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# BMJ Open

## Decision Regret Regarding Treatments among Women with Early-Stage Breast Cancer:A Systematic Review Protocol

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Manuscripts

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3 1 Decision Regret Regarding Treatments among Women with Early-Stage Breast Cancer:  
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6 A Systematic Review Protocol  
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54 23 **Word Count 3728**  
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3 **26 ABSTRACT**  
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5 **27 Introduction:** Women with early-stage breast cancer are commonly required to make  
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**28** treatment decisions. Decision regret regarding treatments is an adverse outcome that  
**29** negatively impacts women's psychological well-being and quality of life. A systematic  
**30** review will be conducted to synthesize evidence about decision regret among patients  
**31** regarding treatments for early-stage breast cancer. The study will focus on levels of decision  
**32** regret, what is regretted, and the factors associated with decision regret.

**34** **Methods and analysis:** A systematic review will be conducted following the Preferred  
**35** Reporting Items for Systematic Review and Meta-Analysis Protocols 2015 checklist.  
**36** Electronic databases, including CINAHL Complete, Embase, PubMed, Medline, and Web of  
**37** Science, will be searched for relevant articles published from 2000 to 2021. The reference  
**38** lists of eligible studies will also be manually searched. All types of quantitative, qualitative,  
**39** and mixed-method studies that report on decision regret regarding treatments among women  
**40** with early-stage breast cancer will be included. The primary outcome of this review will be  
**41** patients' levels of decision regret regarding breast cancer treatments, and the secondary  
**42** outcomes will include the content of their regrets, and the factors contributing to decision  
**43** regret. The methodological quality of the studies will be assessed using the Joanna Briggs  
**44** Institute appraisal tools. Meta-analysis and thematic synthesis approaches will be used to  
**45** synthesize quantitative and qualitative data, respectively. A convergent parallel approach will  
**46** be used to integrate quantitative and qualitative findings.

**48** **Ethics and dissemination:** Ethical approval is not required for this systematic review.  
**49** Findings of this work will be disseminated at international conferences and peer-reviewed

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3 50 journals. The findings of this systematic review will inform the development of decision  
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5 51 interventions to improve the decision outcome of breast cancer treatments.  
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10 53 **Registration:** This protocol was registered with the International Prospective Register of  
11  
12 54 Systematic Reviews (PROSPERO) on 06 September 2021 (No. CRD42021260041).  
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15 56  
16 57  
17 58 **Keywords:** breast neoplasm, regret, systematic review, qualitative, meta-analysis, factors  
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3 75 **ARTICLE SUMMARY**  
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5 76 **Strengths and Limitations of This Study**  
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8 77 1. This systematic review will be the first of its kind to provide in-depth knowledge  
9  
10 78 about decision regret related to treatments among women with early-stage breast  
11  
12 79 cancer.  
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14 80 2. This review incorporated all types of studies which differed from other reviews  
15  
16 that only include randomized control trials.  
17 81  
18 82 3. The findings of this review will be used to develop interventions which address  
19  
20 decision regret among women with early-stage breast cancer.  
21 83  
22 84 4. This review only includes studies published in English; thus, eligible studies  
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24 published in other languages may have been missed.  
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## 100 INTRODUCTION

101 Breast cancer is the most prevalent malignancy among women, contributing to 11.6% of new  
102 cancer cases in 2018 <sup>1</sup>. In many countries, the majority of the women with breast cancer were  
103 found to have early-stage breast cancer (ESBC) at the time of diagnosis <sup>2,3</sup>.

104

105 Women with ESBC have a milder form of the disease, superior cure rates, and more  
106 treatment options than those with advanced and metastatic breast cancer (stages 3 and 4).  
107 Clinical trials suggest that survival rates after mastectomy and breast conservative surgery  
108 (BCS) for women with ESBC are equivalent <sup>4,5</sup>, therefore, it is important to empower these  
109 women to make treatment decisions for themselves in order to achieve “shared decision-  
110 making” in breast cancer care <sup>6</sup>. However, choosing among multiple treatment options can be  
111 difficult. For example, a mastectomy surgery benefits women by a lower risk of recurrence  
112 but causes relatively larger body image impairment, whilst a BCS helps women maintain  
113 breast image but exposure women to a higher risk of local recurrence <sup>5</sup>. Therefore, when  
114 choosing between mastectomy and BCS, women must weigh the benefits and side effects of  
115 each option. Facing the difficult treatment choices, some women with ESBC may make a  
116 decision that they will regret in the future <sup>7,8</sup>. Thus, it is important to understand the decision-  
117 making behaviour of women with ESBC.

118

119 In the context of health care, *decision regret* refers to “distress or remorse after a health care  
120 decision” <sup>9</sup>. Decision regret is a significant indicator of treatment decision efficacy and may  
121 emerge when patients feel that they could have had a better outcome if they had chosen a  
122 different treatment <sup>9,10</sup>.

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3 124 In a study from the US, Advani et al. (2019) reported that 100 out of 421 (23.8%) women  
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5 125 with breast cancer (>67 years) had experienced decision regret regarding some forms of local  
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7 126 therapy (e.g., lumpectomy with radiotherapy, brachytherapy, or endocrine therapy or  
8  
9 127 mastectomy). In this study, decision regret was associated with race, education level, and the  
10  
11 128 extent of nodal dissection performed, but not the type of therapy <sup>11</sup>. In another survey among  
12  
13 129 young women (<51 years), 42.5% of 449 women with breast cancer experienced decision  
14  
15 130 regret five years after treatment. Of these women, 24.2% regretted having primary surgery  
16  
17 131 and 21.5% regretted having chemotherapy or radiotherapy <sup>12</sup>. Qualitative explorations also  
18  
19 132 reported women expressed regret about their surgery <sup>12-14</sup>, and their regrets were mostly  
20  
21 133 associated with not engaging in the decision-making process <sup>13</sup> and inadequate information  
22  
23 134 about treatments <sup>12 14</sup>.

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30 136 The physical and psychosocial consequences associated with decision regret have been  
31  
32 137 discussed in previous literature <sup>10 12 15</sup>. Regretting a treatment decision has been associated  
33  
34 138 with a higher probability of undergoing a second round of treatment, which could result in  
35  
36 139 delayed recovery and additional trauma. Regret regarding cancer treatments has also been  
37  
38 140 associated with poor psychological well-being and quality of life <sup>15 16</sup>. Experiencing regret  
39  
40 141 about a treatment decision may also increase patients' financial burden, especially for  
41  
42 142 patients from economically disadvantaged backgrounds. Additionally, studies show that  
43  
44 143 decision regret may damage the relationship between patients and their healthcare providers  
45  
46 144 <sup>17 18</sup>, such as blame of the doctor <sup>17</sup>. Thus, it is important for health care providers to support  
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48 145 patients' decision making and minimise the occurrence of decision regret in clinical practice.  
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56 147 Previous reviews on decision regret related to breast reconstruction <sup>19</sup> and contralateral  
57  
58 148 prophylactic surgery <sup>20 21</sup> could not provide a holistic understanding of decision regret  
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149 regarding ESBC treatments because other treatments, such as breast-conserving surgery,  
 150 chemotherapy, and radiotherapy, are also common choices for ESBC. To date, there is a lack  
 151 of literature synthesis regarding levels of decision regret, what patients regret, and factors  
 152 associated with decision regret regarding breast cancer treatments among women with ESBC.  
 153 Without such an understanding, it is difficult for healthcare workers to develop supportive  
 154 interventions to help patients make treatment decisions.

### 156 **Review Objectives**

157 A systematic review will be conducted to assess studies dealing with decision regret  
 158 regarding breast cancer treatment among patients with ESBC. The treatment approaches of  
 159 interest will include unilateral mastectomy, breast-conserving surgery, chemotherapy,  
 160 radiotherapy, endocrine therapy, and targeted therapy. The Participants, Interventions,  
 161 Comparators and Outcomes (PICO) elements used for the systematic review are listed in  
 162 Table 1.

163 The detailed objectives are:

- 164 1) To assess levels of decision regret among women with ESBC;
- 165 2) To identify what women regret;
- 166 3) To identify factors associated with decision regret.

168 Table 1. The PICO Elements Used as Selection Criteria in This Systematic Review.

<b>Participants</b>	<ul style="list-style-type: none"> <li>• Women with early-stage breast cancer (stage 0/carcinoma in situ, stage 1 and stage 2).</li> </ul>
<b>Intervention/Exposure</b>	<ul style="list-style-type: none"> <li>• Experienced decision regret regarding their treatments.</li> </ul>

<b>Comparators</b>	<ul style="list-style-type: none"> <li>• No restriction. The comparator depends on the study design.</li> <li>• For example, the comparator could be a group of the normal population for a cohort comparative study; if the included study is a randomized control trial to assess the effectiveness of a decision aid, the comparator could be the group of the population who had not received the decisional intervention.</li> </ul>
<b>Outcomes</b>	<ul style="list-style-type: none"> <li>• Levels of decision regret;</li> <li>• Events/processes/things that women regret;</li> <li>• Factors associated with decision regret.</li> </ul>
<b>Settings</b>	<ul style="list-style-type: none"> <li>• No restriction</li> </ul>

169

## 170 METHODS AND ANALYSIS

171 This protocol has been registered with the International Prospective Register of Systematic  
 172 Reviews (PROSPERO; registration number: CRD42021260041). The Preferred Reporting  
 173 Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) 2015 checklist is  
 174 followed to report this protocol<sup>22</sup> (See supplemental material 1). This systematic review is  
 175 anticipated to be performed during August 2021 and January 2022.

176

### 177 Study Selection

#### 178 Information Sources

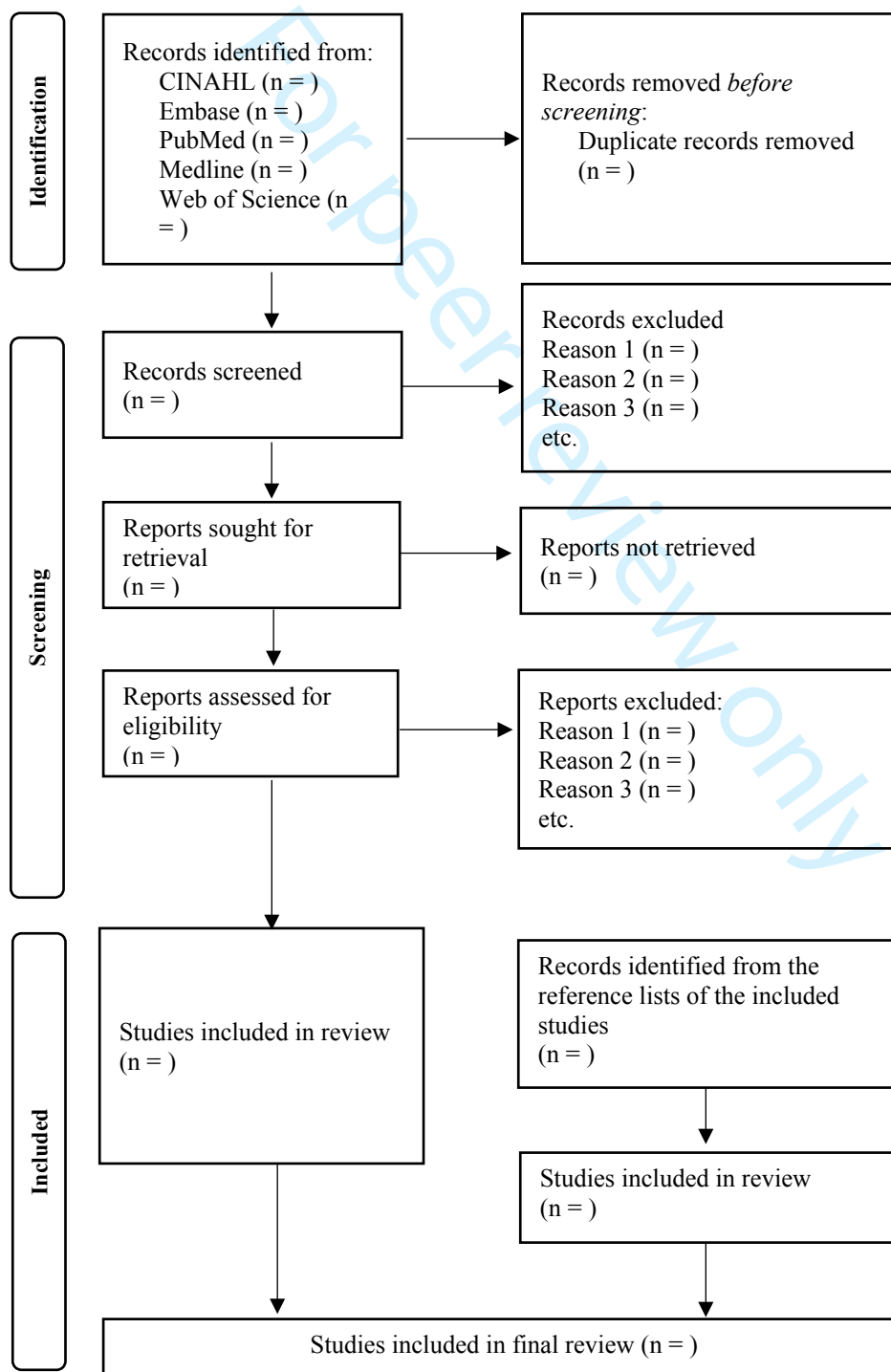
179 The authors will search electronic databases including CINAHL Complete, Embase,  
 180 PubMed, Medline, and Web of Science. A manual search of the reference lists of eligible  
 181 studies will be also performed. This systematic review will include primary studies published  
 182 from January 2000 to June 2021 in order to provide the most recent evidence.

183

#### 184 Selection Process

185 Two authors will independently conduct the literature search (JL and SH). Another researcher  
 186 will validate the search process to ensure accuracy (SC). All studies will be exported using

1  
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3 187 Endnote X9 software for duplicate removal and further screening. Thereafter, two authors  
4  
5 188 will independently review the titles, abstracts, and full texts of these papers to determine their  
6  
7 189 eligibility (JL and SH). Disagreement about study eligibility will be resolved through  
8  
9 190 discussions among all researchers (JL, SH, JMZ, RL, and SC). The selection process will be  
10  
11 191 presented in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses  
12  
13 192 PRISMA flow diagram (see Figure 1).  
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15 192 PRISMA flow diagram (see Figure 1).  
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228 Figure 1. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses  
 229 (PRISMA) Flow Diagram and Selection Process.

230

231 Search Terms

232 The keyword search terms are derived from the main concepts of the research topic. The key  
 233 terms will include: “breast cancer,” “breast tumor,” “breast neoplasm,” “breast carcinoma,”  
 234 “early-stage breast cancer,” “early breast cancer,” “regret,” “decision regret,” “treatment,”  
 235 “intervention,” and “therapy.” An example of the search strategy is presented in Table 2.

236

237 Table 2. Search Strategy Used for CINAHL Complete Database

238

Main Concepts	Search Terms	Outcomes
Breast Cancer	1. Breast cancer or breast tumor or breast neoplasm or breast carcinoma or early-stage breast cancer or early breast cancer	109,841
Regret	2. Regret or decision regret	1,676
Treatment	3. Treatment or intervention or therapy	2,343,406
Combined: 1 and 2 and 3		61
Publication Year Limit from 2000 to 2021		58

239

240

241 Inclusion and Exclusion Criteria

242 All relevant quantitative, qualitative, and mixed-methods studies written in the English  
 243 language will be included. There will be no restrictions regarding the design or setting of the  
 244 study, as long as they are:

- 245 1) primary studies reporting decision regret regarding unilateral mastectomy, breast-  
 246 conserving surgery, chemotherapy, radiotherapy, endocrine therapy, or targeted  
 247 therapy;
- 248 2) among patients with ESBC; and
- 249 3) published in the English language.

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5 251 Studies regarding risk-reducing treatment (e.g., contralateral prophylactic mastectomy) and  
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8 252 reconstructive surgery will be excluded because there have been three published reviews  
9  
10 253 specifically addressing these surgeries. Secondary studies and grey literature will also be  
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12 254 excluded.

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## 17 256 **Analysis**

### 19 257 Outcome Measures

21 258 The primary outcome of the systematic review will be patients' levels of decision regret  
22  
23 259 regarding breast cancer treatment. The secondary outcomes will include what patients regret  
24  
25 260 when they recall their decision-making process and the factors contributing to their decision  
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27  
28 261 regret.

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### 33 263 Data Evaluation

35 264 Three researchers will conduct the data evaluation independently (JL, JMZ, and RL), and  
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37 265 another author's (SC) advice will be sought if there is disagreement. The methodological  
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39 266 quality of eligible studies will be evaluated using critical appraisal tools developed by the  
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41 267 Joanna Briggs Institute. These tools were developed to assist in assessing the trustworthiness,  
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43 268 relevance, and results of quantitative and qualitative studies. For qualitative studies,  
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45 269 researchers are required to respond (*yes, no, unclear, or not applicable*) to ten questions to  
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47 270 determine whether a study has addressed the possibility of bias in its design, conduct, or  
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49 271 analysis<sup>23</sup>. Following these questions, researchers will decide if the study should be included  
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51 272 or excluded, or if additional information should be sought<sup>23</sup>. Disagreements regarding study  
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53 273 inclusion will be discussed by the entire group of researchers.  
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3 275 Data Extraction and Synthesis  
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5 276 Two researchers will analyze the data independently (JL and SH). Included studies will be  
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7 277 first categorized into quantitative, qualitative, or mixed-methods studies according to their  
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9 278 design. Information on the year of publication, author(s), setting, participant characteristics  
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11 279 (e.g., age, number of participants, cancer stage, and treatment received), measures (e.g.,  
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13 280 instruments, time of measurement, and comparative groups), interventions (e.g., blinding and  
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15 281 randomized methods), and findings of interest (e.g., level of decision regret, what patients  
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17 282 regret, and factors associated with decision regret) will be extracted. The extracted data will  
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19 283 be compiled into an Excel spreadsheet by each researcher before being compared by both  
20  
21 284 researchers for completeness and accuracy. Any discrepancies will be resolved through  
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23 285 discussion within the research group (JL, SH, JMZ, RL, and SC).  
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30 286  
31 287 Quantitative results will be pooled into Review Manager Software (RevMan) Version 5 to  
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33 288 conduct a meta-analysis where appropriate<sup>24</sup>. A forest plot will be created to present the  
34  
35 289 pooled results. For example, if there are several interventional studies that have evaluated the  
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37 290 effectiveness of decision aids in reducing patient-perceived regret, odds ratios (for  
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39 291 dichotomous variables) or weighted mean differences (for continuous variables) and their  
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41 292 95% confidence intervals (CIs) will be calculated in order to precisely describe the impact of  
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43 293 decision aids on decision regret. The  $I^2$  statistic will be used to assess heterogeneity, and a  
44  
45 294 value lower than 50% will be considered to indicate low heterogeneity. In case of low  
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47 295 heterogeneity, the fixed-effects model will be applied to assess the pooled results. Otherwise,  
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49 296 the pooled results will be assessed using the random-effects model. Sensitivity analysis will  
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51 297 be conducted if the pooled results have substantial heterogeneity, and the results will be  
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53 298 carefully interpreted. A subgroup analysis on the interventions and types of received  
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55 299 treatment (e.g., chemotherapy or radiotherapy) will be performed where applicable. The  
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3 300 publication bias will be indicated by the asymmetry of the funnel plot <sup>25</sup>. The findings will be  
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5 301 described in narrative form where meta-analysis is impossible. For example, if there is only  
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8 302 one cross-sectional survey reporting regret after chemotherapy, results concerning the level of  
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10 303 regret, what women regret, and related factors will be narratively described.

304

14 305 Qualitative evidence will be analyzed using the thematic synthesis approach proposed by  
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16  
17 306 Thomas and Harden <sup>26</sup>. Qualitative studies will be read and reread by two researchers (JL and  
18  
19 307 SH), and findings associated with the three review questions will be identified and coded  
20  
21 308 line-by-line. These initial codes will be compared and consolidated until a number of  
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23  
24 309 descriptive subthemes emerge. All researchers will discuss the subthemes until a consensus is  
25  
26 310 reached regarding whether the subthemes comply with the meaning of the original study.  
27  
28 311 Thereafter, similar subthemes will be further grouped based on their similarity in order to  
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30  
31 312 produce several analytical themes that are pertinent to the review questions. A coding sheet  
32  
33 313 will be developed by the author to facilitate the data synthesis. The other three researchers  
34  
35 314 (JMZ, RL, and SC) will comment on the synthesis by reviewing the coding sheet until a final  
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37 315 consensus is reached.

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42 317 A third integrative analysis using a convergent parallel approach will be conducted to  
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44 318 incorporate the quantitative and qualitative findings <sup>27</sup>. Quantitative outcomes and qualitative  
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47 319 themes will be combined to provide rich insights into the three review questions. It is  
48  
49 320 anticipated the quantitative outcomes will quantify the qualitative findings, and the  
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51 321 qualitative themes will help explain the quantitative outcomes; thus, the review findings will  
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54 322 be convergent and complimentary <sup>28</sup>.

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324 *Quality of Evidence*

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3 325 The Grading of Recommendations, Assessment, Development and Evaluation (GRADE)  
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5 326 guidelines will be followed to evaluate the certainty of reviewed evidence <sup>29</sup>, and a GRADE  
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7 327 evidence profile will be included when reporting the review findings.  
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9

10 328

### 11 329 *Patient and Public Involvement*

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14 330 Patients and/or the public are not involved in the design, or conduct, or reporting or  
15  
16 331 dissemination plans of this research.  
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19 332

### 20 333 **Ethics and Dissemination**

21  
22  
23 334 Ethical approval is not required for this systematic review because no human participants will  
24  
25 335 be involved. The findings of this study will be disseminated in international peer-reviewed  
26  
27 336 journals and at nursing conferences. This review will also be disseminated as part of Jing  
28  
29 337 Liu's PhD thesis.  
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3 **419 Authors Contributions**  
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5 420 All authors contributed to the design of this review. JL drafted the initial manuscript of this  
6  
7 421 protocol. SH and SC provided important comments to the manuscript. JL and SH will search  
8  
9 422 and select the studies, and conduct the data analysis. JL, RL, and JMZ will appraise the  
10  
11 423 quality of included studies. SC will validate the study selection, study evaluation, and data  
12  
13 424 synthesis process. All authors (JL, SH, SC, RL and JMZ) will involve in resolving  
14  
15 425 disagreement and drafting publications of the systematic review. All authors have approved  
16  
17 426 the publication of this protocol.  
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23  
24 **428 Funding Statement**  
25

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27  
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30 431 preparation of this article.  
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35 **433 Competing Interests Statement**  
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37 434 The authors declare that they have no competing interests.  
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42 **436 Availability of Data and Materials**  
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44 437 Not applicable for this protocol.  
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49 **439 Consent for Publication**  
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51 440 Not applicable.  
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59  
60

# Reporting checklist for protocol of a systematic review and meta-analysis.

Based on the PRISMA-P guidelines.

	Reporting Item	Page Number
<b>Title</b>		
Identification	<a href="#">#1a</a> Identify the report as a protocol of a systematic review	1
Update	<a href="#">#1b</a> If the protocol is for an update of a previous systematic review, identify as such	NA, It is a protocol for a new systematic review.
<b>Registration</b>		
	<a href="#">#2</a> If registered, provide the name of the registry (such as PROSPERO) and registration number	3
<b>Authors</b>		
Contact	<a href="#">#3a</a> Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contribution	<a href="#">#3b</a> Describe contributions of protocol authors and identify the guarantor of the review	17
<b>Amendments</b>		
	<a href="#">#4</a> If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	NA, It is a protocol for a new systematic review.
<b>Support</b>		
Sources	<a href="#">#5a</a> Indicate sources of financial or other support for the review	17
Sponsor	<a href="#">#5b</a> Provide name for the review funder and / or sponsor	17
Role of sponsor or funder	<a href="#">#5c</a> Describe roles of funder(s), sponsor(s), and / or institution(s), if any, in developing the protocol	17
<b>Introduction</b>		
Rationale	<a href="#">#6</a> Describe the rationale for the review in the context of what is already known	5-7

1	Objectives	<a href="#">#7</a>	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	7-8
2				
3				
4	<hr/>			
5	<b>Methods</b>			
6				
7	Eligibility criteria	<a href="#">#8</a>	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	7-8, 10-11
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12				
13	Information sources	<a href="#">#9</a>	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	8-9
14				
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17				
18	Search strategy	<a href="#">#10</a>	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	10
19				
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21				
22	Study records - data management	<a href="#">#11a</a>	Describe the mechanism(s) that will be used to manage records and data throughout the review	11
23				
24				
25	Study records - selection process	<a href="#">#11b</a>	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	11-12
26				
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31	Study records - data collection process	<a href="#">#11c</a>	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	11-12
32				
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36	Data items	<a href="#">#12</a>	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	12
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41	Outcomes and prioritization	<a href="#">#13</a>	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	11
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45	Risk of bias in individual studies	<a href="#">#14</a>	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	12
46				
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50	Data synthesis	<a href="#">#15a</a>	Describe criteria under which study data will be quantitatively synthesised	12-13
51				
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53	Data synthesis	<a href="#">#15b</a>	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I <sup>2</sup> , Kendall's $\tau$ )	12-13
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1	Data synthesis	<a href="#">#15c</a>	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	12-13
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4	Data synthesis	<a href="#">#15d</a>	If quantitative synthesis is not appropriate, describe the type of summary planned	13
5				
6				
7	Meta-bias(es)	<a href="#">#16</a>	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	12-13
8				
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11	Confidence in	<a href="#">#17</a>	Describe how the strength of the body of evidence will be	13-14
12	cumulative		assessed (such as GRADE)	
13	evidence			
14				

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For peer review only

# BMJ Open

## Decision Regret Regarding Treatments among Women with Early-Stage Breast Cancer: A Systematic Review Protocol.

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2021-058425.R1
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Secondary Subject Heading:	Evidence based practice, Nursing, Patient-centred medicine, Mental health
Keywords:	Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Protocols & guidelines < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, MENTAL HEALTH, Breast tumours < ONCOLOGY

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Manuscripts

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3 1 Decision Regret Regarding Treatments among Women with Early-Stage Breast Cancer:  
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6 A Systematic Review Protocol  
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54 23 **Word Count 3931**  
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3 26 **ABSTRACT**  
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5 27 **Introduction:** Women with early-stage breast cancer are commonly required to make  
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7 28 treatment decisions. Decision regret regarding treatments is an adverse outcome that  
8  
9 29 negatively affects women's psychological well-being and quality of life. A systematic review  
10  
11 30 will be conducted to synthesize evidence about decision regret among patients regarding  
12  
13 31 treatments for early-stage breast cancer. The study will focus on levels of decision regret,  
14  
15 32 what is regretted, and the factors associated with decision regret.  
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21 34 **Methods and analysis:** A systematic review will be conducted following the Preferred  
22  
23 35 Reporting Items for Systematic Review and Meta-Analysis Protocols 2015 checklist.  
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25 36 Electronic databases, including CINAHL Complete, Embase, PubMed, Medline, and Web of  
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27 37 Science, will be searched for relevant articles published from 2000 to 2021. The reference  
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29 38 lists of eligible studies will also be manually searched. All types of quantitative, qualitative,  
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31 39 and mixed-method studies that report on decision regret regarding treatments among women  
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33 40 with early-stage breast cancer will be included. The primary outcome of this review will be  
34  
35 41 patients' levels of decision regret regarding breast cancer treatments, and the secondary  
36  
37 42 outcomes will include the content of their regrets, and the factors contributing to decision  
38  
39 43 regret. The methodological quality of the studies will be assessed using the Joanna Briggs  
40  
41 44 Institute appraisal tools. Meta-analysis and thematic synthesis approaches will be used to  
42  
43 45 synthesize quantitative and qualitative data, respectively. A convergent parallel approach will  
44  
45 46 be used to integrate quantitative and qualitative findings.  
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48 48 **Ethics and dissemination:** Ethical approval is not required for this systematic review.  
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50 49 Findings of this work will be disseminated at international conferences and peer-reviewed  
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3 50 journals. The findings of this systematic review will inform the development of decision  
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5 51 interventions to improve the decision outcome of breast cancer treatments.  
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10 53 **Registration:** This protocol was registered with the International Prospective Register of  
11  
12 54 Systematic Reviews (PROSPERO) on 06 September 2021 (No. CRD42021260041).  
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15 56  
16 57  
17 58 **Keywords:** breast neoplasm, regret, systematic review, qualitative, meta-analysis, factors  
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3 75 **ARTICLE SUMMARY**  
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5 76 **Strengths and Limitations of This Study**  
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- 7  
8 77 • This review will include all types of studies which differed from other reviews that  
9  
10 78 only include randomized control trials.  
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12 79 • Meta-analysis and narrative description will be used to analyze quantitative data, and  
13  
14 80 a thematic synthesis approach will be used to synthesize qualitative data, producing  
15  
16 81 robust evidence about decision regret about breast cancer treatments.  
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18 82 • A third integrative analysis using a convergent parallel approach will be conducted to  
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20 83 incorporate the quantitative and qualitative findings; thus, the review findings will be  
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22 84 convergent and complementary.  
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24 85 • This review only includes studies published in English; thus, eligible studies  
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26 86 published in other languages may be missed.  
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## 100 INTRODUCTION

101 Breast cancer is the most prevalent malignancy among women, contributing to 11.7% of new  
102 cancer cases in 2020<sup>1</sup>. In many countries, the majority of the women with breast cancer were  
103 found to have early-stage breast cancer (EBC) at the time of diagnosis<sup>2,3</sup>.

104

105 Women with EBC have a milder form of the disease, superior cure rates, and more treatment  
106 options than those with advanced and metastatic breast cancer (stages 3 and 4). Clinical trials  
107 suggest that survival rates after mastectomy and breast conservative surgery (BCS) for  
108 women with EBC are equivalent<sup>4,5</sup>; therefore, it is important to empower these women to  
109 make treatment decisions for themselves to achieve “shared decision-making” in breast  
110 cancer care<sup>6,7</sup>. However, choosing among multiple treatment options can be difficult. For  
111 example, a mastectomy surgery benefits women by a lower risk of recurrence but causes  
112 relatively larger body image impairment, whilst a BCS helps women maintain breast image  
113 but exposure women to a higher risk of local recurrence<sup>5</sup>. Therefore, when choosing between  
114 mastectomy and BCS, women must weigh the benefits and side effects of each option.  
115 Negative emotions, such as fear, can further complicate the decision-making about breast  
116 cancer treatments<sup>8,9</sup>. Facing the difficult treatment choices, some women with EBC may  
117 make a decision that they will regret in the future<sup>10,11</sup>. Thus, it is important to understand the  
118 decision-making behaviour of women with EBC.

119

120 In the context of health care, *decision regret* refers to “remorse or distress over a decision”<sup>12</sup>.

121 Decision regret is a significant indicator of treatment decision efficacy and may emerge when  
122 patients feel that they could have had a better outcome if they had chosen a different  
123 treatment<sup>12,13</sup>. In a study from the US, Advani et al. (2019) reported that 100 out of 421  
124 (23.8%) older women with breast cancer (>67 years) had experienced decision regret

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3 125 regarding some forms of local therapy (e.g., lumpectomy with radiotherapy, brachytherapy,  
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5 126 or endocrine therapy or mastectomy). In this study, decision regret was associated with race,  
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7 127 education level, and the extent of nodal dissection performed, but not the type of therapy <sup>14</sup>.  
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10 128 In another survey among young women (<51 years), 42.5% of 449 women with breast cancer  
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12 129 experienced decision regret five years after treatment. Of these women, 24.2% regretted  
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14 130 having primary surgery and 21.5% regretted having chemotherapy or radiotherapy <sup>15</sup>.  
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17 131 Qualitative explorations also reported women expressed regret about their treatment decisions  
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19 132 <sup>15-17</sup>, and their regrets were mostly associated with not engaging in the decision-making  
20  
21 133 process <sup>16</sup> and inadequate information <sup>15 17</sup>.  
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24 134  
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26 135 The physical and psychosocial consequences associated with decision regret have been  
27  
28 136 discussed in previous literature <sup>13 15 17 18</sup>. Regretting a treatment decision has been associated  
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30 137 with a higher probability of undergoing a second round of treatment, which could result in  
31  
32 138 delayed recovery and additional trauma. Regret regarding cancer treatments has also been  
33  
34 139 associated with poor psychological well-being and quality of life <sup>18 19</sup>. Experiencing regret  
35  
36 140 about a treatment decision may also increase patients' financial burden, especially for  
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38 141 patients from economically disadvantaged backgrounds. Additionally, studies show that  
39  
40 142 decision regret may damage the relationship between patients and their healthcare providers  
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42 143 <sup>20 21</sup>. Thus, it is important for health care providers to support patients' decision-making and  
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44 144 minimise the occurrence of decision regret in clinical practice.  
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50 145  
51 146 Reviews summarizing evidence about patients' decision-making about breast cancer  
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53 147 treatments have been published <sup>22 23</sup>, However, they have not specifically addressed the issue  
54  
55 148 of regret about treatment decisions, and were not able to generalize to the whole population  
56  
57 149 because these reviews only included older women <sup>22</sup> and women who had a mastectomy <sup>23</sup>.  
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3 150 Previous reviews on decision regret related to breast reconstruction <sup>24</sup> and risk-reducing  
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5 151 treatment <sup>25 26</sup> also could not provide a holistic understanding of decision regret regarding  
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7 152 EBC treatments because other treatments, such as breast-conserving surgery, chemotherapy,  
8  
9 153 and radiotherapy, are also common choices for EBC. To date, there is a lack of literature  
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11 154 synthesis regarding levels of decision regret, what patients regret, and factors associated with  
12  
13 155 decision regret regarding breast cancer treatments among women with EBC. Without such an  
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15 156 understanding, it is difficult for healthcare professionals to develop supportive interventions  
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17 157 to help patients make treatment decisions.  
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### 159 **Review Objectives**

160 A systematic review will be conducted to assess studies dealing with decision regret  
161 regarding breast cancer treatment among patients with EBC. The treatment approaches of  
162 interest will include unilateral mastectomy, breast-conserving surgery, chemotherapy,  
163 radiotherapy, endocrine therapy, and targeted therapy. The Participants, Interventions,  
164 Comparators and Outcomes (PICO) elements used for the systematic review are listed in  
165 Table 1. The detailed objectives are:

- 166 1) To assess levels of decision regret about treatments among women with EBC;  
167 2) To identify what women regret;  
168 3) To identify factors associated with decision regret.

169

170 Table 1. The PICO Elements Used as Selection Criteria in This Systematic Review.

<b>Participants</b>	<ul style="list-style-type: none"> <li>Women with early-stage breast cancer (stage 0/carcinoma in situ, stage 1 and stage 2).</li> </ul>
<b>Intervention/Exposure</b>	<ul style="list-style-type: none"> <li>Experienced decision regret regarding their treatments.</li> </ul>

<b>Comparators</b>	<ul style="list-style-type: none"> <li>• No restriction. The comparator depends on the study design.</li> <li>• For example, the comparator could be a group of the normal population for a cohort comparative study; if the included study is a randomized control trial to assess the effectiveness of a decision aid, the comparator could be the group of the population who had not received the decisional intervention.</li> </ul>
<b>Outcomes</b>	<ul style="list-style-type: none"> <li>• Levels of decision regret;</li> <li>• Events/processes/things that women regret;</li> <li>• Factors associated with decision regret.</li> </ul>
<b>Settings</b>	<ul style="list-style-type: none"> <li>• No restriction</li> </ul>

171

## 172 METHODS AND ANALYSIS

173 This protocol has been registered with the International Prospective Register of Systematic  
 174 Reviews (PROSPERO; registration number: CRD42021260041). The Preferred Reporting  
 175 Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) 2015 checklist is  
 176 followed to report this protocol <sup>27</sup> (See Supplemental Material 1). This systematic review is  
 177 anticipated to be performed during August 2021 and January 2022.

178

### 179 Study Selection

#### 180 Information Sources

181 The authors will search electronic databases including CINAHL Complete, Embase,  
 182 PubMed, Medline, and Web of Science. A manual search of the reference lists of eligible  
 183 studies will be also performed. This systematic review will include primary studies published  
 184 from January 2000 to June 2021 in order to provide the most recent evidence.

185

#### 186 Selection Process

187 Two authors will independently conduct the literature search (JL and SH). Another researcher  
 188 will validate the search process to ensure accuracy (SC). All studies will be exported using

189 Endnote X9 software for duplicate removal and further screening. Thereafter, two authors  
190 will independently review the titles, abstracts, and full texts of these papers to determine their  
191 eligibility (JL and SH). Disagreement about study eligibility will be resolved through  
192 discussions among all researchers (JL, SH, JMZ, RL, and SC). The selection process will be  
193 presented in the Preferred Reporting Items for Systematic Reviews and Meta-Analysis  
194 PRISMA flow diagram (see Figure 1).

#### 196 Search Terms

197 The keyword search terms are derived from the main concepts of the research topic. The key  
198 terms will include “breast cancer,” “breast tumor,” “breast neoplasm,” “breast carcinoma,”  
199 “early-stage breast cancer,” “early breast cancer,” “regret,” “decision regret,” “treatment,”  
200 “intervention,” and “therapy.” Search strategies for all databases are presented in  
201 Supplementary Material 2.

#### 203 Inclusion and Exclusion Criteria

204 All relevant quantitative, qualitative, and mixed-methods studies written in the English  
205 language will be included. There will be no restrictions regarding the design or setting of the  
206 study, as long as they are:

- 207 1) primary studies reporting decision regret regarding unilateral mastectomy, breast-  
208 conserving surgery, chemotherapy, radiotherapy, endocrine therapy, or targeted  
209 therapy;
- 210 2) among patients with EBC; and
- 211 3) published in the English language.

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213 Studies regarding risk-reducing treatment (e.g., contralateral prophylactic mastectomy) and  
214 reconstructive surgery will be excluded because there have been three published reviews



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3 215 specifically addressing these surgeries<sup>19 25 26</sup>. Secondary studies and grey literature will also  
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5 216 be excluded.  
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10 218 **Analysis**

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12 219 Outcome Measures

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14 220 The primary outcome of the systematic review will be patients' levels of decision regret  
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16 221 regarding breast cancer treatments. Levels of decision regret was measured using different  
17  
18 222 methods across the studies. For example, decision regret was measured using the validated 5-  
19  
20 223 item, 5-point Likert Decision Regret Scale in Advani et al.'s (2019) study. Researchers in this  
21  
22 224 study considered scores 1, 2 and 3 as feeling regret, while 4 and 5 indicated no regret<sup>14</sup>.  
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24 225 Martinez et al. (2013) revised the items of the Decision Regret Scale. In this study, the ratings  
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26 226 of each item were summed up as total scores ranging from 0 to 20, where higher scores  
27  
28 227 indicated higher levels of regret<sup>28</sup>. Regret was also measured by a single-item dichotomous  
29  
30 228 choice question in Yamauchi et al.'s (2019) study, in which women were asked to indicate  
31  
32 229 "having no regret" or "having some regret" about breast cancer treatments<sup>29</sup>.  
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40 231 The secondary outcomes will include what patients regret when they recall their  
41  
42 232 decision-making process and the factors contributing to their decision regret.  
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47 234 Data Evaluation

48  
49 235 Three researchers will conduct the data evaluation independently (JL, JMZ, and RL), and  
50  
51 236 another author's (SC) advice will be sought if there is disagreement. The methodological  
52  
53 237 quality of eligible studies will be evaluated using critical appraisal tools developed by the  
54  
55 238 Joanna Briggs Institute. These tools were developed to assist in assessing the trustworthiness,  
56  
57 239 relevance, and results of quantitative and qualitative studies. For qualitative studies,  
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3 240 researchers are required to respond (*yes, no, unclear, or not applicable*) to ten questions to  
4  
5 241 determine whether a study has addressed the possibility of bias in its design, conduct, or  
6  
7 242 analysis<sup>30</sup>. Following these questions, researchers will decide if the study should be included  
8  
9  
10 243 or excluded, or if additional information should be sought<sup>30</sup>. Disagreements regarding study  
11  
12 244 inclusion will be discussed by the entire group of researchers.  
13  
14  
15 245

#### 16 17 246 Data Extraction and Synthesis

18  
19 247 Two researchers will analyze the data independently (JL and SH). Included studies will be  
20  
21 248 first categorized into quantitative, qualitative, or mixed-methods studies according to their  
22  
23 249 design. Information on the year of publication, author(s), setting, participant characteristics  
24  
25 250 (e.g., age, number of participants, cancer stage, and treatment received), measures (e.g.,  
26  
27 251 instruments, time of measurement, and comparative groups), interventions (e.g., blinding and  
28  
29 252 randomized methods), and findings of interest (e.g., level of decision regret, what patients  
30  
31 253 regret, and factors associated with decision regret) will be extracted. The extracted data will  
32  
33 254 be compiled into an Excel spreadsheet by each researcher before being compared by both  
34  
35 255 researchers for completeness and accuracy. Any discrepancies will be resolved through  
36  
37 256 discussion within the research group (JL, SH, JMZ, RL, and SC).  
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258 Quantitative results will be pooled into Review Manager Software (RevMan) Version 5 to  
259 conduct a meta-analysis where appropriate<sup>31</sup>. A forest plot will be created to present the  
260 pooled results. For example, if there are several interventional studies that have evaluated the  
261 effectiveness of decision aids in reducing patient-perceived regret, odds ratios (for  
262 dichotomous variables) or weighted mean differences (for continuous variables) and their  
263 95% confidence intervals (CIs) will be calculated in order to precisely describe the impact of  
264 decision aids on decision regret. The  $I^2$  statistic will be used to assess heterogeneity, and a

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3 265 value lower than 50% will be considered to indicate low heterogeneity. In case of low  
4  
5 266 heterogeneity, the fixed-effects model will be applied to assess the pooled results. Otherwise,  
6  
7 267 the pooled results will be assessed using the random-effects model. Sensitivity analysis will  
8  
9 268 be conducted if the pooled results have substantial heterogeneity, and the results will be  
10  
11 269 carefully interpreted. A subgroup analysis on the interventions and types of received  
12  
13 270 treatment (e.g., chemotherapy or radiotherapy) will be performed where applicable. The  
14  
15 271 publication bias will be indicated by the asymmetry of the funnel plot <sup>32</sup>. The findings will be  
16  
17 272 described in narrative form where meta-analysis is impossible. For example, if there is only  
18  
19 273 one cross-sectional survey reporting regret after chemotherapy, results concerning the level of  
20  
21 274 regret, what women regret, and related factors will be narratively described.  
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28 276 Qualitative evidence will be analyzed using the thematic synthesis approach proposed by  
29  
30 277 Thomas and Harden <sup>33</sup>. Qualitative studies will be read and reread by two researchers (JL and  
31  
32 278 SH), and findings associated with the three review questions will be identified and coded  
33  
34 279 line-by-line. These initial codes will be compared and consolidated until a number of  
35  
36 280 descriptive subthemes emerge. All researchers will discuss the subthemes until a consensus is  
37  
38 281 reached regarding whether the subthemes comply with the meaning of the original study.  
39  
40 282 Thereafter, similar subthemes will be further grouped based on their similarity in order to  
41  
42 283 produce several analytical themes that are pertinent to the review questions. A coding sheet  
43  
44 284 will be developed by the author to facilitate the data synthesis. The other three researchers  
45  
46 285 (JMZ, RL, and SC) will comment on the synthesis by reviewing the coding sheet until a final  
47  
48 286 consensus is reached.  
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56 288 A third integrative analysis using a convergent parallel approach will be conducted to  
57  
58 289 incorporate the quantitative and qualitative findings <sup>34</sup>. Quantitative outcomes and qualitative  
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3 290 themes will be combined to provide rich insights into the three review questions. It is  
4  
5 291 anticipated the quantitative outcomes will quantify the qualitative findings, and the  
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7  
8 292 qualitative themes will help explain the quantitative outcomes; thus, the review findings will  
9  
10 293 be convergent and complementary <sup>35</sup>.

294

### 295 *Quality of Evidence*

17 296 The Grading of Recommendations, Assessment, Development and Evaluation (GRADE)  
18  
19 297 guidelines will be followed to evaluate the certainty of reviewed evidence <sup>36</sup>, and a GRADE  
20  
21 298 evidence profile will be included when reporting the review findings.

299

### 300 *Patient and Public Involvement*

28 301 Patients and/or the public are not involved in the design, or conduct, or reporting or  
29  
30 302 dissemination plans of this research.

303

### 304 **Ethics and Dissemination**

37 305 Ethical approval is not required for this systematic review because no human participants will  
38  
39 306 be involved. The findings of this study will be disseminated in international peer-reviewed  
40  
41 307 journals and at nursing conferences. This review will also be disseminated as part of Jing  
42  
43 308 Liu's PhD thesis.

309

49 310 Figure 1. The Preferred Reporting Items for Systematic Reviews and Meta-Analysis

51 311 (PRISMA) Flow Diagram and Selection Process.

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14  
15 414 **Authors Contributions**

16  
17 415 All authors contributed to the design of this review. JL drafted the initial manuscript of this  
18  
19 416 protocol. SH and SC provided important comments to the manuscript. JL and SH will search  
20  
21 417 and select the studies, and conduct the data analysis. JL, RL, and JMZ will appraise the  
22  
23 418 quality of included studies. SC will validate the study selection, study evaluation, and data  
24  
25 419 synthesis process. All authors (JL, SH, SC, RL and JMZ) will involve in resolving  
26  
27 420 disagreement and drafting publications of the systematic review. All authors have approved  
28  
29 421 the publication of this protocol.

30  
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38  
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40  
41 426 preparation of this article.

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45 427  
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47 428 **Competing Interests Statement**

48  
49 429 The authors declare that they have no competing interests.

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52 430  
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54 431 **Availability of Data and Materials**

55  
56 432 Not applicable for this protocol.

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434 **Consent for Publication**

435 Not applicable.

436

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For peer review only

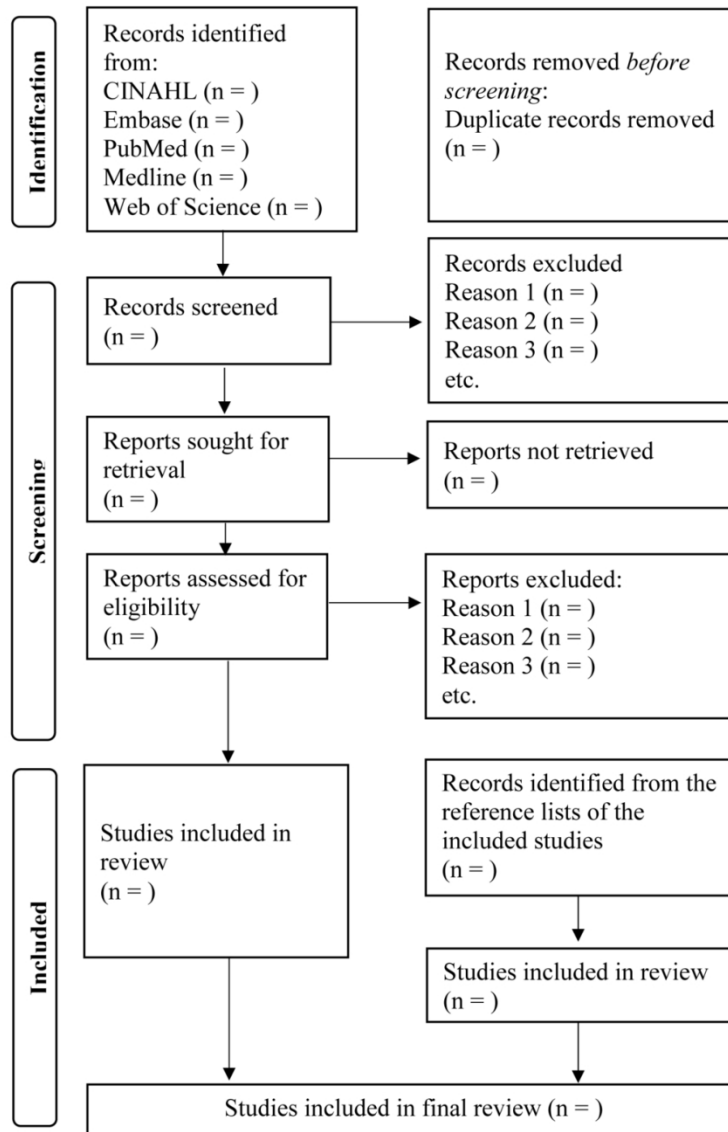


Figure 1. The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) Flow Diagram and Selection Process.

89x139mm (300 x 300 DPI)

## Supplementary Material 1: Reporting Checklist for Protocol of A Systematic Review and Meta-Analysis.

		Reporting Item	Page Number in Manuscript
<b>Title</b>			
Identification	<u>#1a</u>	Identify the report as a protocol of a systematic review	1
Update	<u>#1b</u>	If the protocol is for an update of a previous systematic review, identify as such	NA, It is a protocol for a new systematic review.
<b>Registration</b>			
	<u>#2</u>	If registered, provide the name of the registry (such as PROSPERO) and registration number	3
<b>Authors</b>			
Contact	<u>#3a</u>	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contribution	<u>#3b</u>	Describe contributions of protocol authors and identify the guarantor of the review	18
<b>Amendments</b>			
	<u>#4</u>	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	NA, It is a protocol for a new systematic review.
<b>Support</b>			
Sources	<u>#5a</u>	Indicate sources of financial or other support for the review	18
Sponsor	<u>#5b</u>	Provide name for the review funder and / or sponsor	18
Role of sponsor or funder	<u>#5c</u>	Describe roles of funder(s), sponsor(s), and / or institution(s), if any, in developing the protocol	18
<b>Introduction</b>			
Rationale	<u>#6</u>	Describe the rationale for the review in the context of what is already known	5-7
Objectives	<u>#7</u>	Provide an explicit statement of the question(s) the review will address with	7-8

reference to participants, interventions, comparators, and outcomes (PICO)

## Methods

Eligibility criteria	<u>#8</u>	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	7-10
Information sources	<u>#9</u>	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	8
Search strategy	<u>#10</u>	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	9 and Supplementary Material 2
Study records - data management	<u>#11a</u>	Describe the mechanism(s) that will be used to manage records and data throughout the review	11
Study records - selection process	<u>#11b</u>	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	10-11
Study records - data collection process	<u>#11c</u>	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	11-12
Data items	<u>#12</u>	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	11
Outcomes and prioritization	<u>#13</u>	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	10
Risk of bias in individual studies	<u>#14</u>	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	11-12
Data synthesis	<u>#15a</u>	Describe criteria under which study data will be quantitatively synthesised	11-12
Data synthesis	<u>#15b</u>	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies,	11-12

1			including any planned exploration of	
2			consistency (such as I <sup>2</sup> , Kendall's $\tau$ )	
3	Data synthesis	<u>#15c</u>	Describe any proposed additional analyses	11-12
4			(such as sensitivity or subgroup analyses,	
5			meta-regression)	
6				
7	Data synthesis	<u>#15d</u>	If quantitative synthesis is not appropriate,	12
8			describe the type of summary planned	
9				
10	Meta-bias(es)	<u>#16</u>	Specify any planned assessment of meta-	12
11			bias(es) (such as publication bias across	
12			studies, selective reporting within studies)	
13				
14				
15	Confidence in	<u>#17</u>	Describe how the strength of the body of	13
16	cumulative		evidence will be assessed (such as GRADE)	
17	evidence			

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## Supplementary Material 2: Full Search Strategies for All Databases.

Database	Search Strategy
CINAHL Complete	TX ( breast cancer or breast tumor or breast neoplasm or breast carcinoma or early-stage breast cancer or early breast cancer ) AND TX ( regret or decision regret ) AND TX ( treatment or intervention or therapy ) Filters: publication time from 2000-2021
Embase	1. (breast cancer or breast tumor or breast neoplasm or breast carcinoma or early-stage breast cancer or early breast cancer).mp. 2. Limit 1 to (full text and yr="2000 - 2021") 3. (regret or decision regret).mp. 4. Limit 3 to (full text and yr="2000 - 2021") 5. (treatment or intervention or therapy).mp 6. Limit 5 to (full text and yr="2000 - 2021") 7. 1 and 2 and 3 and 4 and 5 and 6
PubMed	(((((("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND ("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "tumor"[All Fields]) OR "breast tumor"[All Fields])) OR ("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "neoplasm"[All Fields]) OR "breast neoplasm"[All Fields]) OR ("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "carcinoma"[All Fields]) OR "breast carcinoma"[All Fields]) OR ("early"[All Fields] AND ("stage"[All Fields] OR "staged"[All Fields] OR "stages"[All Fields] OR "staging"[All Fields] OR "stagings"[All Fields]) AND ("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields])) OR ("early"[All Fields] AND ("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]))) AND ("emotions"[MeSH Terms] OR "emotions"[All Fields] OR "regret"[All Fields] OR "regrets"[All Fields] OR "regretful"[All Fields] OR "regretted"[All Fields] OR "regretting"[All Fields] OR ("decision"[All Fields] OR "decision s"[All Fields] OR "decisions"[All Fields] OR "decisive"[All Fields] OR "decisively"[All Fields]) AND ("emotions"[MeSH Terms] OR "emotions"[All Fields] OR "regret"[All Fields] OR "regrets"[All Fields] OR "regretful"[All Fields] OR

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"regretted"[All Fields] OR "regretting"[All Fields])) AND ("therapeutics"[MeSH Terms] OR "therapeutics"[All Fields] OR "treatments"[All Fields] OR "therapy"[MeSH Subheading] OR "therapy"[All Fields] OR "treatment"[All Fields] OR "treatment s"[All Fields] OR ("intervention s"[All Fields] OR "interventions"[All Fields] OR "interventive"[All Fields] OR "methods"[MeSH Terms] OR "methods"[All Fields] OR "intervention"[All Fields] OR "interventional"[All Fields]) OR ("therapeutics"[MeSH Terms] OR "therapeutics"[All Fields] OR "therapies"[All Fields] OR "therapy"[MeSH Subheading] OR "therapy"[All Fields] OR "therapy s"[All Fields] OR "therapys"[All Fields])) AND (2000:2021[pdat]))

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**Medline**

1. (breast cancer or breast tumor or breast neoplasm or breast carcinoma or early-stage breast cancer or early breast cancer).mp.
2. Limit 1 to (full text and yr="2000 - 2021")
3. (regret or decision regret).mp.
4. Limit 3 to (full text and yr="2000 - 2021")
5. (treatment or intervention or therapy).mp.
6. Limit 5 to (full text and yr="2000 - 2021")
7. 1 and 2 and 3 and 4 and 5 and 6

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**Web of Science** ((ALL=(breast cancer or breast tumor or breast neoplasm or breast carcinoma or early-stage breast cancer or early breast cancer)) AND ALL=(regret or decision regret)) AND ALL=(treatment or intervention or therapy )  
Filters: publication time from 2000.01.01-2021.06.30

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