May 21, 2025

Risks in Uterus Transplantation: Scoping Review Protocol

Revista Brasileira de Ginecologia e Obstetrícia

DOI
https://dx.doi.org/10.17504/protocols.io.n92ldnxnxv5b/v1

Sibele Maria Schuantes-Paim[1], Dani Ejzenberg[2], Beatriz Souza Braga[3], Gabriela Mininel de Medeiros[4], Anne Caroline Neves Geraldo[3], Bartira de Aguiar Roza[3], Edmund Chada Baracat[2], Janine Schirmer[3]

[1]Paulista School of Nursing;
[2]Gynecology Division, Hospital das Clinicas, Faculdade de Medicina, Universidade de São Paulo (USP), São Paulo, SP, Brazil;
[3]Federal University of São Paulo (UNIFESP), Paulista School of Nursing, São Paulo, SP, Brazil;
[4]Federal University of São Paulo (UNIFESP), Paulista School of Medicine, São Paulo, SP, Brazil

Sibele Maria Schuantes-Paim
Universidade Federal de São Paulo

OPEN ACCESS

DOI: https://dx.doi.org/10.17504/protocols.io.n92ldnxnxv5b/v1

External link: https://doi.org/10.61622/rbgo/2026rbgo14

Protocol Citation: Sibele Maria Schuantes-Paim, Dani Ejzenberg, Beatriz Souza Braga, Gabriela Mininel de Medeiros, Anne Caroline Neves Geraldo, Bartira de Aguiar Roza, Edmund Chada Baracat, Janine Schirmer 2025. Risks in Uterus Transplantation: Scoping Review Protocol. **protocols.io** **https://dx.doi.org/10.17504/protocols.io.n92ldnxnxv5b/v1**

Manuscript citation:
Schuantes-Paim SM, Ejzenberg D, Mergulhão BSB, Medeiros GMd, Geraldo ACN, Ferrari VT, Roza BdA, Schirmer J (2026) Risks of uterus transplantation: a scoping review. Revista Brasileira de Ginecologia e Obstetrícia 48(). doi: **10.61622/rbgo/2026rbgo14**

Protocol status: Working
We use this protocol and it's working

Created: May 21, 2025

Last Modified: May 21, 2025

Protocol Integer ID: 218683

Keywords: Uterus Transplantation, Reproductive Techniques, Assisted, Transplantation, Organ Transplantation, Transplant Recipients, Patient Safety, risks in uterus transplantation, uterus transplantation, modality of transplantation, regarding patient safety, infertility treatment, scoping review, patient safety, scoping review protocol, transplantation, safety of the intervention, scoping review protocol background, specific patient safety tool, risk, management of risk, review protocol, methodological framework of the joanna briggs institute, safety

Funders Acknowledgements:
Coordination for the Improvement of Higher Education Personnel (Coordenação de Aperfeiçoamento de Pessoal de Nível Superior – CAPES)
Grant ID: 88887.817967/2023-00

Disclaimer

The protocol was registered with the Open Science Framework (OSF) on August 16, 2024, and is available at: https://doi.org/10.17605/OSF.IO/524UT

Abstract

Background and Aim: Uterus transplantation represents an innovation in the field of infertility treatment. However, there is a need to advance scientific knowledge regarding patient safety considering all the specificities and complexities of the treatment. Therefore, this scoping review aims to map risks related to uterus transplantation. Method: This scoping review protocol was developed based on the methodological framework of the Joanna Briggs Institute. Research questions and objectives were developed based on population, concept, and context, and search strategies were structured in three stages. Data collection will be independently conducted by four researchers and managed through the Rayyan website. Data analysis will occur through a modified version of the Failure Mode and Effects Analysis with the presentation of results through a cause-and-effect diagram. Expected results: At the end of the review, we expect to develop the first version of a specific patient safety tool for uterus transplantation. This strategy can enhance the safety of the intervention by providing a framework that supports the definition, detection, and management of risks and adverse events during all processes associated with this modality of transplantation.

Attachments

additional file 1_pr...

22KB

additional file 2_in...

17KB

file_scoping review ...

119KB

additional file_PRIS...

33KB

Guidelines

Uterus transplantation (UTx) is an infertility treatment that enables women diagnosed with absolute uterine factor infertility (AUFI) to experience pregnancy and childbirth. AUFI can arise from congenital conditions, such as Mayer-Rokitansky-Küster-Hauser syndrome (MRKH), or acquired conditions, including hysterectomy due to malignancies or severe bleeding disorders. For affected women, traditional motherhood alternatives such as adoption and gestational surrogacy might not align with personal desires, cultural beliefs, or legal contexts(1-2). The UTx process is complex and needs to be meticulously orchestrated. It involves screening both the donor and the recipient. The donor can be living or deceased, and the process of screening and follow-up is different in each case. The process is followed by two surgical procedures: the removal of the uterus from the donor and its transplantation into the recipient, followed by subsequent monitoring of both the living donor and recipient, as well as the viability of the graft. Immunosuppression therapy prevents graft rejection and ensures the long-term functionality of the transplanted uterus, with a specific protocol applied considering the future pregnancy(3-6). After the transplant, the woman begins to have a menstrual cycle; but pregnancy is only achievable through mandatory assisted reproductive techniques, specifically in vitro fertilization (IVF). IVF generates embryos using parental eggs and sperm, which are cryopreserved until the recipient is prepared for pregnancy. Successful pregnancy following UTx are considered high-risk, requiring delivery via cesarean section, with subsequent permanent removal of the transplanted uterus after childbirth(3-6). The entire UTx process involves interdisciplinary collaboration among specialties including obstetrics and gynecology, transplantation surgery, assisted human reproduction, embryology, pathology, intensive care, immunology, nursing, psychology, and social work. Despite recent advances, UTx remains experimental and is not widely implemented globally, underscoring the importance of systematically mapping risks and adverse events to enhance patient safety. Patient safety is defined as "the reduction of risk of unnecessary harm associated with healthcare to an acceptable minimum," considering current knowledge and available resources(7). Therefore, studying the risks linked to medical procedures is key to safer care. UTx offers a new option for uterine-factor infertility, validated by the first live birth from a transplanted uterus in 2014. Understanding its hazards and creating targeted tools can guide public policy and improve clinical decisions. A patient-safety tool should identify, prevent, mitigate, and manage incidents. Developing such a tool aligns with the Global Patient Safety Action Plan (2021-2030) and the Pan American Health Organization’s Strategy and Action Plan on Donation and Equitable Access to Organ, Tissue, and Cell Transplants (2019-2030)(7-10). This scoping review aims to map risks related to UTx, including complications and adverse events, to assemble the evidence needed for a dedicated patient-safety tool suited to UTx. To ensure the novelty of the present study and the methodological reference requirements a preliminary search for existing scoping and systematic reviews on the topic has been conducted, and to the best of our knowledge, no other review or protocol with the same objective has been under development (Additional file 2).

Before start

This review will be conducted as part of **Sibele Maria Schuantes-Paim’s PhD research**, funded by Brazil’s Ministry of Education through the Coordination for the Improvement of Higher Education Personnel (Coordenação de Aperfeiçoamento de Pessoal de Nível Superior – CAPES). The protocol was registered with the Open Science Framework (OSF) on August 16, 2024, and is available at: https://doi.org/10.17605/OSF.IO/524UT

Method

1 Study design

1.1 This protocol was prepared in accordance with the methodological guidance of the Joanna Briggs Institute (JBI) and will be reported following the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR).

1.2 The scoping review method was chosen for this study because it is suitable for exploring the breadth or extent of scientific production in the area, mapping available evidence, identifying knowledge gaps, and developing a conceptual framework. Additionally, the body of literature appears to be complex and heterogeneous.

1.3 Because the pathway to pregnancy after UTx obligatorily includes assisted reproductive technologies (ART) – chiefly in vitro fertilization (IVF/ICSI) – two analytical stages will be conducted within a single scoping review: Stage 1 – ART-related risks and Stage 2 – UTx-related risks. The stages will be conducted independently for search, selection, extraction and synthesis, and integrated during data interpretation and presentation to provide a comprehensive picture of risk across the full clinical pathway.

2 Inclusion criteria

2.1 Research question, objective, title, and inclusion criteria were defined based on the PCC mnemonic strategy (population, concept, and context) presented at table 1. Stage 1 – What risks, adverse events and complications have been reported in systematic reviews of IVF/ICSI pregnancies in adult women? and stage 2 – What risks, adverse events and complications have been reported in clinical studies of uterus transplantation in adult women?

Table 1: Eligibility criteria for the scoping review.

	A	B	C
	PCC element	**Stage 1 – ART (IVF/ICSI)**	**Stage 2 – UTx**
	Population	Adult women (≥18 y) who became pregnant following IVF/ICSI, irrespective of infertility diagnosis, obstetric history or pregnancy outcome.	Adult women (≥18 y) who underwent UTx, irrespective of infertility etiology, donor type, immunosuppression or pregnancy status/outcome.

	A	B	C
	Concept	Risks, adverse events, and complications(15).	Risks, adverse events, and complications(15).
	Context	Any healthcare setting worldwide (outpatient or inpatient).	Any healthcare setting worldwide (outpatient or inpatient).
	Evidence types	Secondary evidence: systematic reviews and meta analyses.	Primary evidence: clinical trials, observational studies, case series/reports.

2.2 In both parts of the study, integrative, narrative, and other non-systematic literature reviews, as well as research abstracts presented at conferences, will not be included. In vitro and animal research will also be excluded. The exclusion of specific types of literature is not strictly recommended by method(11). However, animal studies may produce outcomes that differ significantly from human studies, potentially leading to non-representative results for human subjects, which could bias our analysis. Furthermore, the decision to exclude integrative and narrative reviews is grounded in the risk of duplicating information, which could result in erroneous conclusions in the analysis.

2.3 There will be no language limitations for the articles; however, a temporal cutoff will be applied: studies from 2014. The decision to limit the time is due to changes in the definitions of biovigilance, including risks, adverse events, and complications we are seeking the most current classifications. Additionally, the first successful UTx was performed in 2014, and significant advancements have been made in the field over the past decade.

3 Search Strategy

3.1 A three-step JBI(11) search strategy will be applied separately for each stage:

1. Preliminary search (PubMed, CINAHL) to refine keywords and index terms (Additional file 1).
2. Comprehensive search in five databases (PubMed, CINAHL, Scopus, SciELO, Web of Science) using stage-specific strategies (Table 2).
3. Backward/forward citation chasing of included records.

Table 2: Databases, search strategies, and results found during the development of the scoping review protocol.

	A	B	C
	Assisted Human Reproduction		
	Database	**Search strategy**	**Results**
	PubMed	assisted reproductive techniques. Filters applied: systematic review – last 10 years	4.843
	CINAHL	assisted reproductive techniques. Filters applied: meta-analysis, meta synthesis, systematic review – last 10 years	137
	SCOPUS	assisted reproductive techniques. Filters applied: medicine, nursing, multidisciplinary, health professions, reviews – last 10 years	1.516
	SciELO	assisted reproductive techniques. Filters applied: review articles – last 10 years	97
	Web of Science	assisted reproductive techniques. Filters applied: review article – last 10 years	992
		Total	**7.585**
	Uterus transplantation		
	PubMed	(uterus transplantation) AND (outcomes) – last 10 years	463
	CINAHL	uterus transplantation OR uterus transplant AND adverse effects OR side effects OR negative effects OR complication OR risk – last 10 years	81
	SCOPUS	uterus AND transplantation AND outcomes – last 10 years	508
	SciELO	(uterus transplantation) OR (uterus transplant) – last 10 years	7

	A	B	C
	Web of Science	uterus transplantation (All Fields) AND outcomes (All Fields) OR clinical outcomes –last 10 years	215
		Total	**1.274**
		TOTAL	**8.859**

4 Data extraction

4.1 As this is a scoping review with a high number of references to be analyzed against the inclusion criteria, the study selection process will be carried out independently by four researchers. Initially, all results from each database will be exported to the Rayyan website. On this site, the researchers will read the titles and then the abstracts, seeking to select studies that provide information according to the inclusion criteria. In the event of disagreement, a virtual meeting will be scheduled with all authors. Prior to the meeting, the articles in question will be shared for review. During the meeting, the researchers will discuss each case in detail and reach a consensus to resolve the conflicts.

4.2 After this stage, the database containing all included studies will be shared, and both parts of the research will converge. Data collection will follow recommendations where the information will be collected: authorship, country of study, year of publication, year of data collection, objective, study type (method), population and sample, other sample characteristics, reported risks, adverse events or complications, signs and symptoms related, investigation process (indicators and requested tests, process of determining severity and causality), and management and follow-up strategies. Other information that the researchers deem relevant may also be recorded.

4.3 This information will be recorded on a Microsoft Excel spreadsheet.

5 Data analysis

5.1 Regarding data analysis, the results obtained in this scoping review will be presented in a cause-and-effect diagram(16) describing the entire process of UTx, from donor and recipient selection to the delivery of the baby by cesarean section, including all risks, adverse events and complications identified.

5.2 The cause-and-effect diagram is a quality tool that systematically explores and displays the factors that lead to a specific outcome, in this case shedding light on every stage of the UTx process where complications or adverse events might arise(17-18).

5.3 To populate that diagram with the findings of our scoping review, we will draw on a modified version of Failure Mode and Effects Analysis (mFMEA), a proactive method that examines each component of a system and the ways it could fail(18-20). Traditional FMEA assigns numerical scores to rank risks, but many hazards in healthcare are qualitative or subjective. For that reason, some authors have adapted the method: the mFMEA starts with human anatomy and physiology and estimates risks through rich descriptions from case reports(19-20). For this study, the mFMEA will begin with the UTx procedural phase.

5.4 Using mFMEA for our analysis therefore links directly to the creation of a patient-safety tool. By adding structure and objectivity to qualitative data, it should make it easier to determine risks and design management strategies tailored to UTx(19-20).

6 Presentation of the results

6.1 After the analyses provided by the mFMEA, the cause-and-effect diagram will be formulated, considering the risks at each stage of the UTx process. This formulation will be based on the main clinical characteristics and supported by the investigation and management actions described in the literature included and studied in the review.

Expected Results

7 We expect to recognize risks, adverse events, and complications reported in scientific studies on UTx, including those from assisted human reproduction. These findings will feed into the first version of a patient-safety tool designed specifically for UTx, offering a structured way to define, detect, and manage risks across every step of the procedure.
This tool should, in turn, strengthen both research and clinical practice. By mapping risks and standardizing responses, it can support future studies, guide policy decisions, and help integrate UTx into regular healthcare programs. The expected result will be better-informed patients and health professionals who are more prepared to recognize, manage, and mitigate UTx-related adverse events.

Protocol references

1. Brännström M, Dahm Kähler P, Greite R, Mölne J, Díaz-García C, Tullius SG. Uterus Transplantation: A Rapidly Expanding Field. Transplantation. 2018; doi: 10.1097/TP.0000000000002035.
2. Sallée C, François M, Pierre M, Pascal P, Yves A, Vincent L, Ludivine D, Tristan G. Uterine Factor Infertility, a Systematic Review. Journal of Clinical Medicine. 2022 ; doi: 10.3390/jcm11164907.
3. Brännström M, Johannesson L, Bokström H, Kvarnström N, Mölne J, Dahm-Kähler P, et al. Livebirth after uterus transplantation. The Lancet. 2015; doi: 10.1016/S0140-6736(14)61728-1 .
4. Ejzenberg D, Andraus W, Mendes LRBC, Ducatti L, Song A, Tanigawa R, et al. Livebirth after uterus transplantation from a deceased donor in a recipient with uterine infertility. The Lancet. 2018; doi: 10.1016/S0140-6736(18)31766-5.
5. Brännström M, Tullius SG, Brucker S, Dahm-Kähler P, Flyckt R, Kisu I, et al. Registry of the International Society of Uterus Transplantation: First Report. Transplantation. 2023; doi: 10.1097/TP.0000000000004286.
6. Ejzenberg D, Mendes LRBC, Haddad LBP, Baracat EC, D'Albuquerque LAC, Andraus W. Uterine transplantation: a systematic review. Clinics. 2016; doi: 10.6061/clinics/2016(11)10.
7. WHO. Conceptual Framework for the International Classification for Patient Safety. WHO/IER/PSP/2010.2. 2010. https://www.who.int/publications/i/item/WHO-IER-PSP-2010.2. Accessed 07 May 2024.
8. Sherman H, Castro G, Fletcher M; Hatlie M, Hibbert P, Jakob R, et al. Towards an International Classification for Patient Safety: the conceptual framework. Int J Qual Health Care. 2009; doi: 10.1093/intqhc/mzn054.
9. WHO. Global patient safety action plan 2021–2030: towards eliminating avoidable harm in health care. Geneva: World Health Organization. 2021. https://www.who.int/publications/i/item/9789240032705. Accessed 07 May 2024.
10. WHO. Strategy and Plan of Action on Donation and Equitable Access to Organ, Tissue, and Cell Transplants 2019-2030. Pan American Health Organization (PAHO). 2019. https://iris.paho.org/handle/10665.2/51392. Accessed 07 May 2024.
11. Peters MDJ, Godfrey C, McInerney P, Munn Z, Tricco AC, Khalil, H. Chapter 11: Scoping Reviews (2020 version). In: Aromataris E, Munn Z, editors. JBI Manual for Evidence Synthesis. JBI; 2020. Doi: 10.46658/JBIMES-20-12.
12. Tricco AC, Lillie E, Zarin W, O'Brien K, Colquhoun H, Kastner M, et al. A scoping review on the conduct and reporting of scoping reviews. BMC Med Res Methodol. 2016; doi: 10.1186/s12874-016-0116-4.
13. Peters MD, Godfrey CM, Khalil H, McInerney P, Parker D, Soares CB. Guidance for conducting systematic scoping reviews. Int J Evid Based Healthc. 2015; doi: 10.1097/XEB.0000000000000050.
14. Brazilian Health Regulatory Agency (Anvisa). Manual of biovigilance for human cells, tissues, and organs. https://www.gov.br/anvisa/pt-br/assuntos/fiscalizacao-e-monitoramento/biovigilancia/arquivos/Manualbio_26_12_23_Versofinal.pdf. Accessed 07 May 2024.
15. Pollock D, Peters MDJ, Khalil H, McInerney P, Alexander L, Tricco AC, et al. Recommendations for the extraction, analysis, and presentation of results in scoping reviews. JBI Evid Synth. 2023; doi: 10.11124/JBIES-22-00123.
16. Ishikawa, K. Introduction to Quality Control. 3rd ed. Tokyo: Corporation; 1990. 17. Harel Z, Silver SA, McQuillan RF, Weizman AV, Thomas A, Chertow GM, et al. How to Diagnose Solutions to a Quality-of-Care Problem. Clin J Am Soc Nephrol. 2016; doi: 10.2215/CJN.11481015.
18. Wong KC. How to apply clinical cases and medical literature in the framework of a modified "failure mode and effects analysis" as a clinical reasoning tool--an illustration using the human biliary system. J Med Case

Rep. 2016; doi: 10.1186/s13256-016-0850-6.
19. El-Awady SMM. Overview of Failure Mode and Effects Analysis (FMEA): A Patient Safety Tool. Glob J Qual Saf Healthc. 2023; doi: 10.36401/JQSH-23-X2.
20. Wong, K.C. Using an Ishikawa diagram as a tool to assist memory and retrieval of relevant medical cases from the medical literature. J Med Case Reports. 2022; doi: 10.1186/1752-1947-5-120.

Acknowledgements

Wellington Andraus, José Maria Soares Júnior, Luiz Augusto Carneiro D'Albuquerque, Pedro Augusto Araújo Monteleone from Gynecology Division, Hospital das Clinicas, Faculdade de Medicina, Universidade de São Paulo (USP), São Paulo, SP, Brazil.