on the AP's ethical implications before implementation is necessary to integrate ethical reflection in the technology development. The ethical debate on AP is complex. It involves different stakeholders (e.g. parents, developers, clinicians, ethicists), each with their own perspectives.[6] Further, AP raises many ethical questions beyond treatment of EPIs.[7] For example, should it be offered as an alternative to abortion? Hence, we conducted a systematic argument-based review[8,9] to identify, distinguish, and organize the different ethical questions and arguments described in the AP literature. This could help experts to better understand the current debate and identify potentially overlooked issues. This, in turn, contributes to further inclusion of ethical considerations in the further development and implementation of the AP.[6]

Methods

A systematic search of Medline®, Embase®, Web of Science™, and Scopus® electronic databases was conducted on November 17th 2022, and updated on November 13th 2023. The complete search strings are reported in *Appendix 1*. A librarian from the Leiden University Medical Centre assisted with the development of the search strings. We used the "snowball method" and citation tracking on every included article to identify additional relevant publications.[10]

Eligible articles were selected based on predefined inclusion/exclusion criteria (*Table 1*). We are aware that a plethora of different terms are used to identify artificial placentas or partial ectogenesis. To ensure consistency, we only included articles discussing technologies able to maintain part of the gestation outside the human womb, regardless of the term used for the technology or the process. Further, to ensure scientific rigor, we excluded articles that did not define the technology discussed or whose definition was too ambiguous to determine what technology was being discussed. Two authors (AC and ADB) independently screened titles, abstracts, and full texts. Disagreements were resolved by discussion with a third author (LDP) until consensus was reached. A PRISMA flow diagram[11] summarizes the literature search process (*Figure 1*).

1 Authors use different terms to identify this type of technology depending on whether they are referring to a specific prototype (e.g. biobag or EVE), an aspect of the technology (e.g. artificial amnion and placenta technology), or its general aim (e.g. artificial womb technology). We use the term artificial placenta as it encompasses all the different specific prototypes while differentiating it from artificial wombs able of maintaining an entire pregnancy outside the human womb.

Table 1 Inclusion and exclusion criteria for selection of articles

	Included	Excluded
Types of publication	· Published articles.	· Dissertations, books, book chapters, guidelines, ethics policies and codes, because these publications cannot be systematically searched, which will affect the reproducibility.
Topic	· Publications focusing on the artificial placenta as a technology that mimics the placenta and amniotic sac, and that partially maintain the foetus outside the human womb. · Publications focusing on artificial placenta specifically for infants born at 22-25 weeks of gestation (domain 3 in De Bie et al. 2023). · Publications focusing on partial ectogenesis. · Publications containing original ethical arguments. Articles that use existing concepts and theories to develop an original normative stance, or a new theory or concept are included. Similarly, articles that develop new concepts or theories to support an existing position are included.	· Publications on artificial wombs as a technology able to maintain the whole gestation outside the human womb. · Publications focusing on full ectogenesis; e.g. Smajdor 2007.[68] · Publications that do not clarify whether they refer to artificial placentas or artificial wombs as previously defined; e.g. Räsänen 2017.[69] These two technologies are different and different ethical arguments might apply. Our aim is to review arguments related to the artificial placenta technology specifically. Including articles that do not specify what technology they are referring to will introduce vagueness and bias. · Publication focusing on IVF as partial ectogenesis. · Publications describing clinical trials or the technical functioning of the artificial placenta without ethical reflection. · Publications describing what legal provisions would regulate AP, how, and how these provisions would change without ethical reflection on these changes and/or without taking a position on which changes are advisable. · Reviews that present a mere overview of existing ethical arguments without elaborating a normative stance, because (1) no new original content is presented, and (2) reviewed articles are already included with the risk of duplicating results and over emphasising certain positions.
Language	· Publication language is English.	· Non-English language publications.
Date	· Screening of articles was not limited by publication date; entire date range was included in searches of Medline®, Embase™, Web of Science™, Scopus® databases.	· NA

We relied on the journals' peer review process to assume that the quality of included articles was sufficient. This is acceptable as the aim of our review is descriptive not normative.[12]

Data analysis and synthesis followed the Qualitative Analysis Guide of Leuven (*Table 2*).[13,14] The analysis was conducted in an interdisciplinary research team comprising expertise in medicine (EJV, ADB), and bioethics (AC, LDP, CG).

Table 2 Data analysis and synthesis

Step[a]	Description
1. Familiarization with the publications	We repeatedly read the articles to familiarize ourselves with the material.
2. Development of individual conceptual schemes	For each article, AC developed an individual conceptual scheme summarizing the concepts and arguments emerging from the included articles. The schemes were refined based on team discussion.
3. Development of overall conceptual scheme	The individual conceptual schemes were compared to identify recurring concepts and arguments as well as relevant differences and nuances. AC merged these elements into a single overall conceptual scheme and refined the scheme after team discussion.
4. Reporting of results	We reported the results based on the overall conceptual scheme.

[a]*An interactive relationship between publications, individual schemes, and overall scheme was maintained during the whole process to avoid overlooking relevant nuances and to ensure that we preserved the original meaning of the included publications.*

Results

We identified forty-five eligible publications, whose characteristics are described in *Table 3*. Most publications were published from 2020 and originated mainly from UK, North America, and Australia. Many articles were written by the same first author. Most authors are scholars in philosophy, bioethics, or health law.

Table 3 Characteristics of included publications (N=45)

CHARACTERISTICS	# OF PUBLICATIONS
Article type	
Full article	26
Commentary	19
Year of publication	
2020-2023	38
2015-2019	7
First author's number of included publications	
Romanis E.C.	6
Colgrove N.	3
Horn C.	3
Kendal E.S.	2
Kingma E.	2
Mercurio M.R.	2
Simkulet W.	2
Verweij E.J.	2
Werner K.M.	2
Cohen G.I, Kennedy S., Nelson A., Overall C., Rodger D., Segers S., Stratman C.M, Wozniak P.S., De Proost L., Krom A., Cordeiro J.J., De Bie F.R., Esquerda M., Hine K., Holmes J., Kimberly L.L., Roesner N., Takashima K., Muhsin S.M., Kukora S.	1 (each)
Country of first author's affiliation	
USA	20
UK	14
The Netherlands	4
Australia	2
Canada, Belgium, Spain, Japan, Singapore	1 (each country)
First author's professional background[1,2]	
Philosophy, bioethics	14
Healthcare	6
Law	6
Not found	3

[1]*To determine the first author background we looked at the professional titles indicated in the papers and at the professional biography in the indicated institution website.*
[2]*Authors with multiple publications were only counted once.*

We identified three main themes: foundational-ethical issues; reproductive ethics issues; and research-ethics issues (*Figure 2*).

Foundational-ethical issues: The moral status of the AP subject

Several terms were coined to identify the AP subject, e.g. gestateling, fetonate or perinate.[15] Further, disagreements exists on the moral status of the AP subject. Some stated that the AP subject is "a foetus (physiologically) that we treat as a neonate (morally)",[15] but the main discussion is on whether the AP subject is a new moral entity or an infant.[16-19]

The AP subject is a new moral entity

Some authors claimed that the AP subject is a new moral entity.[20-27] Hence, concepts and rules that apply to foetuses or infants do not apply to AP subjects, who require ad-hoc protections.[20,21,23-27] These authors conceptualize the AP subject as a new moral entity for several reasons.

First, some authors claimed that AP subjects are not physiologically born.[20,21,23-25] They explained that birth implies a change of location from the womb to the external environment *and* a change of physiology, e.g. the lungs inflate. The AP subject is only geographically born because it did not change physiology.[20,23-25]

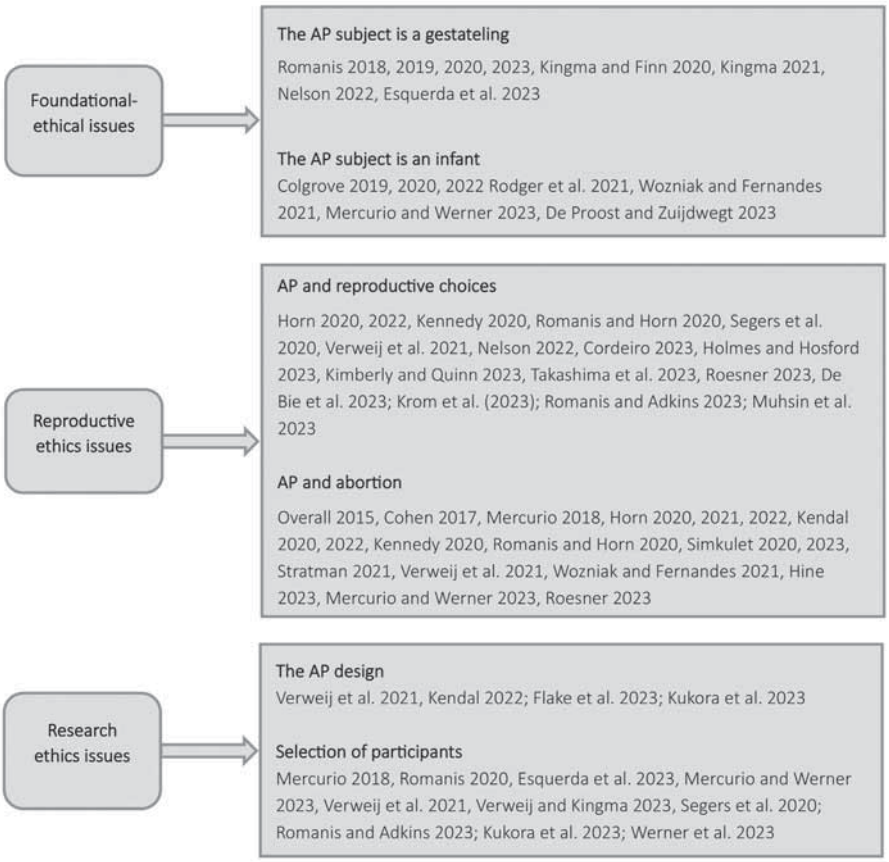

Figure 2 Distribution of included publications based on the identified themes and sub-themes.

Second, according to Romanis, AP subjects, which she has termed "gestatelings", have no capacity to live independently.[23-25] Romanis explained that the physiological change grants infants independent capacity for life, whereas AP subjects did not physiologically change and, consequently, are still completely dependent on the AP.[23-25]

Third, according to Romanis, while the preterm infant has direct contact with the parents and the external environment, the AP subject is completely isolated from the external environment. For Romanis, "this isolation will influence the perception of and, on occasion, the feeling attached to each entity".[23;] Implying, in this way, that AP subjects will be perceived and treated differently than infants.[23-25]

The AP subject is an infant

Others claimed that the AP subject is an infant[15-18,28-30] for several reasons.
First, they believe that the AP subject is born because,[16-18,28,29] based on the conventional definition of birth, "being born" means being completely expelled from the womb, and showing evidence of life, such as breathing or having a heartbeat.[16-18,28] The AP subject is completely expelled from the womb and shows evidence of life as it has a heartbeat, thus it is born.

Second, they maintained that the AP subject has some capacity to live independently.[29] For example, the subject must be sufficiently developed to survive the surgery required for the transfer in the AP. Further, Colgrove elicited that the conventional definition of birth does not require independency as it refers to evidence for life "however supported".[16,17] Finally, Wozniak & Fernandez reminded that no infant has independent capacity for life because they all need care to survive, and, therefore, this is not a distinctive characteristic of AP subjects.[29]

Third, they argued that EPIs are also more similar to foetuses than infants, but parents and clinicians treat them as children.[15,30] Two publications conceded that Romanis' term gestateling could identify an infant treated with AP, but this does not imply that the AP subject is not an infant in the same way in which EPIs are specific infants born prematurely, but they are infants nonetheless.[16,30] Conversely, Mercurio warned that introducing a new term could suggest that AP subjects are not given the same level of care and compassion as other infants.[30] Therefore, these authors believed that AP subjects have the same rights and protections of infants.[16-18,28]

Reproductive ethics issues: Impact on reproductive choices

Krom et al. proposed to use the capabilities approach to obtain a comprehensive and nuanced understanding of how AP will affect the pregnant person and the infant.[31] For example, a risk of prematurity is survival with severe disability, meaning that AP needs to be incorporated in a broader system of healthcare to ensure long-term support.[31] Two specific

reproductive ethics issues were identified: how AP will affect reproductive choices, and how it will affect abortion rights in particular.

AP and reproductive choices

A first question in the literature is whether AP will increase or decrease reproductive choices. Kennedy elicited that AP might increase reproductive autonomy by increasing reproductive choices, e.g. choosing AP as an alternative to abortion. To the opposite, seven publications warned that AP might reduce reproductive autonomy.[32-38] Three publications explained that AP might increase social pressure to use it for the foetus' benefit.[36-38] Five publications warned that access to AP might be limited to traditional family units, as it already happens in some countries for IVF, or it might be too expensive.[32-36] Therefore, AP implementation should be preceded by structural interventions to prevent inequalities.[32-36]

A second question is whether pregnant people should be allowed to choose AP as an alternative delivery option even when not medically indicated. Nelson maintained that whether to choose AP is a reproductive choice. As such, access to AP should not be limited because this would be an infringement of autonomy, which could generate anxiety, distress, and delivery-related post-traumatic stress disorder.[22] Holmes and Hosford concluded that AP might be acceptable for non-medical reasons, e.g. to pursue career or education, as these will benefit the pregnant person, the child, and society.[39] To the opposite, two publications maintained that the AP medical risks are too high to justify it when non-medically indicated.[40,41] In analyzing AP acceptability based on Islamic legal maxims, Muhsin et al. concluded that using AP when not medically indicated – specifically to avoid the burdens of pregnancy, for single fathers or gay couples, and for abortion - is not consistent with Islamic precepts.[42]

A third question is whether a pregnant person should be allowed to refuse AP if medically indicated. Two publications concluded that pregnant persons should not be obliged to choose AP,[43,44] although Takashima et al. believed that they could be subjected to some sort of mild punishment like blame.[43]

AP and abortion

There are two main points discussed: if and how the AP will affect abortion rights; and whether it should be an alternative to abortion.

Will the AP affect abortion rights?

Six publications claimed that AP might lower the viability threshold, i.e. the week at which a foetus is considered capable to support life.[30,34,38,45-48] Depending on how we reinterpret viability, it might reduce or expand abortion rights because several laws use viability thresholds to determine when abortion is permissible. Cohen theorized that, if AP will lower the viability threshold, jurisdictions that only allow abortion up to viability could lower the abortion threshold. However, countries that prohibit abortion could allow AP instead of a total ban on abortion.[45] Kendal answered that viability is not an intrinsic characteristic of

the foetus, but it depends on external factors (e.g. resources available in the hospital), and indeed, it varies greatly worldwide. As AP is not the only technology challenging viability, it must not affect abortion laws.[48]

Should AP be an alternative to abortion?

Two authors explained that historically the abortion debate focused on whether there is a right to terminate the pregnancy, regardless of whether the foetus could survive, as survival was impossible. As AP will allow to terminate a pregnancy without terminating the foetus, they elicited that the abortion debate is now focusing on whether AP should be a compulsory alternative to abortion.[45,49]

Simkulet and Stratman claimed that, assuming that AP is safe and not riskier than abortion, AP should substitute abortion because it allows a cessation of pregnancy without killing the foetus.[49,50] Stratman bases this statement on two assumptions. First, parents do not own a child or a foetus, so they do not have right to its destruction, and even if they do own it, this does not make its destruction moral. Second, the harms of having a biologically related human against their will are not grave enough to warrant the death of the foetus.

To the opposite, others claimed that AP is *not* an alternative to abortion, and that considering it as such is ethically problematic.[33,34,46,48,51-54] On a practical level, they said, most abortions occur in the first trimester and are minimally invasive, whereas AP can only be effective from 22/23 weeks and requires a C-section.[33,34] Enforcing AP instead of abortion means obliging pregnant people to stay pregnant longer than they want, and to undergo an invasive surgery instead of the safer and less invasive option, and to become biological parents against their wish, which is an infringement of bodily autonomy.[33,36,48,52,54] Two publications added that substituting abortion with AP will increase the infants in the adoption system.[52,53] Further, conceptually these authors reject that abortion is a moral issue to be solved.[32-34,46,48] They explained that abortion is a basic form of reproductive care and, as such, abortion and AP can coexist: a pregnant person should be allowed to decide whether to continue the pregnancy, have an abortion, or choose AP. Finally, Horn warned that, as AP will likely be an expensive technology, making it compulsory will penalize poorer people, because they might be punished for not using a technology they cannot afford.[32,33] She explained that this is not farfetched as in the US women can already be punished for behaviors that place the foetus at risk.[32,33]

Research-ethics issues: Development and trial

Mercurio and Romanis stated that the safety and efficacy of AP should be assessed through clinically and ethically solid trials that prioritize participants' safety.[25,41,47] Two publications explained that different AP prototypes work differently.[55,56] Hence, while some ethical considerations apply to all prototypes, e.g. the importance of minimizing risks, other are prototype-dependent, e.g. considering the C-section risks because not all prototypes require a C-section. Therefore, the risks of each prototype should be assessed individually.[56]

Two main aspects of the development and trial are considered: The AP design, and the selection of participants.

The AP design

Included publications explained that it is important to consider the AP design as its aesthetic can contribute to how it is perceived and used.[38,51] For example, Kendal explained that much of the distrust toward AP can be explained by the fact that we already have a long history of sci-fi imaginary (e.g. The Matrix) that included artificial wombs sustaining entire gestations in pods as a crucial negative element of their dystopias. People tend to associate the two, which lead to negative attitudes toward AP.[57] Because of that, Verweij et al. emphasized the importance of involving parents and caregivers in the design process and to consider their input on design choices. For example, if we know that parents prefer to always see their foetus, the AP could be made transparent.[38,51]

Selection of participants

Seven publications focused on which foetuses should be selected for the first in-human trial based on potential risks (e.g. psychosocial development risks) and benefits (e.g. higher chances of survival).[25,27,30,47,58] According to them, EPIs of 22-23 weeks have a high mortality rate with current care and, therefore, the experimental AP treatment could be justifiable as compassionate care. EPIs of 24-25 weeks already have better survival rates, meaning that AP treatment might be even more beneficial to them, but it could also mean that the experimental treatment would be less justifiable. Four publications took an explicit stance claiming that it is acceptable to include in the trial infants so premature that without AP death or severe disability is the likely outcome.[30,55,58,59]

Included publications also focused on which parents should be involved in the clinical trial and how to counsel them to allow them to make a proper informed decision on whether to participate in the AP trial, to choose standard of treatment (i.e., intensive care), or, in countries that allow it, to choose palliative care.[37,38,44,47,58] First, AP should only be proposed to pregnant persons for whom the caesarean is already indicated and for whom it would be better not to be pregnant.[38] Second, the pregnant person (and if present the partner) should receive appropriate counselling. They should receive all necessary information related to the AP trial and the possible alternatives (i.e. intensive or palliative care), including the fact that the pregnant person will also be a research subject [38,44,47,55,58] Further, counsellors must avoid therapeutic misconception, i.e., the mistaken belief that the experimental treatment will be curative. [38,58] Counselling also needs to be nondirective[37,38] to avoid undermining pregnant people's safety for the sake of the foetus.[37,55] To this regard, Romanis and Adkins advocated for a non-fetal-centric counselling.[44] They explained that much of the literature only focuses on fetal risks, whereas AP might affect the pregnant person beyond the physical risks of the C-section, such as generating feelings of pregnancy loss and failure. Counsellors should communicate and minimize these risks, for example, by providing psychological support.[44] Finally, parents should have enough time to decide.[38,58]

Discussion

Based on our analysis of the forty-five eligible publications, we identified two main gaps in the existing literature.

Lack of consistent terminology

There is no agreement on the correct terminology for the AP subject.[15] While new terms (e.g. gestateling, fetonate) are proposed,[7] some articles refer to the AP subject as "infant".[16] Similarly, we found different terms identifying the technology itself. We chose the term artificial placenta but others refer to it as artificial womb. [60] Although all included articles discussing the moral status of the AP subject well explain and justify their terminological choices, the existence of so many different terms might be confusing. This terminological confusion is aggravated by the fact that the technology is often too ambiguously described conflating the AP with full ectogenesis. Conflating the two misrepresents how the AP functions, its applications, and the ethical issues it raises.[41,61,62] Using terms like 'artificial wombs' may suggest that APs can substitute pregnancy and create public hostility towards it. This could hinder the implementation of a potentially better treatment for EPIs.[41,57] This misrepresentation is probably most evident in the abortion debate. Those in favor of substituting abortion with AP often imply that AP can be used at any point in pregnancy,[60] or do not appropriately consider the possibilities and limitations of existing APs.[49,50] Current APs are unable to maintain EPIs of less than 22 weeks and in many cases a C-section will be necessary. Advocating for substituting abortion with AP in the current technological context would oblige pregnant persons to be pregnant longer than they wanted and to undergo a major surgery instead of opting for earlier safer and less invasive abortion. On that, we agree with Romanis and Horn that in discussing proposals that would affect people's autonomy and wellbeing so heavily, we need to either clearly state that we are speculating about a non-existing technology or refer to the description of existing technologies.[34] To clarify, we are not advocating for the end of speculative thinking. We are advocating for a more consistent and responsible use of language. One that correctly identifies the technology at hand and the related ethical issues.

Lack of ethical reflection on issues related to the first in-human trial and implementation

The AP is a clinical device being developed to treat EPIs, so the first in-human trial will inevitably involve vulnerable EPIs.[25] Furthermore, the in-human trial and implementation of the AP for EPIs are expected to occur in quick succession,[63,64] which makes the ethical reflection on the trial and implementation necessary and urgent. Despite that, only twelve out of forty-five included articles discussed research ethics and clinical-ethics issues related specifically to EPIs.

Most included articles discussed the moral status of the subject or the possibility of using the AP as an alternative to abortion or as an alternative delivery method, which will only

occur in a distant future, if it will ever occur. The AP ethical issues for EPIs and their families are currently understudied. We believe this is ethically problematic as EPIs and pregnant persons will be the ones bearing the risks of the first AP trial and implementation. We do not exclude that the AP could be used beyond its original scope, nor do we undermine the importance of discussing potential future applications of AP and their impact on pregnant people. What we found problematic is the current imbalance between the articles discussing these future scenarios and the articles discussing short-terms applications of AP. Hence, we advocate for more research on the ethical issues related to the trial and implementation of AP.

A related issue is the lack of empirical studies, particularly of studies involving prospective AP users, such as neonatal professionals or EPIs' parents. We found only two empirical studies on the topic,[65,66] of which only one involved prospective users, i.e. neonatologists.[65] The other involved reproductive rights advocates and discussed assisted reproductive technologies in general. We advocate for integrating more empirical studies on users' perspective in the development of the technology. Importantly, researchers should make an active effort to include the views of minorities, such as people with disabilities or people of colour, in their studies to ensure a comprehensive but nuanced understanding of all stakeholders' perspectives.[31] Stakeholder engagement could help produce a technology that truly answers the needs of the users. This could also help us identify potentially overlooked but important ethical issues. For example, determining the subject's moral status and name is important in the legal and academic sphere. Ambiguity in terminology and definitions might hinder communication and affect AP acceptability. Further, different moral entities have different rights and, therefore, whether the AP subject is a foetus, an infant, or a new moral entity does matter. However, scientific terms are not always appropriate in the clinical context. For example, if parents consider the AP subject "their child" clinicians should call it a child rather than gestateling, fetonate, or AP subject, even if these terms might be scientifically more correct.[15] Beyond terminological differences, this also implies that parents might perceive different ethical issues than clinicians and academics. Hence, it is important to engage with parents and other stakeholders to obtain a comprehensive understanding of the ethical issues raised by AP and to address all the relevant issues. To achieve that, though, it is important that researchers address potential obstacles to participation, especially for participants from minority groups, for example by covering the costs of transportation or by accommodating participants' requests in terms of timing and modality of data collection.[67]

Strengths and limitations

To our knowledge, this is the first review that systematically presents ethical arguments related to the AP specifically rather than discussing it along with other artificial womb or reproductive technologies. This allowed us to isolate arguments specific to the AP and to give an in-depth and nuanced overview of this debate. However, due to the narrow focus of the review and the ambiguity regarding terminology and technology description that

still permeates the ethical literature on artificial womb technologies, some articles and arguments were ineligible.

All but two publications originated from high-income western countries. Several articles had the same first authors. Six first authors are healthcare professionals; all other articles are written by scholars in ethics or law. This might limit the generalizability of results as ethical arguments are at least partially culturally sensitive. This could also indicate that despite the considerable number of included articles, the AP debate is still in its infancy and that there is not much interaction between scholars, clinicians, and developers.

Conclusions

Our review shows that the AP ethical literature is imbalanced. Most included publications focused on the possible use of AP as an alternative to abortion or healthy pregnancy instead of for the treatment of EPIs – for which it is in fact being developed and will be used. Consequently, reflection on the ethical implications of the AP for treatment of EPIs and pregnant persons is urgently needed as they will be the ones bearing the risks of the AP first.

References

1. Myrhaug HT, Brurberg KG, Hov L, Markestad T. Survival and Impairment of Extremely Premature Infants: A Meta-analysis. *Pediatrics.* 2019;143(2).
2. Backes CH, Söderström F, Ågren J, et al. Outcomes following a comprehensive versus a selective approach for infants born at 22 weeks of gestation. *J Perinatol.* 2019;39(1):39-47.
3. Marlow N, Ni Y, Lancaster R, et al. No change in neurodevelopment at 11 years after extremely preterm birth. *Arch Dis Child Fetal Neonatal Ed.* 2021;106(4):418-424.
4. Pascal A, Naulaers G, Ortibus E, et al. Neurodevelopmental outcomes of very preterm and very-low-birthweight infants in a population-based clinical cohort with a definite perinatal treatment policy. *Eur J Paediatr Neurol.* 2020;28:133-141.
5. Bird SD. Artificial placenta: Analysis of recent progress. *European Journal of Obstetrics & Gynecology and Reproductive Biology.* 2017;208:61-70.
6. Jongsma KR, Bredenoord AL. Ethics parallel research: an approach for (early) ethical guidance of biomedical innovation. *BMC Medical Ethics.* 2020;21(1):81.
7. De Bie FR, Kim SD, Bose SK, et al. Ethics Considerations Regarding Artificial Womb Technology for the Fetonate. *American Journal of Bioethics.* 2023;23(5):67-78.
8. McCullough LB, Coverdale JH, Chervenak FA. Constructing a systematic review for argument-based clinical ethics literature: the example of concealed medications. *J Med Philos.* 2007;32(1):65-76.
9. Mertz M, Kahrass H, Strech D. Current state of ethics literature synthesis: a systematic review of reviews. *BMC Medicine.* 2016;14(152).
10. Greenhalgh T, Peacock R. Effectiveness and efficiency of search methods in systematic reviews of complex evidence: audit of primary sources. *BMJ.* 2005;331(7524):1064.
11. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. *BMJ.* 2009;339.
12. Mertz M. How to tackle the conundrum of quality appraisal in systematic reviews of normative literature/information? Analysing the problems of three possible strategies (translation of a German paper). *BMC Medical Ethics.* 2019;20(1):81.
13. Dierckx de Casterle B, Gastmans C, Bryon E, Denier Y. QUAGOL: a guide for qualitative data analysis. *Int J Nurs Stud.* 2012;49(3):360-371.
14. Dierckx de Casterlé B, De Vliegher K, Gastmans C, Mertens E. Complex Qualitative Data Analysis: Lessons Learned From the Experiences With the Qualitative Analysis Guide of Leuven. *Qualitative Health Research.* 2020;31(6):1083-1093.
15. De Proost L, Zuijdwegt G. Lost in Gestation: On Fetonates, Perinates, and Gestatelings. *Am J Bioeth.* 2023;23(5):108-110.
16. Colgrove N. Subjects of ectogenesis: are 'gestatelings' foetuses, newborns or neither? *Journal of medical ethics.* 2019;45(11):723-726.
17. Colgrove N. Artificial wombs, birth and 'birth': a response to Romanis. *Journal of medical ethics.* 2020;46(8):554-556.
18. Colgrove N. In defence of newborns: a response to Kingma. *Journal of Medical Ethics.* 2022;48(8):551-553.
19. Werner KM, Mercurio MR. Ethical considerations in the use of artificial womb/placenta technology. *Seminars in Perinatology.* 2022;46(3).
20. Kingma E, Finn S. Neonatal incubator or artificial womb? Distinguishing ectogestation and ectogenesis using the metaphysics of pregnancy. *Bioethics.* 2020;34(4):354-363.
21. Kingma E. In defence of gestatelings: response to Colgrove. *Journal of Medical Ethics.* 2021;47(5):355-356.
22. Nelson A. Should Delivery by Partial Ectogenesis Be Available on Request of the Pregnant Person? *International Journal of Feminist Approaches to Bioethics.* 2022;15(1):1-26.

23. Romanis EC. Artificial womb technology and the frontiers of human reproduction: conceptual differences and potential implications. *Journal of Medical Ethics.* 2018;44(11):751-755.
24. Romanis EC. Artificial womb technology and the significance of birth: Why gestatelings are not newborns (or foetuses). *Journal of Medical Ethics.* 2019;45(11):727-729.
25. Romanis EC. Artificial womb technology and clinical translation: Innovative treatment or medical research? *Bioethics.* 2020;34(4):392-402.
26. Romanis EC. The Ethical and Legal Status of 'Fetonates' Or 'Gestatelings'. *Am J Bioeth.* 2023;23(5):90-92.
27. Esquerda M, Lorenzo D, Bofarull M. Beyond the Domains: What Would be the Fundamental Ethical Questions in the Development of the Artificial Womb. *American Journal of Bioethics.* 2023;23(5):125-127.
28. Rodger D, Colgrove N, Blackshaw BP. Gestaticide: killing the subject of the artificial womb. *Journal of Medical Ethics.* 2021;47(12):6.
29. Wozniak PS, Fernandes AK. Conventional revolution: the ethical implications of the natural progress of neonatal intensive care to artificial wombs. *Journal of Medical Ethics.* 2021;47(12):5.
30. Mercurio MR, Werner KM. Thinking Inside the Bag: Patient Selection, Framing the Ethical Discourse, and the Importance of Terminology in Artificial Womb Technology. *American Journal of Bioethics.* 2023;23(5):79-82.
31. Krom A, de Boer A, Geurtzen R, de Vries MC. Capabilities and Stakeholders - Two Ways of Enriching the Ethical Debate on Artificial Womb Technology. *American Journal of Bioethics.* 2023;23(5):110-113.
32. Horn C. Ectogenesis, inequality, and coercion: a reproductive justice-informed analysis of the impact of artificial wombs. *BioSocieties.* 2022.
33. Horn C. Ectogenesis is for Feminists. Reclaiming Artificial Wombs from Antiabortion Discourse *Catalyst.* 2020;6(1).
34. Romanis EC, Horn C. Artificial Wombs and the Ectogenesis Conversation: A Misplaced Focus? Technology, Abortion, and Reproductive Freedom. *International Journal of Feminist Approaches to Bioethics.* 2020;13(2):174-194.
35. Kimberly LL, Quinn GP. Toward a Broader Conception of Equity in Artificial Womb Technology. *American Journal of Bioethics.* 2023;23(5):114-116.
36. Roesner N. Beyond a Medicalized View of Reproduction: Recentering Pregnant People in the Ethics of Ectogenesis. *American Journal of Bioethics.* 2023;23(5):102-104.
37. Segers S, Pennings G, Mertes H. The ethics of ectogenesis-aided foetal treatment. *Bioethics.* 2020;34(4):364-370.
38. Verweij EJ, De Proost L, van Laar JOEH, et al. Ethical Development of Artificial Amniotic Sac and Placenta Technology: A Roadmap. *Frontiers in Pediatrics.* 2021;9.
39. Holmes J, Hosford L. Artificial Womb Technology, Catholic Health Care, and Social Justice. *American Journal of Bioethics.* 2023;23(5):123-125.
40. Cordeiro JJ. On the Permissibility of Elective Ectogestation. *American Journal of Bioethics.* 2023;23(5):116-118.
41. De Bie FR, Flake AW, Feudtner C. Life Support System for the Fetonate and the Ethics of Speculation. *Jama Pediatrics.* 2023.
42. Muhsin SM, Chin AHB, Padela AI. An Ethico-Legal Analysis of Artificial Womb Technology and Extracorporeal Gestation Based on Islamic Legal Maxims. *New Bioeth.* 2023:1-13.
43. Takashima K, Ibuki T, Yamamoto K. Is the Mother's Decision to Opt for Artificial Womb Technology Always "Supererogatory"? *American Journal of Bioethics.* 2023;23(5):119-121.
44. Romanis EC, Adkins V. Artificial placentas, pregnancy loss and loss-sensitive care. *J Med Ethics.* 2023.
45. Cohen IG. Artificial Wombs and Abortion Rights. *The Hastings Center report.* 2017;47(4):inside back cover.
46. Horn C. Abortion Rights after Artificial Wombs: Why Decriminalisation is Needed Ahead of Ectogenesis. *Medical law review.* 2021;29(1):80-105.
47. Mercurio MR. The EXTEND system for extrauterine support of extremely premature neonates: opportunity and caution. *Pediatric Research.* 2018;84(6):795-796.

48. Kendal E. Pregnant people, inseminators and tissues of human origin: how ectogenesis challenges the concept of abortion. *Monash bioethics review.* 2020;38(2):197-204.
49. Stratman CM. Ectogestation and the Problem of Abortion. *Philosophy and Technology.* 2021;34(4):683-700.
50. Simkulet W. Abortion and Ectogenesis: Moral Compromise. *Journal of Medical Ethics.* 2020;46(2):93-98.
51. Kendal ES. Form, Function, Perception, and Reception: Visual Bioethics and the Artificial Womb. *Yale Journal of Biology and Medicine.* 2022;95(3):371-377.
52. Overall C. Rethinking Abortion, Ectogenesis, and Fetal Death. *Journal of Social Philosophy.* 2015;46(1):126-140.
53. Kennedy S. Willing mothers: ectogenesis and the role of gestational motherhood. *Journal of medical ethics.* 2020;46(5):320-327.
54. Hine K. Partial ectogestation and the right to choose the method by which one ends one's pregnancy. *Journal of Social Philosophy.* 2023.
55. Kukora SK, Mychaliska GB, Weiss EM. Ethical challenges in first-in-human trials of the artificial placenta and artificial womb: not all technologies are created equally, ethically. *J Perinatol.* 2023;43(11):1337-1342.
56. Flake AW, De Bie FR, Munson DA, Feudtner C. The artificial placenta and EXTEND technologies: one of these things is not like the other. *J Perinatol.* 2023;43(11):1343-1348.
57. Kendal E. Form, Function, Perception, and Reception: Visual Bioethics and the Artificial Womb. *Yale Journal of Biology and Medicine.* 2022;95(3):371-377.
58. Verweij EJ, Kingma E. Artificial Placenta - Imminent Ethical Considerations for Research Trials and Clinical Translation. *American Journal of Bioethics.* 2023;23(5):85-87.
59. Werner KM, Baker AC, Mercurio MR. Unique ethical considerations of the artificial womb and placenta: the threshold for patient eligibility in clinical trials. In: *J Perinatol.* Vol 43. United States2023:1335-1336.
60. Kaczor C. Could artificial wombs end the abortion debate? *The national Catholic bioethics quarterly.* 2005;5(2):283-301.
61. Usuda H, Fee EL, Takahashi T, et al. The artificial placenta: sci-fi or reality? *Revista Medica Clinica Las Condes.* 2021;32(6):699-706.
62. Brown BP, Watson K. No Substitute: The False Promise of Artificial Womb Technology as an Alternative to Abortion. *American Journal of Bioethics.* 2023;23(5):87-89.
63. Zimmer K. Artificial wombs are science fiction. But artificial placentas are on the horizon. *Ieee Spectrum.* 2021;58(4):22-29.
64. Kozlov M. Human trials of artificial wombs could start soon. Here's what you need to know. 2023;7979(621):458-460.
65. Di Stefano L, Mills C, Watkins A, Wilkinson D. Ectogestation ethics: The implications of artificially extending gestation for viability, newborn resuscitation and abortion. *Bioethics.* 2020;34(4):371-384.
66. Romanis EC. Equality-enhancing potential of novel forms of assisted gestation: Perspectives of reproductive rights advocates. *Bioethics.* 2023.
67. Chescheir NC, D'Alton M. Evidence-based medicine and fetal treatment: How to get involved. *Obstetrics and Gynecology.* 2005;106(3):610-613.
68. Smajdor A. The moral imperative for ectogenesis. *Cambridge Quarterly of Healthcare Ethics.* 2007;16(3):336-345.
69. Räsänen J. Ectogenesis, abortion and a right to the death of the foetus. *Bioethics.* 2017;31(9):697-702.

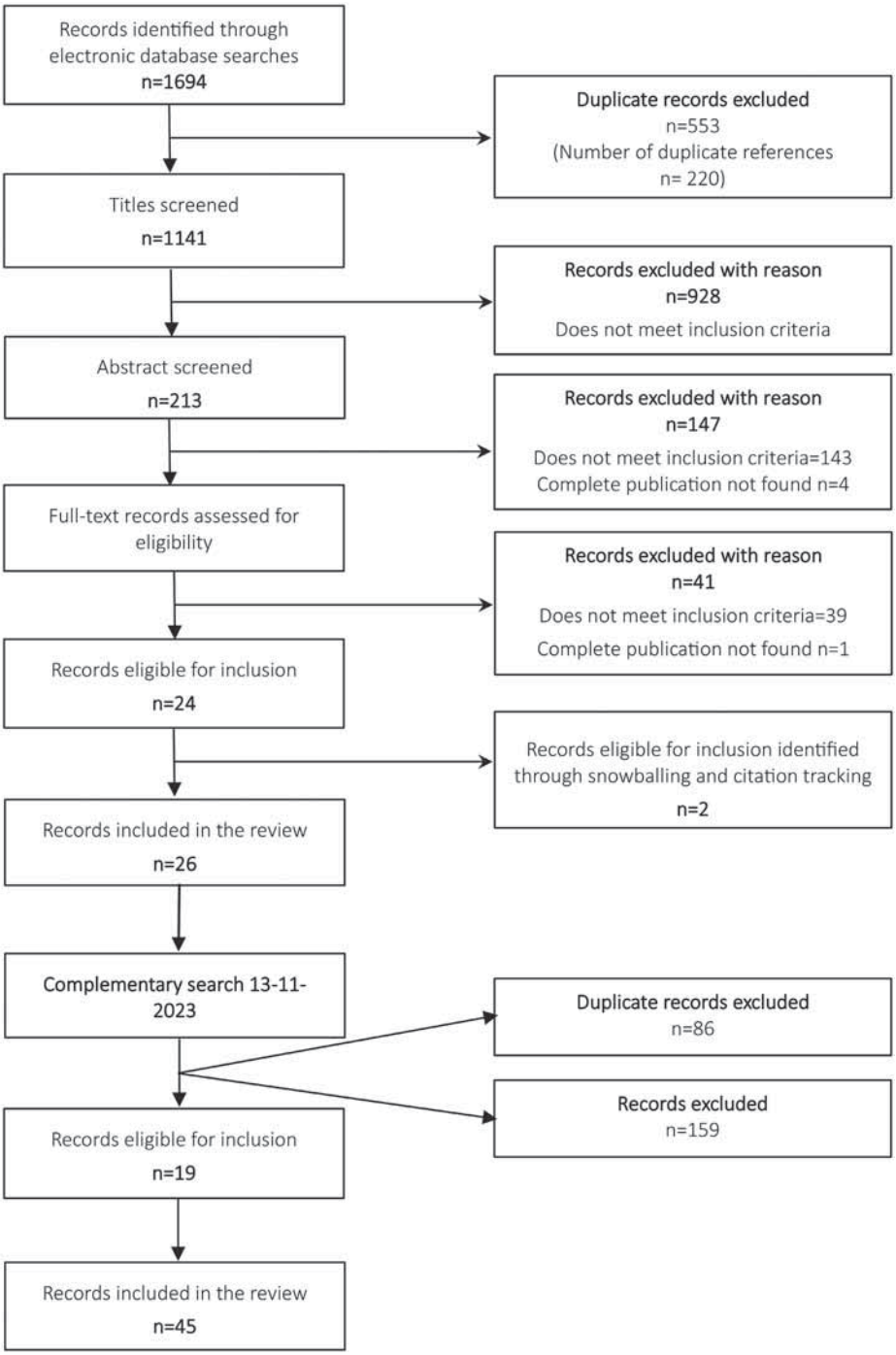

Figure 1 Process of electronic literature search for identifying and selecting articles. Flowchart is organised according to PRISMA guidelines outlined in Liberati et al.

Appendix 1 search strategy

Database	Group 1 Technology	Group 2 Ethics	Results first search (17-11-2022)	Results updated search (13-11-2023)
Medline®	artificial placenta OR artificial womb OR partial ectogenesis OR full ectogenesis OR ectogenesis OR ectogestation OR artificial womb technology OR artificial womb technologies OR artificial utero OR full ectogestation OR partial ectogestation OR biobag OR ex vivo uterine therapy OR extracorporeal life support OR extracorporeal membrane	"Ethics"[Mesh] OR "Philosophy"[Mesh] OR ethic* OR philosophy OR bioethic*[tiab] OR philosophical[tiab] OR moral[tiab] OR morals[tiab]	n=868	n=113
Embase™	'artificial placenta':ti,ab,kw OR 'artificial womb':ti,ab,kw OR 'partial ectogenesis':ti,ab,kw OR 'full ectogenesis':ti,ab,kw OR ectogenesis:ti,ab,kw OR ectogestation:ti,ab,kw OR 'artificial womb technology':ti,ab,kw OR 'artificial womb technologies':ti,ab,kw OR 'artificial utero':ti,ab,kw OR 'full ectogestation':ti,ab,kw OR 'partial ectogestation':ti,ab,kw OR biobag:ti,ab,kw OR 'ex vivo uterine therapy':ti,ab,kw OR 'extracorporeal life support':ti,ab,kw OR 'extracorporeal membrane':ti,ab,kw	ethics:ti,ab,kw OR ethical:ti,ab,kw OR philosophy:ti,ab,kw OR philosophical:ti,ab,kw OR bioethics:ti,ab,kw OR bioethical:ti,ab,kw OR moral:ti,ab,kw OR morals:ti,ab,kw	n=392	n=81
Web of Science™	All field: artificial placenta OR artificial womb OR partial ectogenesis OR full ectogenesis OR ectogenesis OR ectogestation OR artificial womb technology OR artificial womb technologies OR artificial utero OR full ectogestation OR partial ectogestation OR biobag OR ex vivo uterine therapy OR extracorporeal life support OR extracorporeal membrane	All fields: ethics OR ethical OR philosophy OR philosophical OR bioethics OR bioethical OR moral OR morals	n=396	n=64
Scopus®	TITLE-ABS-KEY: artificial AND placenta OR artificial AND womb OR partial AND ectogenesis OR full AND ectogenesis OR ectogenesis OR biobag	TITLE-ABS-KEY: ethics OR ethical OR moral OR morals OR philosophy OR philosophical OR bioethics OR bioethical	n=38	n=6