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Symptom-related experience and sexual health of female patients with pulmonary arterial hypertension: protocol for a systematic review and qualitative meta-synthesis

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Abstract

Introduction

Pulmonary arterial hypertension (PAH) is a complex condition affecting quality of life, characterized by high blood pressure in the pulmonary arteries leading to heart strain. PAH's impact extends beyond physical symptoms, influencing emotional and social well-being, particularly in women where it affects sexual health and pregnancy outcomes. Despite medical advancements, the disease's full impact on women's lives is under-researched, especially regarding sexual experiences and health. This systematic review and qualitative meta-synthesis aim to address this gap by examining women's experiences with PAH, informing clinical practice and patient-centered care. The protocol outlines a methodology for synthesizing qualitative research to amplify women's voices and enhance our understanding of PAH's impact on female patients.

Methods and analysis

Search strategy

A systematic review and thematic meta-synthesis of qualitative research studies and qualitative components of mixed-methods studies will be conducted. The systematic review will be guided by the Joanna Briggs Institute methodological framework. A comprehensive search will encompass seven electronic databases and search engine (Ovid Medline, CINAHL, EMBASE, APA PsycINFO, Cochrane Database of Systematic Reviews, PubMed, Scopus) and grey literature sources (ProQuest Dissertations, Clinical Trials. gov). Building on insights from previous reviews centered on symptom-related experience and sexual health. Two review authors will independently conduct the screening and data extraction processes. Discrepancies will be resolved through consensus or discussion with a third review author. The review will include English studies from database inception. Findings will be presented graphically and tabularly, together with a narrative description.

Assessment of Confidence and Data Synthesis

The meta-synthesis used thematic analysis, importing study transcripts and notes into NVivo software. Data-derived codes formed categories, which were then iteratively refined into broader themes reflecting women's experiences with sex and childbirth while living with PAH.

Registration details

PROSPERO(CRD42024529342)

Strengths and limitations of this study

- The systematic review will employ a comprehensive methodology aligned with the Cochrane methodological framework, underpinned by the framework of Hilary Thomson and Mhairi Campbell with the support of Dario Sambunjak and colleague from Cochrane's People Services Department.
- The heterogeneity in PAH patients across gender and countries regarding age, roles and symptoms means significant diversity in their experience and response affecting the disease; we hope to capture this through the review findings as an important link between female patients' response in influencing sexual health and health related quality of life.
- Two reviewers will independently screen titles/abstracts and full-text articles using ReviewManager (RevMan) and then extract data using an adapted Cochrane data extraction

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- This systematic review will exclusively concentrate on publications written in the English language.

- To ensure rigor and transparency, the review will document each step and any discrepancies between reviewers will be resolved through consensus or third-party arbitration, ensuring a thorough and unbiased synthesis of the evidence.

Background

Pulmonary arterial hypertension (PAH) is a complex form of pulmonary arterial hypertension characterized by progressive occlusive vascular lesions in the distal pulmonary circulation, usually leading to right ventricular failure and death if without treatment, that significantly impairs the quality of life for affected individuals¹. The disease is not only defined by its physiological manifestations but also by the diverse and often underexplored symptom-related experiences of patients. Despite the improvement of right heart catheterization technology and the emergence of new targeted drugs such as Ambrisentan, Sildenafil and Treprostinil, PAH remains a complex condition with a profound impact on patients' physical, emotional, and social well-being². Patients may present with physical symptoms such as dyspnea, fatigue, and chest pain, as well as psychosocial problems like anxiety, depression and financial burden³. The symptom-related experience of adults with PAH is multifaceted, encompassing not only the physiological challenges but also the psychological and social consequences of managing a life-altering disease. Sexual health is a particularly important aspect of quality of life for women with PAH, as the majority of idiopathic PAH patients—nearly 80%—are female, with many in their reproductive years⁴. For women with PAH, the physical symptoms may limit sexual activity, while psychological symptoms can affect desire and relationship dynamics, even maternal injuries during pregnancy and childbirth can be severe, permanent and even fatal⁵. All these can severely impaired health-related quality of life (HRQOL)⁶.

Sexual health encompasses a broad range of issues, including sexual function, satisfaction, and overall well-being⁷. The symptoms and treatment modalities can have profound implications on sexual experiences of patients with PAH. Furthermore, the fear of intimacy due to concerns about disease progression or the potential impact on pregnancy adds another layer of complexity to their sexual health⁸. Understanding the lived experiences of female patients with PAH is crucial for healthcare providers to deliver patient-centered care and improving quality of life that addresses the holistic needs of patients⁹. However, the voices of those women living with PAH often go unheard, and there is a need for research that centers on their perspectives and experiences. Despite the recognized importance of sexual health in the overall well-being of individuals with chronic illnesses, there remains a paucity of research focusing on the experiences of female PAH patients in this domain¹⁰. Qualitative research offers valuable insights into the subjective experiences, perceptions, and coping strategies of individuals living with chronic illnesses¹¹. Existing literature is often centered on the physiological aspects of PAH, with less emphasis on the lived experiences and subjective realities of patients. In addition, many qualitative research findings remain isolated and unavailable for use in practice and policy formation as they have not been rigorously and systematically reviewed¹². This gap in knowledge is particularly evident in the context of sexual health, where the voices and perspectives of female patients are underrepresented⁸. Several qualitative studies have explored the lived experiences of patients with PAH, highlighting the

challenges of diagnosis, the impact on daily life, coping mechanisms, and emotional well-being¹³⁻¹⁶. These studies have shed light on the physical and emotional toll of living with a chronic and life-threatening condition, as well as the resilience and resourcefulness of patients in managing their symptoms and navigating the healthcare system. The previous synthesis by Rawlings GH and colleagues¹⁷ included 19 articles published between 2005 and 2020, that reflected the experiences of over 1900 individuals impacted by PH from various regions. The findings highlighted six descriptive themes related to participants' experiences with diagnosis, treatment, prognosis, healthcare professionals, the impact of PH, and coping strategies. Additionally, four higher-order analytical themes were developed, reflecting the uncertainties and anxieties associated with PH, the lack of recognition of the condition's impact, frustration with the limited awareness of PH, and participants' accounts of transitioning through different stages of living with the disease. The review concludes that while PH significantly impacts patients' quality of life, there are gaps in the literature that warrant further research, and it emphasizes the role of educational and psychological therapies in supporting those with the disease.

With myriad treatment options now available, the health-related quality of life (HRQoL) has been greatly improved in disease management¹⁸. Despite a more consistent focus on HRQoL in PAH research, we do not fully understand the Sexual Health-Related Quality of Life (SHRQoL) of PAH patients especially of female PAH patients¹⁹. This systematic review and qualitative meta-synthesis will conduct a comprehensive search and aim to fill this gap by synthesizing the qualitative research on the experiences of women living with PAH. These studies investigated a specific question by interviewing individuals with a series of semi-structured questions by endorsing predefined responses²⁰. Through an exploration of the narratives from individuals impacted by the disease, this review aims to elucidate the challenges encountered, coping mechanisms adopted, and support needed by these individuals. The findings have the potential to inform clinical practice, guide the development of interventions that are patient-centered, and advocate for improved services and policies to support this population.

This protocol outlines the methodology and approach that will be taken to conduct a systematic review and qualitative meta-synthesis of the symptom-related experiences and sexual health of female patients with PAH. It sets the stage for a research endeavor that seeks to amplify the voices of women with PAH and contribute to a more patient-centered understanding of the impact and management on the disease.

Methods

Design

The protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO) in April 2024, and the registration number is CRD42024529342. This protocol was designed following the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) 2015 statement²¹, and was developed following the guidelines set forth by the Cochrane Effective Practice and Organization of Care: Qualitative Evidence Synthesis²². The study will run tentatively from 1 April 2024 to 30 November 2024.

Search strategy

The search strategy will be used for the literature search by three steps²³. For step 1, a preliminary search of the PubMed database will be performed on 1 April 2024, analyzing the titles, abstracts, subject terms and Mesh terms in the articles. For step 2, a comprehensive search will be undertaken

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across all included databases using keywords, subject word and random word; the databases will include Ovid Medline, CINAHL, EMBASE, APA PsycINFO, Cochrane Database of Systematic Reviews, PubMed, Scopus and grey literature sources (ProQuest Dissertations, ClinicalTrials.gov). This task would be finished on 1 May 2024. For step 3, all reference lists of the included literature published before 1 June 2024 will be searched to complement other relevant literature. The search strategy for databases is shown in online supplemental Appendix I. The data synthesis for this study is expected to begin in July 2024.

Eligibility criteria

The inclusion criteria for literature in this study are qualitative studies. And the types of participants focusing on female patients diagnosed with pulmonary arterial hypertension (aged ≥ 18 years), regardless of whether or not they were pregnant. The eligible research is in English and the full text can be obtained. Studies focusing on PAH without female patients included will be excluded.

Identification and selection of studies

The results of the electronic database searching will be imported to EndNote V.X9 reference management software and will use the automated 'Find Duplicates' function to exclude any duplicates. The literature will be independently screened by two researchers (YL, HY) trained in systematic review methodology, who will read the titles and abstracts for the preliminary screening, and then read the full texts for secondary screening and eligibility using a standardized form. Ineligible studies will be excluded, and the reason for exclusion will be recorded. Eligible studies will be included in the analysis. Differences encountered during the screening process will be resolved by the two investigators through negotiation or by discussion with a third investigator (MF). The screening process will be reported using a PRISMA flow chart. We plan to complete the selection of studies on 31 October 2024.

Assessment of methodological quality of included studies

The GRADE-CERQual (Confidence in the Evidence from Reviews of Qualitative Research) evidence grading method will be used to grade the quality of evidence of the synthesized findings²⁴. The GRADE CERQual approach is designed to help researcher of qualitative evidence make informed judgments about the trustworthiness and applicability of the findings^{25,26}. The Critical Appraisal Skills Programme (CASP) checklist for qualitative research will be used to assess methodological limitations of qualitative research²⁷ of which the utilization methods is presented in table 1. The final confidence rating would be classified into one of the following categories: 'high', 'moderate', 'low' or 'very low'.

Two researchers (YL, HY) will independently use the 10-item Critical Appraisal Checklist for qualitative research to assess the methodological quality of the included studies²⁴. Each question is rated 'yes', 'no', 'cannot tell'. it was necessary to achieve a minimum affirmative response in at least six of the domains. Studies fully meeting the above criteria, indicating a low risk of bias, will be graded A. Studies partially meeting the minimum criteria, indicating a moderate risk of bias, will be graded B. Finally, studies not meeting the above quality standards at all, indicating a high risk of bias, will be graded C. Studies with grades of A and B will be included in the qualitative meta-synthesis. Differences encountered by the two investigators (YL, HY) during the evaluation process will be resolved through negotiation or discussion with a third investigator (MF).

Table 1 The utilization of CASP tool for assessing methodological limitations of qualitative studies

Content of Evaluation	
1. Was there a clear statement of the aims of the research?	<input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> cannot tell
2. Was there a clear statement of the aims of the research?	<input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> cannot tell
3. Was the research design appropriate to address the aims of the research?	<input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> cannot tell
4. Was the recruitment strategy appropriate to the aims of the research?	<input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> cannot tell
5. Were the data collected in a way that addressed the research issue?	<input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> cannot tell
6. Has the relationship between researcher and participants been adequately considered?	<input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> cannot tell
7. Have ethical issues been taken into consideration?	<input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> cannot tell
8. Was the data analysis sufficiently rigorous?	<input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> cannot tell
9. Is there a clear statement of findings?	<input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> cannot tell
10. Overall assessment	<input type="checkbox"/> no or few limitations <input type="checkbox"/> minor limitations <input type="checkbox"/> major limitations

Data extraction

Data extraction was performed by two reviewers (YZ, ZR) using a standardized extraction form. The form was pilot-tested on a sample of articles and refined as necessary. In addition to parameters required for quality appraisal of included studies and thematic analyses, data extraction will contain the following data parameters:

- ▶ Study identifiers (including authors, publication date and country)
- ▶ Context
- ▶ Aims and objectives
- ▶ Study design
- ▶ Sampling frame and recruitment
- ▶ Participants
- ▶ Method of data collection and analysis
- ▶ Summary of major study findings

Data synthesis

The meta-synthesis process involved a thematic analysis approach²⁸. Transcripts and field notes from the included studies were imported into NVIVO (Lumivero) qualitative analysis software. Codes were inductively generated from the data and organized into categories²⁹. Through an iterative process, these categories were refined and synthesized into overarching themes that captured the essence of the women's experiences with sex and delivery during pregnancy with PAH.

Patient and public involvement

The qualitative meta-synthesis will involve a secondary analysis of publicly available primary data; consequently, there will be no participant or public involvement.

Ethics and dissemination

External ethical approval is not required as this review is a retrospective review, which is undertaking secondary analysis of publicly available primary data. The results will be disseminated

in peer-reviewed journals and presented in conference papers and elsewhere.

Discussion

This synthesis will establish what is known about the components and processes of experience and sexual health concern for female patients with PAH. It is hoped that the conclusion of this study can provide a theoretical basis for medical staff to combine multiple resources for PAH patients and provide a new perspective for improving their health-related quality of life.

Significance and impact of this review

In the published literature, pulmonary hypertension related qualitative research has mainly focused on social, cultural, and psychological aspects and the impact of disease-related symptoms on emotional and sexual health, and some qualitative research has explored these attributes and behaviors by individuals experiencing and reporting symptoms. This review represents a novel approach to illness perception research. The synthesis and interpretation of the preliminary research of this study will increase the breadth and depth of the findings of the contribution, listen to and understand the feelings and needs of patients with pulmonary hypertension, and provide reference for better health care and guidance for them.

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1 **Symptom-related experience and sexual health of female patients with pulmonary**
2 **arterial hypertension: protocol for a systematic review and qualitative meta-**
3 **synthesis**

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19 **Competing interests**

20 All authors have stated that there are no competing non-financial/financial interests to
21 disclose.

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- To ensure rigor and transparency, the review will document each step and any discrepancies between reviewers will be resolved through consensus or third-party arbitration, ensuring a thorough and unbiased synthesis of the evidence.

Background

Pulmonary arterial hypertension (PAH) is a disease marked by elevated blood pressure within the pulmonary arteries. This condition can cause the narrowing, obstruction, or destruction of lung blood vessels, which in turn slows blood flow and raises pulmonary arterial pressure. As a result, the heart has to exert more effort to circulate blood through the lungs. If left untreated, this increased workload can ultimately result in right ventricular failure and death¹. Despite the improvement of right heart catheterization technology and the emergence of new targeted drugs, PAH remains a complex condition with a profound impact on patients' physical, psychological. Despite advancements in right heart catheterization technology and new targeted drugs, PAH continues to significantly impact patients' physical, psychological, and social well-being. Patients experience symptoms such as dyspnea, fatigue, chest pain, anxiety, depression, and financial burden^{2,3}. Sexual health is a particularly important aspect of quality of life for women with PAH, as the majority of idiopathic PAH patients—nearly 80%—are female, with many in their reproductive years⁴. For women with PAH, the physical symptoms may limit sexual activity, while psychological symptoms can affect desire and relationship dynamics, even maternal injuries during pregnancy and childbirth can be severe, permanent and even fatal⁵. All these can severely impaired health-related quality of life (HRQOL)⁶.

Sexual health encompasses a broad range of issues, including sexual function, satisfaction, and overall well-being⁷. The symptoms and treatment modalities can have profound implications on sexual experiences of patients with PAH. Furthermore, the fear of intimacy due to concerns about disease progression or the potential impact on pregnancy adds another layer of complexity to their sexual health⁸. Understanding the lived experiences of female patients with PAH is crucial for healthcare providers to deliver patient-centered care and improving quality of life that addresses the holistic needs of patients⁹. Despite the recognized importance of sexual health in the overall well-being of individuals with chronic illnesses, the voices of women living with PAH often go unheard, highlighting a need for research that focuses on their unique perspectives and experiences in this under-researched domain. ¹⁰. Several qualitative studies have explored the experiences of PAH patients, highlighting challenges in diagnosis, daily life impact, coping mechanisms, and emotional well-being¹¹⁻¹⁶. A synthesis by Rawlings GH and colleagues included articles reflecting the experiences of over 1900 individuals with PH, identifying themes related to diagnosis, treatment, prognosis, healthcare professionals, the impact of PH, and coping strategies¹⁷. This review emphasizes the role of educational and psychological therapies in supporting patients with PAH.

With myriad treatment options now available, the HRQoL has been greatly improved in disease management¹⁸. Despite a more consistent focus on HRQoL in PAH research, we do not fully understand the Sexual Health-Related Quality of Life (SHRQoL) of PAH patients especially of female PAH patients^{19, 20}. This systematic review and qualitative meta-synthesis will conduct a comprehensive search and aim to fill this gap by synthesizing the qualitative research on the

experiences of women living with PAH. We aim to elucidate the challenges encountered, coping mechanisms adopted, and support needed by these individuals.

This protocol outlines the methodology and approach that will be taken to conduct a systematic review and qualitative meta-synthesis of the symptom-related experiences and sexual health of female patients with PAH. It sets the stage for a research endeavor that seeks to amplify the voices of women with PAH and contribute to a more patient-centered understanding of the impact and management on the disease.

Methods

Design

The protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO) in April 2024, and the registration number is CRD42024529342. This protocol was designed following the guidelines set forth by the Cochrane Effective Practice and Organization of Care: Qualitative Evidence Synthesis²¹, while the reporting follows the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) 2015 statement²² shown in Appendix 1. The study will run tentatively from 1 April 2024 to 30 November 2024. In the event of this protocol was registered but not yet published, we will update the registration record by submitting a modification request through the PROSPERO portal, detailing the changes and their rationale, ensuring all revisions are documented and auditable within the registry.

Search strategy

The search strategy will be used for the literature search by three steps²³. For step 1, a preliminary search of the PubMed database will be performed on 1 April 2024, analyzing the titles, abstracts, subject terms and Mesh terms in the articles. For step 2, a comprehensive search will be undertaken across all included databases using keywords, subject word and random word; the databases will include Ovid Medline, CINAHL, EMBASE, APA PsycINFO, Cochrane Database of Systematic Reviews, PubMed, Scopus and grey literature sources (ProQuest Dissertations, ClinicalTrials.gov). This task would be finished on 1 May 2024. For step 3, all reference lists of the included literature published before 1 June 2024 will be searched to complement other relevant literature. The search strategy for databases is shown in online supplemental Appendix II. The data synthesis for this study is expected to begin in July 2024.

Eligibility criteria

The inclusion criteria for literature in this study are qualitative studies. And the types of participants focusing on female patients diagnosed with pulmonary arterial hypertension (aged \geq 18 years), regardless of whether or not they were pregnant. The eligible research is in English, and the full text can be obtained. Studies focusing on PAH without female patients included will be excluded.

Identification and selection of studies

The results of the electronic database searching will be imported to EndNote V.X9 reference management software and will use the automated 'Find Duplicates' function to exclude any duplicates. The literature will be independently screened by two researchers (YL, HY) trained in systematic review methodology, who will read the titles and abstracts for the preliminary screening, and then read the full texts for secondary screening and eligibility using a standardized form. Ineligible studies will be excluded, and the reason for exclusion will be recorded. Eligible studies will be included in the analysis. Differences encountered during the screening process will be

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resolved by the two investigators through negotiation or by discussion with a third investigator (MF). The screening process will be reported using a PRISMA flow chart. We plan to complete the selection of studies on 31 October 2024.

Assessment of methodological quality of included studies

The GRADE-CERQual (Confidence in the Evidence from Reviews of Qualitative Research) evidence grading method will be used to grade the quality of evidence of the synthesized findings²⁴. The GRADE CERQual approach is designed to help researcher of qualitative evidence make informed judgments about the trustworthiness and applicability of the findings^{25,26}. The Critical Appraisal Skills Programme (CASP) checklist for qualitative research will be used to assess methodological limitations of qualitative research²⁷ of which the utilization methods is presented in table 1. The final confidence rating would be classified into one of the following categories: 'high', 'moderate', 'low' or 'very low'.

Two researchers (YL, HY) will independently use the 10-item Critical Appraisal Checklist for qualitative research to assess the methodological quality of the included studies²⁴. Each question is rated 'yes', 'no', 'cannot tell'. it was necessary to achieve a minimum affirmative response in at least six of the domains. Studies fully meeting the above criteria, indicating a low risk of bias, will be graded A. Studies partially meeting the minimum criteria, indicating a moderate risk of bias, will be graded B. Finally, studies not meeting the above quality standards at all, indicating a high risk of bias, will be graded C. Studies with grades of A and B will be included in the qualitative meta-synthesis. Differences encountered by the two investigators (YL, HY) during the evaluation process will be resolved through negotiation or discussion with a third investigator (MF).

Table 1 The utilization of CASP tool for assessing methodological limitations of qualitative studies

Content of Evaluation	
1. Was there a clear statement of the aims of the research?	<input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> cannot tell
2. Was there a clear statement of the aims of the research?	<input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> cannot tell
3. Was the research design appropriate to address the aims of the research?	<input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> cannot tell
4. Was the recruitment strategy appropriate to the aims of the research?	<input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> cannot tell
5. Were the data collected in a way that addressed the research issue?	<input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> cannot tell
6. Has the relationship between researcher and participants been adequately considered?	<input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> cannot tell
7. Have ethical issues been taken into consideration?	<input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> cannot tell
8. Was the data analysis sufficiently rigorous?	<input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> cannot tell
9. Is there a clear statement of findings?	<input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> cannot tell
10. Overall assessment	<input type="checkbox"/> no or few limitations <input type="checkbox"/> minor limitations <input type="checkbox"/> major limitations

Data extraction

Data extraction was performed by two reviewers (YZ, ZR) using a standardized extraction form. The form was pilot-tested on a sample of articles and refined as necessary. In addition to parameters

required for quality appraisal of included studies and thematic analyses, data extraction will contain the following data parameters:

- ▶ Study identifiers (including authors, publication date and country)
- ▶ Context
- ▶ Aims and objectives
- ▶ Study design
- ▶ Sampling frame and recruitment
- ▶ Participants
- ▶ Method of data collection and analysis
- ▶ Summary of major study findings

Data synthesis

The meta-synthesis process involved a thematic analysis approach²⁸. Transcripts and field notes from the included studies were imported into NVIVO (Lumivero) qualitative analysis software. Codes were inductively generated from the data and organized into categories²⁹. Through an iterative process, these categories were refined and synthesized into overarching themes that captured the essence of the women's experiences with sex and delivery during pregnancy with PAH.

Patient and public involvement

The qualitative meta-synthesis will involve a secondary analysis of publicly available primary data; consequently, there will be no participant or public involvement.

Ethics and dissemination

External ethical approval is not required as this review is a retrospective review, which is undertaking secondary analysis of publicly available primary data. The results will be disseminated in peer-reviewed journals and presented in conference papers and elsewhere.

Potential bias and Countermeasures

In the realm of qualitative research synthesis, potential biases can undermine the dependability and potency of study outcomes. These biases include information bias from inaccurate variable measurement, sampling bias when the sample fails to mirror the intended population, and both researcher and reporting biases that can skew result interpretation or lead to selective outcome reporting³⁰. To mitigate such risks, we've implemented standardized training for our research team, enforced consistent data collection protocols, and employed a strategy of collaborative, independent analysis by multiple researchers.

Discussion

This synthesis will establish what is known about the components and processes of experience and sexual health concern for female patients with PAH. It is hoped that the conclusion of this study can provide a theoretical basis for medical staff to combine multiple resources for PAH patients and provide a new perspective for improving their health-related quality of life.

Significance and impact of this review

In the published literature, pulmonary hypertension related qualitative research has mainly focused on social, cultural, and psychological aspects and the impact of disease-related symptoms on emotional and sexual health, and some qualitative research has explored these attributes and

behaviors by individuals experiencing and reporting symptoms. This review represents a novel approach to illness perception research. The synthesis and interpretation of the preliminary research of this study will increase the breadth and depth of the findings of the contribution, listen to and understand the feelings and needs of patients with pulmonary hypertension, and provide reference for better health care and guidance for them.

Contributorship statement

Fangfang Ma and Lixiao Yang had contributed equally to this work. Miss He was responsible for study design and data integration. Ma assisted for study design and literature search as well as editing the manuscript. Lixiao Yang and Zhu Yang were responsible for Literature analysis and data extraction. All authors approved the final version of the manuscript submitted and have agreed to be accountable for all aspects of the work. Fangfang M. is responsible for the overall content as guarantor.

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Appendix II The search strategy for databases

P(Participants): female PAH patients
I(Interest of phenomena): patients’ experiences related to disease and sexual health
Co(Context): self-care or being cared for by others
S(study design): qualitative interview research methods

Pubmed	#1	("Pulmonary Arterial Hypertension"[MeSH Terms]) OR (pulmonary hypertension[Title/Abstract] OR pulmonary arterial hypertension[Title/Abstract] OR "PH"[Title/Abstract] OR "PAH"[Title/Abstract])	618576
	#2	((("Women"[MeSH Terms]) OR (women[Title/Abstract])) OR (female[Title/Abstract])) OR (maternal[Title/Abstract])	2233530
	#3	qualitative research*[Title/Abstract] OR qualitative stud*[Title/Abstract] OR narrative*[Title/Abstract] OR unstructured interview*[Title/Abstract] OR semistructured interview*[Title/Abstract]	194661
	#4	#1 AND #2 AND #3	44
Web of Science	#1	qualitative research* OR qualitative stud* OR narrative* OR unstructured interview* OR semistructured interview* (All Fields)	353195
	#2	women OR female OR maternal (Topic)	1893085
	#3	pulmonary hypertension OR pulmonary arterial hypertension OR PH OR PAH (Topic)	811047
	#4	#1 AND #2 AND #3	224
Embase	#1	'pulmonary arterial hypertension'/exp OR 'pulmonary arterial hypertension' OR ((pulmonary:ab AND hypertension:ab OR pulmonary:ab) AND arterial:ab AND hypertension:ab) OR 'ph':ab OR 'pah':ab	781814
	#2	women OR female OR maternal:ab	13103197
	#3	((qualitative AND research* OR qualitative) AND stud* OR narrative* OR unstructured) AND interview* OR semistructured) AND interview*	212033
	#4	#1 AND #2 AND #3	171
CINAHL	#1	AB: pulmonary hypertension OR pulmonary arterial hypertension OR PH OR PAH	24855
	#2	AB: female OR women OR meternal	626903
	#3	TX:qualitative research* OR qualitative stud* OR narrative* OR unstructured interview* OR semistructured interview*	321651
	#4	#1 AND #2 AND #3	39
APA PsycINFO	#1	AB: pulmonary hypertension OR pulmonary arterial hypertension OR PH OR PAH	1247
	#2	AB: female OR women OR meternal	278965
	#3	TX:qualitative research* OR qualitative stud* OR narrative* OR	186679

		unstructured interview* OR semistructured interview*	
	#4	#1 AND #2 AND #3	8
Cochrane	#1	Title/Abstract/Key words: pulmonary hypertension OR pulmonary arterial hypertension OR PH OR PAH	24914
	#2	All text: female OR women OR meternal	1122852
	#3	All text: qualitative research* OR qualitative stud* OR narrative* OR unstructured interview* OR semistructured interview*	35613
	#4	#1 AND #2 AND #3	156
SCOPUS	#1	Title/Abstract/Key words: pulmonary hypertension OR pulmonary arterial hypertension OR PH OR PAH	39870
	#2	Title/Abstract/Key words: female OR women OR meternal	12699961
	#3	All text: qualitative research* OR qualitative stud* OR narrative* OR unstructured interview* OR semistructured interview*	688729
	#4	#1 AND #2 AND #3	45

BMJ Open

Symptom-related experience and sexual health of female patients with pulmonary arterial hypertension: protocol for a systematic review and qualitative meta-synthesis

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Manuscript ID	bmjopen-2024-089095.R2
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Primary Subject Heading:	Qualitative research
Secondary Subject Heading:	Sexual health
Keywords:	Health, Cardiovascular Disease, Patient-Centered Care, Nursing Care

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Symptom-related experience and sexual health of female patients with pulmonary arterial hypertension: protocol for a systematic review and qualitative meta-synthesis

Abstract

Introduction

Pulmonary arterial hypertension (PAH) is a complex condition affecting quality of life, characterized by high blood pressure in the pulmonary arteries leading to heart strain. PAH's impact extends beyond physical symptoms, influencing emotional and social well-being, particularly in women where it affects sexual health and pregnancy outcomes. Despite medical advancements, the disease's full impact on women's lives is under-researched, especially regarding sexual experiences and health. This systematic review and qualitative meta-synthesis aim to address this gap by examining women's experiences with PAH, informing clinical practice and patient-centered care. The protocol outlines a methodology for synthesizing qualitative research to amplify women's voices and enhance our understanding of PAH's impact on female patients.

Methods and analysis

Search strategy

A systematic review and thematic meta-synthesis of qualitative research studies and qualitative components of mixed-methods studies will be conducted. The systematic review will be guided by the Joanna Briggs Institute methodological framework. A comprehensive search will encompass seven electronic databases and search engine (Ovid Medline, CINAHL, EMBASE, APA PsycINFO, Cochrane Database of Systematic Reviews, PubMed, Scopus) and grey literature sources (ProQuest Dissertations, Clinical Trials. gov). Building on insights from previous reviews centered on symptom-related experience and sexual health. Two review authors will independently conduct the screening and data extraction processes. Discrepancies will be resolved through consensus or discussion with a third review author. The review will include English studies from database inception. Findings will be presented graphically and tabularly, together with a narrative description.

Assessment of Confidence and Data Synthesis

The meta-synthesis used thematic analysis, importing study transcripts and notes into NVivo software. Data-derived codes formed categories, which were then iteratively refined into broader themes reflecting women's experiences with sex and childbirth while living with PAH.

Registration details

PROSPERO(CRD42024529342)

Strengths and limitations of this study

-The systematic review will employ a comprehensive methodology aligned with the Cochrane methodological framework, underpinned by the framework of Hilary Thomson and Mhairi Campbell with the support of Dario Sambunjak and colleague from Cochrane's People Services Department.

-The heterogeneity in PAH patients across gender and countries regarding age, roles and symptoms means significant diversity in their experience and response affecting the disease; we hope to capture this through the review findings as an important link between female patients' response in influencing sexual health and health related quality of life.

-Two reviewers will independently screen titles/abstracts and full-text articles using

ReviewManager (RevMan) and then extract data using an adapted Cochrane data extraction template.

- To ensure rigor and transparency, the review will document each step and any discrepancies between reviewers will be resolved through consensus or third-party arbitration, ensuring a thorough and unbiased synthesis of the evidence.

- This systematic review focused exclusively on English-language publications, which may introduce potential biases that could limit the reliability and validity of the study findings.

Background

Pulmonary arterial hypertension (PAH) is a disease marked by elevated blood pressure within the pulmonary arteries. This condition can cause the narrowing, obstruction, or destruction of lung blood vessels, which in turn slows blood flow and raises pulmonary arterial pressure. As a result, the heart has to exert more effort to circulate blood through the lungs. If left untreated, this increased workload can ultimately result in right ventricular failure and death¹. Despite advancements in right heart catheterization technology and new targeted drugs, PAH continues to significantly impact patients' physical, psychological, and social well-being. Patients experience symptoms such as dyspnea, fatigue, chest pain, anxiety, depression, and financial burden^{2, 3}. Sexual health is a particularly important aspect of quality of life for women with PAH, as the majority of idiopathic PAH patients—nearly 80%—are female, with many in their reproductive years⁴. For women with PAH, the physical symptoms may limit sexual activity, while psychological symptoms can affect desire and relationship dynamics, even maternal injuries during pregnancy and childbirth can be severe, permanent and even fatal⁵. Moreover, previous studies have found that high degrees of sexual dysfunction were observed in women treated with parenteral prostanoids⁶. All these can severely impaired health-related quality of life (HRQOL)⁷.

Sexual health encompasses a broad range of issues, including sexual function, satisfaction, and overall well-being⁸. The symptoms and treatment modalities can have profound implications on sexual experiences of patients with PAH. Furthermore, the fear of intimacy due to concerns about disease progression or the potential impact on pregnancy adds another layer of complexity to their sexual health⁹. Understanding the lived experiences of female patients with PAH is crucial for healthcare providers to deliver patient-centered care and improving quality of life that addresses the holistic needs of patients¹⁰. Despite the recognized importance of sexual health in the overall well-being of individuals with chronic illnesses, the voices of women living with PAH often go unheard, highlighting a need for research that focuses on their unique perspectives and experiences in this under-researched domain. This study focuses on women with PAH as pregnancy and childbirth can significantly affect their condition, and an aspect that is less explored in studies including male patients¹¹. Several qualitative studies have explored the experiences of PAH patients, highlighting challenges in diagnosis, daily life impact, coping mechanisms, and emotional well-being¹²⁻¹⁷. A synthesis by Rawlings GH and colleagues included articles reflecting the experiences of over 1900 individuals with PH, identifying themes related to diagnosis, treatment, prognosis, healthcare professionals, the impact of PH, and coping strategies¹⁸. This review emphasizes the role of educational and psychological therapies in supporting patients with PAH.

With myriad treatment options now available, the HRQoL has been greatly improved in disease management¹⁹. Despite a more consistent focus on HRQoL in PAH research, we do not fully understand the Sexual Health-Related Quality of Life (SHRQoL) of PAH patients especially of

female PAH patients^{20, 21}. This systematic review and qualitative meta-synthesis will conduct a comprehensive search and aim to fill this gap by synthesizing the qualitative research on the experiences of women living with PAH. We aim to elucidate the challenges encountered, coping mechanisms adopted, and support needed by these individuals.

This protocol outlines the methodology and approach that will be taken to conduct a systematic review and qualitative meta-synthesis of the symptom-related experiences and sexual health of female patients with PAH. It sets the stage for a research endeavor that seeks to amplify the voices of women with PAH and contribute to a more patient-centered understanding of the impact and management on the disease.

Methods

Design

The protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO) in April 2024, and the registration number is CRD42024529342. This protocol was designed following the guidelines set forth by the Cochrane Effective Practice and Organization of Care: Qualitative Evidence Synthesis²², while the reporting follows the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) 2015 statement²³ shown in Appendix 1. The study will run tentatively from 1 April 2024 to 31 January 2025. In the event of this protocol was registered but not yet published, we will update the registration record by submitting a modification request through the PROSPERO portal, detailing the changes and their rationale, ensuring all revisions are documented and auditable within the registry.

Search strategy

The search strategy will be used for the literature search by three steps²⁴. For step 1, a preliminary search of the PubMed database will be performed on 1 April 2024, analyzing the titles, abstracts, subject terms and Mesh terms in the articles. For step 2, a comprehensive search will be undertaken across all included databases using keywords, subject word and random word; the databases will include Ovid Medline, CINAHL, EMBASE, APA PsycINFO, Cochrane Database of Systematic Reviews, PubMed, Scopus and grey literature sources (ProQuest Dissertations, ClinicalTrials.gov). This task would be finished on 1 May 2024. For step 3, all reference lists of the included literature published before 1 June 2024 will be searched to complement other relevant literature. The search strategy for databases is shown in online supplemental Appendix II. The data synthesis for this study is expected to begin in December 2024.

Eligibility criteria

The inclusion criteria for literature in this study are qualitative studies. And the types of participants focusing on female patients diagnosed with pulmonary arterial hypertension (aged \geq 18 years), regardless of whether or not they were pregnant. The eligible research is in English and the full text can be obtained. Studies focusing on PAH without female patients included will be excluded.

Identification and selection of studies

The results of the electronic database searching will be imported to EndNote V.X9 reference management software and will use the automated 'Find Duplicates' function to exclude any duplicates. The literature will be independently screened by two researchers (YL, HY) trained in systematic review methodology, who will read the titles and abstracts for the preliminary screening, and then read the full texts for secondary screening and eligibility using a standardized form.

Ineligible studies will be excluded, and the reason for exclusion will be recorded. Eligible studies will be included in the analysis. Differences encountered during the screening process will be resolved by the two investigators through negotiation or by discussion with a third investigator (MF). The screening process will be reported using a PRISMA flow chart. We plan to complete the selection of studies on 31 October 2024.

Assessment of methodological quality of included studies

The GRADE-CERQual (Confidence in the Evidence from Reviews of Qualitative Research) evidence grading method will be used to grade the quality of evidence of the synthesized findings²⁵. The GRADE CERQual approach is designed to help researcher of qualitative evidence make informed judgments about the trustworthiness and applicability of the findings^{26,27}. The Critical Appraisal Skills Programme (CASP) checklist for qualitative research will be used to assess methodological limitations of qualitative research²⁸ of which the utilization methods is presented in table 1. The final confidence rating would be classified into one of the following categories: 'high', 'moderate', 'low' or 'very low'.

Two researchers (YL, HY) will independently use the 10-item Critical Appraisal Checklist for qualitative research to assess the methodological quality of the included studies²⁵. Each question is rated 'yes', 'no', 'cannot tell'. it was necessary to achieve a minimum affirmative response in at least six of the domains. Studies fully meeting the above criteria, indicating a low risk of bias, will be graded A. Studies partially meeting the minimum criteria, indicating a moderate risk of bias, will be graded B. Finally, studies not meeting the above quality standards at all, indicating a high risk of bias, will be graded C. Studies with grades of A and B will be included in the qualitative meta-synthesis. Differences encountered by the two investigators (YL, HY) during the evaluation process will be resolved through negotiation or discussion with a third investigator (MF).

Table 1 The utilization of CASP tool for assessing methodological limitations of qualitative studies

Content of Evaluation	
1. Was there a clear statement of the aims of the research?	<input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> cannot tell
2. Was there a clear statement of the aims of the research?	<input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> cannot tell
3. Was the research design appropriate to address the aims of the research?	<input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> cannot tell
4. Was the recruitment strategy appropriate to the aims of the research?	<input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> cannot tell
5. Were the data collected in a way that addressed the research issue?	<input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> cannot tell
6. Has the relationship between researcher and participants been adequately considered?	<input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> cannot tell
7. Have ethical issues been taken into consideration?	<input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> cannot tell
8. Was the data analysis sufficiently rigorous?	<input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> cannot tell
9. Is there a clear statement of findings?	<input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> cannot tell
10. Overall assessment	<input type="checkbox"/> no or few limitations <input type="checkbox"/> minor limitations <input type="checkbox"/> major limitations

Data extraction

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1 Data extraction was performed by two reviewers (YZ, ZR) using a standardized extraction form.
2 The form was pilot-tested on a sample of articles and refined as necessary. In addition to parameters
3 required for quality appraisal of included studies and thematic analyses, data extraction will contain
4 the following data parameters:

- 5 ▶ Study identifiers (including authors, publication date and country)
- 6 ▶ Context
- 7 ▶ Aims and objectives
- 8 ▶ Study design
- 9 ▶ Sampling frame and recruitment
- 10 ▶ Participants
- 11 ▶ Method of data collection and analysis
- 12 ▶ Summary of major study findings

13 **Data synthesis**

14 The meta-synthesis process involved a thematic analysis approach²⁹. Transcripts and field notes
15 from the included studies were imported into NVIVO (Lumivero) qualitative analysis software.
16 Codes were inductively generated from the data and organized into categories³⁰. Through an
17 iterative process, these categories were refined and synthesized into overarching themes that
18 captured the essence of the women's experiences with sex and delivery during pregnancy with PAH.

20 **Ethics and dissemination**

21 External ethical approval is not required as this review is a retrospective review, which is
22 undertaking secondary analysis of publicly available primary data. The results will be disseminated
23 in peer-reviewed journals and presented in conference papers and elsewhere.

25 **Patient and public involvement**

26 The qualitative meta-synthesis will involve a secondary analysis of publicly available primary
27 data; consequently, there will be no participant or public involvement.

29 **Potential bias and Countermeasures**

30 In the realm of qualitative research synthesis, potential biases can undermine the dependability
31 and potency of study outcomes. These biases include information bias from inaccurate variable
32 measurement, sampling bias when the sample fails to mirror the intended population, and both
33 researcher and reporting biases that can skew result interpretation or lead to selective outcome
34 reporting³¹. To mitigate such risks, we've implemented standardized training for our research team,
35 enforced consistent data collection protocols, and employed a strategy of collaborative, independent
36 analysis by multiple researchers.

38 **Discussion**

39 This synthesis will establish what is known about the components and processes of experience
40 and sexual health concern for female patients with PAH. It is hoped that the conclusion of this study
41 can provide a theoretical basis for medical staff to combine multiple resources for PAH patients and
42 provide a new perspective for improving their health-related quality of life.

44 **Strengths and limitations of this study**

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The strengths of this study include the adoption of a comprehensive methodology in line with the Cochrane methodological framework. We aim to capture the significant diversity in experiences and responses among female PAH patients, particularly focusing on the relationship between female patients' responses and their sexual health and quality of life. The review process will be rigorous, with two independent reviewers using RevMan to screen titles/abstracts and full-text articles, and an adapted Cochrane data extraction template to ensure consistency. Discrepancies will be resolved through consensus or third-party arbitration, maintaining the integrity and transparency of the review. However, a limitation is the focus on English-language publications, which may introduce biases affecting the reliability and validity of the study's findings.

Significance and impact of this review

In the published literature, pulmonary hypertension related qualitative research has mainly focused on social, cultural, and psychological aspects and the impact of disease-related symptoms on emotional and sexual health, and some qualitative research has explored these attributes and behaviors by individuals experiencing and reporting symptoms. This review represents a novel approach to illness perception research. The synthesis and interpretation of the preliminary research of this study will increase the breadth and depth of the findings of the contribution, listen to and understand the feelings and needs of patients with pulmonary hypertension, and provide reference for better health care and guidance for them.

Funding and Contributorship statement

This research is conducted without any funding. Fangfang Ma and Lixiao Yang had contributed equally to this work. Miss He was responsible for study design and data integration. Ma assisted for study design and literature search as well as editing the manuscript. Lixiao Yang and Zhu Yang were responsible for Literature analysis and data extraction. All authors approved the final version of the manuscript submitted and have agreed to be accountable for all aspects of the work. Fangfang M. is responsible for the overall content as guarantor.

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Appendix II The search strategy for databases

P(Participants): female PAH patients
I(Interest of phenomena): patients’ experiences related to disease and sexual health
Co(Context): self-care or being cared for by others
S(study design): qualitative interview research methods

Pubmed	#1	("Pulmonary Arterial Hypertension"[MeSH Terms]) OR (pulmonary hypertension[Title/Abstract] OR pulmonary arterial hypertension[Title/Abstract] OR "PH"[Title/Abstract] OR "PAH"[Title/Abstract])	618576
	#2	((("Women"[MeSH Terms]) OR (women[Title/Abstract])) OR (female[Title/Abstract])) OR (maternal[Title/Abstract])	2233530
	#3	qualitative research*[Title/Abstract] OR qualitative stud*[Title/Abstract] OR narrative*[Title/Abstract] OR unstructured interview*[Title/Abstract] OR semistructured interview*[Title/Abstract]	194661
	#4	#1 AND #2 AND #3	44
Web of Science	#1	qualitative research* OR qualitative stud* OR narrative* OR unstructured interview* OR semistructured interview* (All Fields)	353195
	#2	women OR female OR maternal (Topic)	1893085
	#3	pulmonary hypertension OR pulmonary arterial hypertension OR PH OR PAH (Topic)	811047
	#4	#1 AND #2 AND #3	224
Embase	#1	'pulmonary arterial hypertension'/exp OR 'pulmonary arterial hypertension' OR ((pulmonary:ab AND hypertension:ab OR pulmonary:ab) AND arterial:ab AND hypertension:ab) OR 'ph':ab OR 'pah':ab	781814
	#2	women OR female OR maternal:ab	13103197
	#3	((qualitative AND research* OR qualitative) AND stud* OR narrative* OR unstructured) AND interview* OR semistructured) AND interview*	212033
	#4	#1 AND #2 AND #3	171
CINAHL	#1	AB: pulmonary hypertension OR pulmonary arterial hypertension OR PH OR PAH	24855
	#2	AB: female OR women OR meternal	626903
	#3	TX:qualitative research* OR qualitative stud* OR narrative* OR unstructured interview* OR semistructured interview*	321651
	#4	#1 AND #2 AND #3	39
APA PsycINFO	#1	AB: pulmonary hypertension OR pulmonary arterial hypertension OR PH OR PAH	1247
	#2	AB: female OR women OR meternal	278965
	#3	TX:qualitative research* OR qualitative stud* OR narrative* OR	186679

		unstructured interview* OR semistructured interview*	
	#4	#1 AND #2 AND #3	8
Cochrane	#1	Title/Abstract/Key words: pulmonary hypertension OR pulmonary arterial hypertension OR PH OR PAH	24914
	#2	All text: female OR women OR meternal	1122852
	#3	All text: qualitative research* OR qualitative stud* OR narrative* OR unstructured interview* OR semistructured interview*	35613
	#4	#1 AND #2 AND #3	156
SCOPUS	#1	Title/Abstract/Key words: pulmonary hypertension OR pulmonary arterial hypertension OR PH OR PAH	39870
	#2	Title/Abstract/Key words: female OR women OR meternal	12699961
	#3	All text: qualitative research* OR qualitative stud* OR narrative* OR unstructured interview* OR semistructured interview*	688729
	#4	#1 AND #2 AND #3	45

BMJ Open

Symptom-related experience and sexual health of female patients with pulmonary arterial hypertension: protocol for a systematic review and qualitative meta-synthesis

Journal:	BMJ Open
Manuscript ID	bmjopen-2024-089095.R3
Article Type:	Protocol
Date Submitted by the Author:	26-Nov-2024
Complete List of Authors:	Ma, Fangfang; Peking Union Medical College Hospital, Cardiac Intensive Care Unit, Department of Cardiology Yang, Lixiao; Peking Union Medical College Hospital, Cardiac Intensive Care Unit, Department of Cardiology He, Ye; Peking Union Medical College Hospital, Cardiac Intensive Care Unit, Department of Cardiology Yang, Zhu; Peking Union Medical College Hospital, Cardiac Intensive Care Unit, Department of Cardiology
Primary Subject Heading:	Qualitative research
Secondary Subject Heading:	Sexual health
Keywords:	Health, Cardiovascular Disease, Patient-Centered Care, Nursing Care

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Symptom-related experience and sexual health of female patients with pulmonary arterial hypertension: protocol for a systematic review and qualitative meta-synthesis

Abstract

Introduction

Pulmonary arterial hypertension (PAH) is a complex condition affecting quality of life, characterized by high blood pressure in the pulmonary arteries leading to heart strain. PAH's impact extends beyond physical symptoms, influencing emotional and social well-being, particularly in women where it affects sexual health and pregnancy outcomes. Despite medical advancements, the disease's full impact on women's lives is under-researched, especially regarding sexual experiences and health. This systematic review and qualitative meta-synthesis aim to address this gap by examining women's experiences with PAH, informing clinical practice and patient-centered care. The protocol outlines a methodology for synthesizing qualitative research to amplify women's voices and enhance our understanding of PAH's impact on female patients.

Methods and analysis

Search strategy

A systematic review and thematic meta-synthesis of qualitative research studies and qualitative components of mixed-methods studies will be conducted. The systematic review will be guided by the Joanna Briggs Institute methodological framework. A comprehensive search will encompass seven electronic databases and search engine (Ovid Medline, CINAHL, EMBASE, APA PsycINFO, Cochrane Database of Systematic Reviews, PubMed, Scopus) and grey literature sources (ProQuest Dissertations, Clinical Trials. gov). Building on insights from previous reviews centered on symptom-related experience and sexual health. Two review authors will independently conduct the screening and data extraction processes. Discrepancies will be resolved through consensus or discussion with a third review author. The review will include English studies from database inception. Findings will be presented graphically and tabularly, together with a narrative description.

Assessment of Confidence and Data Synthesis

The meta-synthesis used thematic analysis, importing study transcripts and notes into NVivo software. Data-derived codes formed categories, which were then iteratively refined into broader themes reflecting women's experiences with sex and childbirth while living with PAH.

Ethics and dissemination

External ethical approval is not required as this review is a retrospective review, which is undertaking secondary analysis of publicly available primary data. The results will be disseminated in peer-reviewed journals and presented in conference papers and elsewhere. This protocol is registered with PROSPERO prospective database of systematic review.

PROSPERO Registration number CRD42024529342

Strengths and limitations of this study

- The systematic review will employ a comprehensive methodology aligned with the Cochrane methodological framework, underpinned by the framework of Hilary Thomson and Mhairi Campbell with the support of Dario Sambunjak and colleague from Cochrane's People Services Department.
- The heterogeneity in PAH patients across gender and countries regarding age, roles and symptoms

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means significant diversity in their experience and response affecting the disease; we hope to capture this through the review findings as an important link between female patients' response in influencing sexual health and health related quality of life.

-Two reviewers will independently screen titles/abstracts and full-text articles using ReviewManager (RevMan) and then extract data using an adapted Cochrane data extraction template.

- To ensure rigor and transparency, the review will document each step and any discrepancies between reviewers will be resolved through consensus or third-party arbitration, ensuring a thorough and unbiased synthesis of the evidence.

- This systematic review focused exclusively on English-language publications, which may introduce potential biases that could limit the reliability and validity of the study findings.

Background

Pulmonary arterial hypertension (PAH) is a disease marked by elevated blood pressure within the pulmonary arteries. This condition can cause the narrowing, obstruction, or destruction of lung blood vessels, which in turn slows blood flow and raises pulmonary arterial pressure. As a result, the heart has to exert more effort to circulate blood through the lungs. If left untreated, this increased workload can ultimately result in right ventricular failure and death¹. Despite advancements in right heart catheterization technology and new targeted drugs, PAH continues to significantly impact patients' physical, psychological, and social well-being. Patients experience symptoms such as dyspnea, fatigue, chest pain, anxiety, depression, and financial burden²⁻³. Sexual health is a particularly important aspect of quality of life for women with PAH, as the majority of idiopathic PAH patients—nearly 80%—are female, with many in their reproductive years⁴. For women with PAH, the physical symptoms may limit sexual activity, while psychological symptoms can affect desire and relationship dynamics, even maternal injuries during pregnancy and childbirth can be severe, permanent and even fatal⁵. Moreover, previous studies have found that high degrees of sexual dysfunction were observed in women treated with parenteral prostanoids⁶. All these can severely impaired health-related quality of life (HRQOL)⁷.

Sexual health encompasses a broad range of issues, including sexual function, satisfaction, and overall well-being⁸. The symptoms and treatment modalities can have profound implications on sexual experiences of patients with PAH. Furthermore, the fear of intimacy due to concerns about disease progression or the potential impact on pregnancy adds another layer of complexity to their sexual health⁹. Understanding the lived experiences of female patients with PAH is crucial for healthcare providers to deliver patient-centered care and improving quality of life that addresses the holistic needs of patients¹⁰. Despite the recognized importance of sexual health in the overall well-being of individuals with chronic illnesses, the voices of women living with PAH often go unheard, highlighting a need for research that focuses on their unique perspectives and experiences in this under-researched domain. This study focuses on women with PAH as pregnancy and childbirth can significantly affect their condition, and an aspect that is less explored in studies including male patients¹¹. Several qualitative studies have explored the experiences of PAH patients, highlighting challenges in diagnosis, daily life impact, coping mechanisms, and emotional well-being¹²⁻¹⁷. A synthesis by Rawlings GH and colleagues included articles reflecting the experiences of over 1900 individuals with PH, identifying themes related to diagnosis, treatment, prognosis, healthcare professionals, the impact of PH, and coping strategies¹⁸. This review emphasizes the role of

educational and psychological therapies in supporting patients with PAH.

With myriad treatment options now available, the HRQoL has been greatly improved in disease management¹⁹. Despite a more consistent focus on HRQoL in PAH research, we do not fully understand the Sexual Health-Related Quality of Life (SHRQoL) of PAH patients especially of female PAH patients^{20, 21}. This systematic review and qualitative meta-synthesis will conduct a comprehensive search and aim to fill this gap by synthesizing the qualitative research on the experiences of women living with PAH. We aim to elucidate the challenges encountered, coping mechanisms adopted, and support needed by these individuals.

This protocol outlines the methodology and approach that will be taken to conduct a systematic review and qualitative meta-synthesis of the symptom-related experiences and sexual health of female patients with PAH. It sets the stage for a research endeavor that seeks to amplify the voices of women with PAH and contribute to a more patient-centered understanding of the impact and management on the disease.

Methods

Design

The protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO) in April 2024, and the registration number is CRD42024529342. This protocol was designed following the guidelines set forth by the Cochrane Effective Practice and Organization of Care: Qualitative Evidence Synthesis²², while the reporting follows the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) 2015 statement²³ shown in Appendix I. The study will run tentatively from 1 April 2024 to 31 January 2025. In the event of this protocol was registered but not yet published, we will update the registration record by submitting a modification request through the PROSPERO portal, detailing the changes and their rationale, ensuring all revisions are documented and auditable within the registry.

Search strategy

The search strategy will be used for the literature search by three steps²⁴. For step 1, a preliminary search of the PubMed database will be performed on 1 April 2024, analyzing the titles, abstracts, subject terms and Mesh terms in the articles. For step 2, a comprehensive search will be undertaken across all included databases using keywords, subject word and random word; the databases will include Ovid Medline, CINAHL, EMBASE, APA PsycINFO, Cochrane Database of Systematic Reviews, PubMed, Scopus and grey literature sources (ProQuest Dissertations, ClinicalTrials. gov). This task would be finished on 1 May 2024. For step 3, all reference lists of the included literature published before 1 June 2024 will be searched to complement other relevant literature. The search strategy for databases is shown in online supplemental Appendix II. The data synthesis for this study is expected to begin in December 2024.

Eligibility criteria

The inclusion criteria for literature in this study are qualitative studies. And the types of participants focusing on female patients diagnosed with pulmonary arterial hypertension (aged \geq 18 years), regardless of whether or not they were pregnant. The eligible research is in English and the full text can be obtained. Studies focusing on PAH without female patients included will be excluded.

Identification and selection of studies

The results of the electronic database searching will be imported to EndNote V.X9 reference

management software and will use the automated 'Find Duplicates' function to exclude any duplicates. The literature will be independently screened by two researchers (YL, HY) trained in systematic review methodology, who will read the titles and abstracts for the preliminary screening, and then read the full texts for secondary screening and eligibility using a standardized form. Ineligible studies will be excluded, and the reason for exclusion will be recorded. Eligible studies will be included in the analysis. Differences encountered during the screening process will be resolved by the two investigators through negotiation or by discussion with a third investigator (MF). The screening process will be reported using a PRISMA flow chart. We plan to complete the selection of studies on 31 October 2024.

Assessment of methodological quality of included studies

The GRADE-CERQual (Confidence in the Evidence from Reviews of Qualitative Research) evidence grading method will be used to grade the quality of evidence of the synthesized findings²⁵. The GRADE CERQual approach is designed to help researcher of qualitative evidence make informed judgments about the trustworthiness and applicability of the findings^{26,27}. The Critical Appraisal Skills Programme (CASP) checklist for qualitative research will be used to assess methodological limitations of qualitative research²⁸ of which the utilization methods is presented in table 1. The final confidence rating would be classified into one of the following categories: 'high', 'moderate', 'low' or 'very low'.

Two researchers (YL, HY) will independently use the 10-item Critical Appraisal Checklist for qualitative research to assess the methodological quality of the included studies²⁵. Each question is rated 'yes', 'no', 'cannot tell'. it was necessary to achieve a minimum affirmative response in at least six of the domains. Studies fully meeting the above criteria, indicating a low risk of bias, will be graded A. Studies partially meeting the minimum criteria, indicating a moderate risk of bias, will be graded B. Finally, studies not meeting the above quality standards at all, indicating a high risk of bias, will be graded C. Studies with grades of A and B will be included in the qualitative meta-synthesis. Differences encountered by the two investigators (YL, HY) during the evaluation process will be resolved through negotiation or discussion with a third investigator (MF).

Table 1 The utilization of CASP tool for assessing methodological limitations of qualitative studies

Content of Evaluation	
1. Was there a clear statement of the aims of the research?	<input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> cannot tell
2. Was there a clear statement of the aims of the research?	<input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> cannot tell
3. Was the research design appropriate to address the aims of the research?	<input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> cannot tell
4. Was the recruitment strategy appropriate to the aims of the research?	<input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> cannot tell
5. Were the data collected in a way that addressed the research issue?	<input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> cannot tell
6. Has the relationship between researcher and participants been adequately considered?	<input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> cannot tell
7. Have ethical issues been taken into consideration?	<input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> cannot tell
8. Was the data analysis sufficiently rigorous?	<input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> cannot tell
9. Is there a clear statement of findings?	<input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> cannot tell
10. Overall assessment	<input type="checkbox"/> no or few limitations

	<input type="checkbox"/> minor limitations
	<input type="checkbox"/> major limitations

Data extraction

Data extraction was performed by two reviewers (YZ, ZR) using a standardized extraction form. The form was pilot-tested on a sample of articles and refined as necessary. In addition to parameters required for quality appraisal of included studies and thematic analyses, data extraction will contain the following data parameters:

- ▶ Study identifiers (including authors, publication date and country)
- ▶ Context
- ▶ Aims and objectives
- ▶ Study design
- ▶ Sampling frame and recruitment
- ▶ Participants
- ▶ Method of data collection and analysis
- ▶ Summary of major study findings

Data synthesis

The meta-synthesis process involved a thematic analysis approach²⁹. Transcripts and field notes from the included studies were imported into NVIVO (Lumivero) qualitative analysis software. Codes were inductively generated from the data and organized into categories³⁰. Through an iterative process, these categories were refined and synthesized into overarching themes that captured the essence of the women's experiences with sex and delivery during pregnancy with PAH.

Ethics and dissemination

External ethical approval is not required as this review is a retrospective review, which is undertaking secondary analysis of publicly available primary data. The results will be disseminated in peer-reviewed journals and presented in conference papers and elsewhere.

Patient and public involvement

The qualitative meta-synthesis will involve a secondary analysis of publicly available primary data; consequently, there will be no participant or public involvement.

Potential bias and Countermeasures

In the realm of qualitative research synthesis, potential biases can undermine the dependability and potency of study outcomes. These biases include information bias from inaccurate variable measurement, sampling bias when the sample fails to mirror the intended population, and both researcher and reporting biases that can skew result interpretation or lead to selective outcome reporting³¹. To mitigate such risks, we've implemented standardized training for our research team, enforced consistent data collection protocols, and employed a strategy of collaborative, independent analysis by multiple researchers.

Discussion

This synthesis will establish what is known about the components and processes of experience and sexual health concern for female patients with PAH. It is hoped that the conclusion of this study can provide a theoretical basis for medical staff to combine multiple resources for PAH patients and

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provide a new perspective for improving their health-related quality of life.

Strengths and limitations of this study

The strengths of this study include the adoption of a comprehensive methodology in line with the Cochrane methodological framework. We aim to capture the significant diversity in experiences and responses among female PAH patients, particularly focusing on the relationship between female patients' responses and their sexual health and quality of life. The review process will be rigorous, with two independent reviewers using RevMan to screen titles/abstracts and full-text articles, and an adapted Cochrane data extraction template to ensure consistency. Discrepancies will be resolved through consensus or third-party arbitration, maintaining the integrity and transparency of the review. However, a limitation is the focus on English-language publications, which may introduce biases affecting the reliability and validity of the study's findings.

Significance and impact of this review

In the published literature, pulmonary hypertension related qualitative research has mainly focused on social, cultural, and psychological aspects and the impact of disease-related symptoms on emotional and sexual health, and some qualitative research has explored these attributes and behaviors by individuals experiencing and reporting symptoms. This review represents a novel approach to illness perception research. The synthesis and interpretation of the preliminary research of this study will increase the breadth and depth of the findings of the contribution, listen to and understand the feelings and needs of patients with pulmonary hypertension, and provide reference for better health care and guidance for them.

Funding and Contributorship statement

This research is conducted without any funding. Fangfang Ma and Lixiao Yang had contributed equally to this work. Miss He was responsible for study design and data integration. Ma assisted for study design and literature search as well as editing the manuscript. Lixiao Yang and Zhu Yang were responsible for Literature analysis and data extraction. All authors approved the final version of the manuscript submitted and have agreed to be accountable for all aspects of the work. Fangfang M. is responsible for the overall content as guarantor.

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Appendix II The search strategy for databases

P(Participants): female PAH patients
I(Interest of phenomenon): patients’ experiences related to disease and sexual health
Co(Context): self-care or being cared for by others
S(study design): qualitative interview research methods

Pubmed	#1	("Pulmonary Arterial Hypertension"[MeSH Terms]) OR (pulmonary hypertension[Title/Abstract] OR pulmonary arterial hypertension[Title/Abstract] OR "PH"[Title/Abstract] OR "PAH"[Title/Abstract])	618576
	#2	((("Women"[MeSH Terms]) OR (women[Title/Abstract])) OR (female[Title/Abstract])) OR (maternal[Title/Abstract])	2233530
	#3	qualitative research*[Title/Abstract] OR qualitative stud*[Title/Abstract] OR narrative*[Title/Abstract] OR unstructured interview*[Title/Abstract] OR semistructured interview*[Title/Abstract]	194661
	#4	#1 AND #2 AND #3	44
Web of Science	#1	qualitative research* OR qualitative stud* OR narrative* OR unstructured interview* OR semistructured interview* (All Fields)	353195
	#2	women OR female OR maternal (Topic)	1893085
	#3	pulmonary hypertension OR pulmonary arterial hypertension OR PH OR PAH (Topic)	811047
	#4	#1 AND #2 AND #3	224
Embase	#1	'pulmonary arterial hypertension'/exp OR 'pulmonary arterial hypertension' OR ((pulmonary:ab AND hypertension:ab OR pulmonary:ab) AND arterial:ab AND hypertension:ab) OR 'ph':ab OR 'pah':ab	781814
	#2	women OR female OR maternal:ab	13103197
	#3	((qualitative AND research* OR qualitative) AND stud* OR narrative* OR unstructured) AND interview* OR semistructured) AND interview*	212033
	#4	#1 AND #2 AND #3	171
CINAHL	#1	AB: pulmonary hypertension OR pulmonary arterial hypertension OR PH OR PAH	24855
	#2	AB: female OR women OR maternal	626903
	#3	TX:qualitative research* OR qualitative stud* OR narrative* OR unstructured interview* OR semistructured interview*	321651
	#4	#1 AND #2 AND #3	39
APA PsycINFO	#1	AB: pulmonary hypertension OR pulmonary arterial hypertension OR PH OR PAH	1247
	#2	AB: female OR women OR maternal	278965
	#3	TX:qualitative research* OR qualitative stud* OR narrative* OR	186679

		unstructured interview* OR semistructured interview*	
	#4	#1 AND #2 AND #3	8
Cochrane	#1	Title/Abstract/Key words: pulmonary hypertension OR pulmonary arterial hypertension OR PH OR PAH	24914
	#2	All text: female OR women OR maternal	1122852
	#3	All text: qualitative research* OR qualitative stud* OR narrative* OR unstructured interview* OR semistructured interview*	35613
	#4	#1 AND #2 AND #3	156
SCOPUS	#1	Title/Abstract/Key words: pulmonary hypertension OR pulmonary arterial hypertension OR PH OR PAH	39870
	#2	Title/Abstract/Key words: female OR women OR maternal	12699961
	#3	All text: qualitative research* OR qualitative stud* OR narrative* OR unstructured interview* OR semistructured interview*	688729
	#4	#1 AND #2 AND #3	45