

BMJ Open Reproductive concerns among young adult women with breast cancer: a systematic review protocol

Li Hu ^{1,2}, Binbin Xu,³ Pui Hing Chau ,¹ Edmond Pui Hang Choi ¹

To cite: Hu L, Xu B, Chau PH, *et al.* Reproductive concerns among young adult women with breast cancer: a systematic review protocol. *BMJ Open* 2023;**13**:e071160. doi:10.1136/bmjopen-2022-071160

► Prepublication history for this paper is available online. To view these files, please visit the journal online (<http://dx.doi.org/10.1136/bmjopen-2022-071160>).

Received 16 December 2022
Accepted 29 June 2023



© Author(s) (or their employer(s)) 2023. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

¹School of Nursing, The University of Hong Kong, Hong Kong, China

²Breast Surgical Department, The Affiliated Hospital of Guizhou Medical University, Guiyang, China

³The Nethersole School of Nursing, The Chinese University of Hong Kong, Hong Kong, China

Correspondence to

Dr Edmond Pui Hang Choi;
h0714919@connect.hku.hk

ABSTRACT

Introduction Reproductive concerns refer to worries about impaired or lost reproductive ability due to disease or/and treatment. Many young female patients with breast cancer experience reproductive concerns because they still desire to have children at the time of diagnosis. Reproductive concerns can impact patients' treatment decision-making as well as their psychological health and quality of life. Understanding the situation, contributing factors and health-related consequences of reproductive concerns among patients with breast cancer is essential to minimise their impacts.

Methods and analysis A systematic review will be conducted. We will search five English databases (PubMed, Embase, CINAHL, Web of Science and APA PsycInfo) and four Chinese databases (Wang Fang database, VIP, CBM and CNKI) for pertinent studies. Other relevant studies will be identified from the reference lists of included studies. Two reviewers will independently perform study selection, data extraction and quality appraisal. Any discrepancies between the two reviewers will be resolved through consultation and discussion with the senior reviewer. A formal narrative synthesis will be performed to summarise the findings of individual studies. This review aims to improve understanding of the level of reproductive concerns, factors associated with reproductive concerns and health-related consequences of reproductive concerns among patients with breast cancer. The findings can contribute to the development of tailored interventions to alleviate reproductive concerns of patients with breast cancer, enhancing their psychological health and quality of life.

Ethics and dissemination Ethical approval is not required for this review, as it will be based on published studies. The findings will be disseminated by publishing in a journal.

PROSPERO registration number CRD42022375247.

INTRODUCTION

Worldwide, there are approximately 2.26 million new breast cancer cases in women yearly, and around 29% of them are under the age of 50.^{1,2} The survival rate of breast cancer has lately increased due to advancements in diagnosis, screening and treatments,³ but chemotherapy and radiotherapy may cause early menopause, ovarian failure and an increased risk of infertility.⁴⁻⁶ Additionally,

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This will be the first systematic review that not only focuses on the level of reproductive concerns but also summarises their influencing factors and relevant health-related consequences among patients with breast cancer.
- ⇒ This review will only identify articles published in Chinese and English language from journals.
- ⇒ A potential limitation of this review may be the exclusion of qualitative studies, which may provide important insights into understanding the topic of reproductive concerns among young adult women with breast cancer.
- ⇒ Meta-analysis will not be performed due to the anticipated high heterogeneity of study outcomes in this review, limiting the level of evidence of this study.

patients who receive endocrine therapy need to postpone their pregnancy plans.⁴ All these side effects point to the fact that it is more difficult for patients with breast cancer to have children. However, many young women who have been diagnosed with breast cancer nevertheless still desire to have children.⁷ Thus, they may have a concern related to fertility.

The term 'reproductive concerns' was used to reflect concerns about the reproductive ability being impaired or removed because of disease or/and treatment.⁸ It can be used interchangeably with terms such as fertility concerns or childbearing concerns.^{9,10} As identified by breast cancer survivors, their feelings and experience of reproductive concerns mainly include concerns of the effect of fertility on disease prognosis and survival, concerns about their fertility ability, concerns about the health and care of children and feelings of guilt towards spouses and parents for not having children.^{11,12} These findings are consistent with Gorman and colleagues' claims that the main elements of reproductive concerns include fertility potential, partner disclosure, child's health,

personal health, acceptance of infertility and becoming pregnant.¹³

In a web-based study conducted in the USA, 57% of young patients with breast cancer under 40 years old expressed concerns about their ability to conceive after their diagnosis.¹⁴ Similar to this, a Swedish study found that 58% of patients with breast cancer had high levels of at least one aspect of reproductive concerns.¹⁵ For individuals who wanted additional children and had difficulty in conceiving in the past, the reproductive concerns were higher.^{14 16} It is important to note that women who do not want children may also have reproductive concerns. According to a systematic review, even women who do not desire for children felt emotional stress at the prospect of not being able to become pregnant.¹⁶

Patients with breast cancer are negatively impacted by reproductive concerns in many ways. In a previous study, it was discovered that 29% of patients with breast cancer treatment decisions were influenced by concerns about their fertility.¹⁴ Even though endocrine therapy should last at least 5 years for women with hormone receptor-positive breast cancer, those who wish to become pregnant did not begin endocrine therapy or stop the medication before the specified time.^{17 18} Reproductive concerns were also linked to psychological health among patients with cancer.¹⁹ According to previous studies, reproductive concerns contribute to depressive symptoms in patients with breast cancer.^{19 20} Furthermore, the development of reproductive concerns has a negative impact on the long-term quality of life for patients with breast cancer.^{8 21 22}

Numerous studies have been conducted to help understand the issue of reproductive concerns in patients with breast cancer, which in turn have produced varying outcomes. Yu *et al* and Ren *et al* reported relatively lower reproductive concerns,^{23–25} while other researchers found relatively higher concerns of reproduction.^{26 27} The total average score of reproductive concerns measured by Reproductive Concerns after cancer Scale (RCAC) ranged from 47.34 to 63.65.^{23–28} In addition, the level of patients with breast cancer reproductive concerns was affected by many different factors, which include age, educational level, wish for children, number of prior pregnancies, prior difficulty conceiving, social relationship quality and emotion regulation.^{14 24–27} To provide a better understanding of this issue, a systematic review on reproductive concerns is necessary to summarise the level of reproductive concerns as well as their influencing factors and relevant health-related consequences among patients with breast cancer. Recently, a scoping review has been conducted to evaluate the literature on reproductive concerns among adolescent and adult cancer patients in general, which provides some information on reproductive concerns among cancer patients.²⁹ When it is specific to women with breast cancer, there have been two identified reviews related to reproductive concerns of patients with breast cancer in 2009 and 2012, respectively.^{10 16} However, we believe that a more updated review is necessary. On the one hand, many more studies have

been conducted and published since Gorman *et al* developed and published their RCAC in 2014.^{13 15 23–27} On the other hand, the earlier reviews did not consider the influencing factors and negative outcomes of reproductive concerns among patients with breast cancer. To address this knowledge gap, an updated review that incorporates new studies and considers influencing factors and negative effects of reproductive concerns is required. Therefore, we plan to conduct this systematic review to: (1) determine the level of reproductive concerns faced by patients with breast cancer, (2) synthesise factors influencing the reproductive concerns of patients with breast cancer, (3) summarise the health-related consequences (psychological health, physical health or quality of life) caused by the reproductive concerns of patients with breast cancer. The findings of this review will help us understand the issue of reproductive concerns among patients with breast cancer and will provide data for creating specialised interventions to alleviate such concerns and enhance quality of life.

METHODS AND ANALYSIS

This systematic review protocol was developed according to the Preferred Items of Systematic Reviews and Meta-Analysis Protocol 2015 Statement.³⁰ The anticipated start and completion date of the review are 20 April and 30 July 2023, respectively. We registered this review protocol on PROSPERO.

Eligibility criteria

Inclusion criteria

Population

The population of interest will be young adult women diagnosed with breast cancer. Young age at breast cancer diagnosis is defined inconsistently according to previous studies. Some studies reported it as ≤ 50 years old,^{10 25 31–33} some defined it as ≤ 45 years old^{34 35} and some used ≤ 40 years old.^{20 22 36 37} Considering that 15–49 years old is an indicator for reproductive-aged women.³⁸ The present review will define young adult women as those aged 18–49 years old.

Main outcome

The review will include studies that report at least one of the following results: (1) the level of reproductive concerns of patients with breast cancer, (2) the influencing factors of reproductive concerns of patients with breast cancer, (3) the health-related consequences of reproductive concerns on patients with breast cancer (psychological health issues such as depression, anxiety, or quality of life).

Study design

The review will include quantitative studies.

Exclusion criteria

The exclusion criteria of the review include: (1) studies that were not published in Chinese or English language;

Table 1 Literature search strategies in database of PubMed

Search	Query
#1	“breast neoplasms”(MeSH Terms)
#2	(“breast”(Title/Abstract)OR “mamma”(Title/Abstract)) AND (“cancer”(Title/Abstract)OR “tumor”(Title/Abstract)OR “tumour”(Title/Abstract)OR “malignan”(Title/Abstract)OR “neoplas”(Title/Abstract)OR “carcinoma”(Title/Abstract))
#3	#1 OR #2
#4	(“reproduc”(Title/Abstract)OR “fertility”(Title/Abstract)OR “childbearing”(Title/Abstract)OR “parenthood”(Title/Abstract)OR “sexual”(Title/Abstract)) AND (“concern”(Title/Abstract)OR “worr”(Title/Abstract)OR “anxi”(Title/Abstract) OR “distress”(Title/Abstract))
#5	#3 AND #4
#6	Filter-Language: Chinese and English

(2) studies that included all cancer patients, and the interested results of patients with breast cancer cannot be identified; (3) studies that the age of participants was unclear; (4) studies that focused on the psychometric validation of instruments; (5) book chapters, abstract and conference paper; (6) interventional studies.

Databases and search strategy

We will search for studies in four Chinese electronic databases (China National Knowledge Infrastructure, Wan Fang Database, VIP Chinese Journal Database and China Biological Medicine Database) and four English electronic databases (PubMed, Embase, Cumulative Index to Nursing and Allied Health Literature, APA PsycInfo). Reference lists of selected articles will also be checked for additional papers. A comprehensive search strategy will be performed to identify studies relevant to the review outcomes. The free-text terms and Medical Subject Headings retrieved from review questions will be combined by Boolean logic operators for literature searching. No time and region restriction will be placed for literature searching. The search strategy applied in PubMed is provided in [table 1](#). Database-specific search strategies will be created for literature searching in other electronic databases.

Study selection

All the search findings will be imported into EndNote V.20. Duplicated articles will be removed with the help of the software, generating a list of identified articles for review. The list of search findings will be screened and selected by two researchers (LH and BX) according to the established inclusion and exclusion criteria. First, the two researchers will scan the title and abstract to determine whether the article should be classified as potentially meeting the eligibility criteria group or ineligible criteria group. The full text will be retrieved for all studies

potentially meeting eligibility criteria. Then the two researchers will read independently the full text to decide whether the study will be included for review according to the predesigned eligibility criteria, generating the final list of selected articles. The final list of selected articles decided by the two researchers will be compared, and the discrepancies will be resolved by consulting and discussing with the third researcher (EPHC). Finally, the reference list of included studies will be examined for additional articles that may be eligible. The study selection process will be summarised in a flow diagram as recommended by the PRISMA 2020 statement.³⁹

Data extraction

A data extraction form will be designed for data collection. The form will be piloted using a random sample of five included studies by two researchers independently. Adjustments and modifications will be made to the form according to the feedback of two researchers. At the beginning, two researchers (LH and BX) will independently extract data of included studies into the predesigned data extraction form for cross-checking. Data of all studies (both English and Chinese studies) will be extracted by using English language. Then the two researchers will review included studies together and reach consensus on what they extract from the studies. Two researchers will maintain frequent communication and discussion during data collection process to resolve any content discrepancies identified. The data will be extracted include: (1) study characteristics (authors, publication year, study design, objectives, study setting, sample size, data collection time, etc); (2) patients’ characteristics (age, breast cancer stage, treatment, reproductive information such as number of children, reproductive intention after diagnosis, reproductive preservation before treatment, etc); (3) outcome variables and measurement instruments; (4) key findings of the study (the level of reproductive concerns, factors influencing reproductive concerns and health-related consequence caused by reproductive concerns).

Assessment of risk of bias

Critical appraisal of the study quality will be conducted using Joanna Briggs Institute Critical Appraisal Checklist for Analytical Cross-Sectional Studies or Joanna Briggs Institute Critical Appraisal Checklist for Cohort Studies. Two reviewers will conduct the critical appraisal independently, and the disagreements will be addressed by discussion with the third researchers (EPHC) to reach a consensus.

Data synthesis

A formal narrative synthesis will be performed to summarise the findings of this review due to the anticipated heterogeneous outcomes of studies. The findings will be presented systematically, which include patients’ characteristics, the level of reproductive concerns, factors associated with reproductive concerns and health-related

consequences of reproductive concerns. Data will be presented under the relevant subheadings appropriately, and the absence of data in some areas will be mentioned.

DISCUSSION

Due to incomplete fertility planning at the time of diagnosis, many young adult women with breast cancer may still wish to have children despite their diagnosis.^{40 41} Reproductive concerns may surface among women with breast cancer for the impact of breast cancer treatment on reproductive functioning. Numerous studies on the issue of reproductive concerns among patients with breast cancer exist and some findings are conflicting. This review seeks to summarise the current literature on the level of reproductive concerns, their associated factors and health-related outcomes.

The findings of the review will help better understand the issue of reproductive concerns among patients with breast cancer. Additionally, the review's findings will guide healthcare professionals to develop relevant interventions or strategies to address reproductive concerns among patients with breast cancer. Finally, our study will identify knowledge gaps in area of reproductive concerns among patients with breast cancer, providing recommendations for future study priority. To our best knowledge, this will be the first review that focuses explicitly on reproductive concerns among patients with breast cancer. However, the predicted high heterogeneity of outcomes among studies prevents the performance of meta-analysis, which will be the main limitation of this review.

Twitter Edmond Pui Hang Choi @edmondchoihku

Contributors EPHC and LH conceived and designed the systematic review. LH and BX contributed to the search strategy of the systematic review. LH drafted the manuscript. EPHC and PPHC critically reviewed and offered comments on the draft manuscript and approved the final manuscript. All authors read and approved the final manuscript for submission.

Funding Publication made possible in part by support from the HKU Libraries Open Access Author Fund sponsored by the HKU Libraries.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.

ORCID iDs

Li Hu <http://orcid.org/0000-0002-8413-8757>

Pui Hing Chau <http://orcid.org/0000-0003-0287-8020>

Edmond Pui Hang Choi <http://orcid.org/0000-0001-9062-3540>

REFERENCES

- International Agency for Research on Cancer. Estimated number of new cases in 2020, worldwide, female, all ages. n.d. Available: <https://gco.iarc.fr/today/online-analysis-table>
- International Agency for Research on Cancer. Estimated number of new cases in 2020, worldwide, females, ages 0-49 (Excl. NMSC). n.d. Available: <https://gco.iarc.fr/today/online-analysis-table>
- Maaajani K, Jalali A, Alipour S, et al. The global and regional survival rate of women with breast cancer: A systematic review and meta-analysis. *Clin Breast Cancer* 2019;19:165-77.
- Hickey M, Peate M, Saunders CM, et al. Breast cancer in young women and its impact on reproductive function. *Hum Reprod Update* 2009;15:323-39.
- Jacobs LA, Pucci DA. Adult survivors of childhood cancer: the medical and Psychosocial late effects of cancer treatment and the impact on sexual and reproductive health. *J Sex Med* 2013;10:120-6.
- Lambertini M, Goldrat O, Clatot F, et al. Controversies about fertility and pregnancy issues in young patients with breast cancer: Current state of the art. *Curr Opin Oncol* 2017;29:243-52.
- Ju J, Zhang LX, Yue J, et al. An investigation of the fertility needs of young patients with breast cancer. *Chin J Oncol* 2020;42:408-12.
- Wenzel L, Dogan-Ates A, Habbal R, et al. Defining and measuring reproductive concerns of female cancer survivors. *J Natl Cancer Inst Monogr* 2005;34:94-8.
- Holton S, Kirkman M, Rowe H, et al. The childbearing concerns and related information needs and preferences of women of reproductive age with a chronic, Noncommunicable health condition: a systematic review. *Womens Health Issues* 2012;22:e541-52.
- Howard-Anderson J, Ganz PA, Bower JE, et al. Quality of life, fertility concerns, and behavioral health outcomes in younger breast cancer survivors: A systematic review. *J Natl Cancer Inst* 2012;104:386-405.
- Gorman JR, Su HI, Pierce JP, et al. A multidimensional scale to measure the reproductive concerns of young adult female cancer survivors. *J Cancer Surviv* 2014;8:218-28.
- Wang X, Wang Y, Pang J, et al. Qualitative study of fertility concerns experience in of childbearing-aged patients with breast cancer. *J Nurs Tain* 2021;36:329-38.
- Li N, Huang W, Zhang L, et al. Fertility Intension and concern of young breast cancer patients from the perspective of need theory: a qualitative study. *Chin J Mod Nurs* 2021;27:3390-6.
- Partridge AH, Gelber S, Peppercorn J, et al. Web-based survey of fertility issues in young women with breast cancer. *J Clin Oncol* 2004;22:4174-83.
- Ljungman L, Ahlgren J, Petersson L-M, et al. Sexual dysfunction and reproductive concerns in young women with breast cancer: type, prevalence, and predictors of problems. *Psychooncology* 2018;27:2770-7.
- Peate M, Meiser B, Hickey M, et al. The fertility-related concerns, needs and preferences of younger women with breast cancer: a systematic review. *Breast Cancer Res Treat* 2009;116:215-23.
- Sella T, Poorvu PD, Ruddy KJ, et al. Impact of fertility concerns on endocrine therapy decisions in young breast cancer survivors. *Cancer* 2021;127:2888-94.
- Llarena NC, Estevez SL, Tucker SL, et al. Impact of fertility concerns on tamoxifen initiation and persistence. *J Natl Cancer Inst* 2015;107:djv202.
- Logan S, Perz J, Ussher JM, et al. Systematic review of fertility-related psychological distress in cancer patients: informing on an improved model of care. *Psychooncology* 2019;28:22-30.
- Gorman JR, Malcarne VL, Roesch SC, et al. Depressive symptoms among young breast cancer survivors: the importance of reproductive concerns. *Breast Cancer Res Treat* 2010;123:477-85.
- Kang T, Zheng W, Liu M, et al. Fertility concerns and its influence on quality of life in young women with breast cancer during convalescence. *Chin J Prev Contr Chron Dis* 2021;29:387-90.
- Bártolo A, Santos IM, Valério E, et al. Depression and health-related quality of life among young adult patients with breast cancer: the mediating role of reproductive concerns. *J Adolesc Young Adult Oncol* 2020;9:431-5.
- Yu Y, Liu S, Tao Y, et al. The mechanism of self-disclosure and marital intimacy in patients with breast cancer in relation to their mental resilience and reproductive concerns after cancer. *Chin J Nurs Educ* 2020;18:644-9.
- Tan Y, Li X, Fan R, et al. Current situation and influencing factors of fertility anxiety in patients with breast cancer of childbearing age. *Nurs Prac Res* 2022;19:10-6.
- Ren H, Jiao N, Zhao Y. The current situation and influencing factors of reproductive concerns in patients with breast cancer in breeding age. *Chin Nurs Manag* 2022;22:359-63.

- 26 Qiu J, Tang L, Li P, *et al.* An investigation into the reproductive concerns of young women with breast cancer. *Asia Pac J Oncol Nurs* 2022;9:100055.
- 27 Chen Y, Zhang Y, Bao J. The level of reproductive concerns of reproductive-aged patients with breast cancer and its influencing factors. *Matern Child Healthc Chin* 2022;37:117–9.
- 28 Kang T, Zheng W, Liu M, *et al.* Current status of fertility concerns among young women recovering from breast cancer and its impact on quality of life. *Chin J Prev Contr Chron Dis* 2021;29:387–9.
- 29 Xie J, Sun Q, Duan Y, *et al.* Reproductive concerns among adolescent and young adult cancer survivors: A Scoping review of current research situations. *Cancer Medicine* 2022;11:3508–17. 10.1002/cam4.4708 Available: <https://onlinelibrary.wiley.com/toc/20457634/11/18>
- 30 Shamseer L, Moher D, Clarke M, *et al.* Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. *BMJ* 2015;350:g7647.
- 31 Ahmad S, Fergus K, McCarthy M. Psychosocial issues experienced by young women with breast cancer: the minority group with the majority of need. *Curr Opin Support Palliat Care* 2015;9:271–8.
- 32 Liu F, Pang J, Wang X, *et al.* The mediating effect of psychological resilience of breast cancer patients on reproductive concern and quality of life. *Modern Clin Nurs* 2021;20:7–12.
- 33 Sun Y, Chen L, Zhao C, *et al.* The study on relationship between perception of partner responsiveness and reproductive anxiety in breast cancer patients of childbearing age. *J Nurs Adm* 2022;22:134–8.
- 34 Pop F, Iancu M, Achimas Cadariu P, *et al.* Developing a needs assessment questionnaire for women of reproductive age following breast cancer treatment: a cross-sectional pilot study in a Romanian sample. *J BUON* 2018;23:1606–15.
- 35 Lambertini M, Fontana V, Massarotti C, *et al.* Prospective study to optimize care and improve knowledge on ovarian function and/or fertility preservation in young breast cancer patients: results of the pilot phase of the pregnancy and fertility (PREFER) study. *Breast* 2018;41:51–6.
- 36 Xiao Y, Li J, Lei J, *et al.* Qualitative study of the fertility information support experiences of young breast cancer patients. *Eur J Oncol Nurs* 2023;62:S1462-3889(23)00009-1.
- 37 Gorman JR, Usita PM, Madlensky L, *et al.* Young breast cancer survivors: their perspectives on treatment decisions and fertility concerns. *Cancer Nurs* 2011;34:32–40.
- 38 World Health Organization. Reproductive health indicators: guidelines for their generation, interpretation and analysis for global monitoring. 2006. Available: https://apps.who.int/iris/bitstream/handle/10665/43185/924156315X_eng.pdf
- 39 Page MJ, McKenzie JE, Bossuyt PM, *et al.* The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *Syst Rev* 2021;10:89.
- 40 Geue K, Richter D, Schmidt R, *et al.* The desire for children and fertility issues among young German cancer survivors. *J Adolesc Health* 2014;54:527–35.
- 41 Mahey R, Kandpal S, Gupta M, *et al.* Knowledge and awareness about fertility preservation among female patients with cancer: a cross-sectional study. *Obstet Gynecol Sci* 2020;63:480–9.