



# Exploring the Association Between Breastfeeding and Risk of Rheumatoid Arthritis

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## ABSTRACT

**Background:** Rheumatoid arthritis (RA) is a progressive autoimmune disease that leads to impaired physical function. The treatment focuses on disease management since it is an irremediable condition. As such, prevention is crucial. However, relatively few prevention strategies exist because of the unknown etiology. RA affects 0.9% of Canadians; however, this is expected to increase.

**Objective:** The purpose of this study was to review the existing literature and assess evidence pertaining to the association between breastfeeding and development of rheumatoid arthritis.

**Methods:** A structured literature review was conducted. Articles were retrieved from PubMed and SCOPUS using the keywords "rheumatoid arthritis" AND ("breastfeeding" OR "lactation"). The articles were limited to those written in the English language with full text available. Systematic reviews and meta-analyses were excluded.

**Results:** Nine articles were deemed relevant to the study. Five indicated breastfeeding to be protective against the development of rheumatoid arthritis while two suggested breastfeeding increased the risk of RA. In two studies, neither a positive nor negative association could be determined. Additionally, there was no consensus as to the duration of breastfeeding required to elicit a reduced risk.

**Conclusions:** The literature reviewed in this study supports the association between breastfeeding and reduced risk of rheumatoid arthritis. However, due to the varying results in the literature and the uncertain etiology of RA, further research is needed to reinforce the relationship and determine a causal mechanism. Additional research is also required to establish the duration of breastfeeding necessary to reduce risk.

## INTRODUCTION

### Background

- RA is a progressive autoimmune disease commonly affecting joints in the hands, wrists, knees, and ankles. Individuals with RA often experience stiffness and pain. The chronic inflammation may lead to instability, deformity, and impaired physical function.
- In 2011, RA affected 0.9 percent of Canadians.<sup>1</sup> The global prevalence is estimated to be between 0.3 and 1 percent.<sup>2</sup> RA is more common in women and in developed countries.<sup>2</sup> In fact, below the age of fifty, the incidence of RA is four to five times higher in women than men.<sup>3</sup>
- Current treatment focuses on disease management since RA is an irremediable condition.
- RA has an uncertain etiology. However, its development is thought to be a result of a combination of genetic and environmental factors including hormones.
- There is a decreased risk of developing RA while pregnant but an increased risk postpartum, particularly within the first 3 months.<sup>4</sup>
- There have been inconsistent findings in regards to the effect of breastfeeding on RA.

### Research Question

Does the practice of breastfeeding reduce the risk of developing rheumatoid arthritis in women over the age of 17?

## METHODS

### Study Design: Structured review

- Databases: Pubmed, SCOPUS
- Search Terms: "Rheumatoid Arthritis" AND ("Breastfeeding" OR "Lactation")
- Inclusion Criteria:
  - Peer-reviewed articles
  - English
  - Full text available
- Exclusion Criteria
  - Systematic review or meta-analysis
  - Existing cases of RA or otherwise irrelevant articles

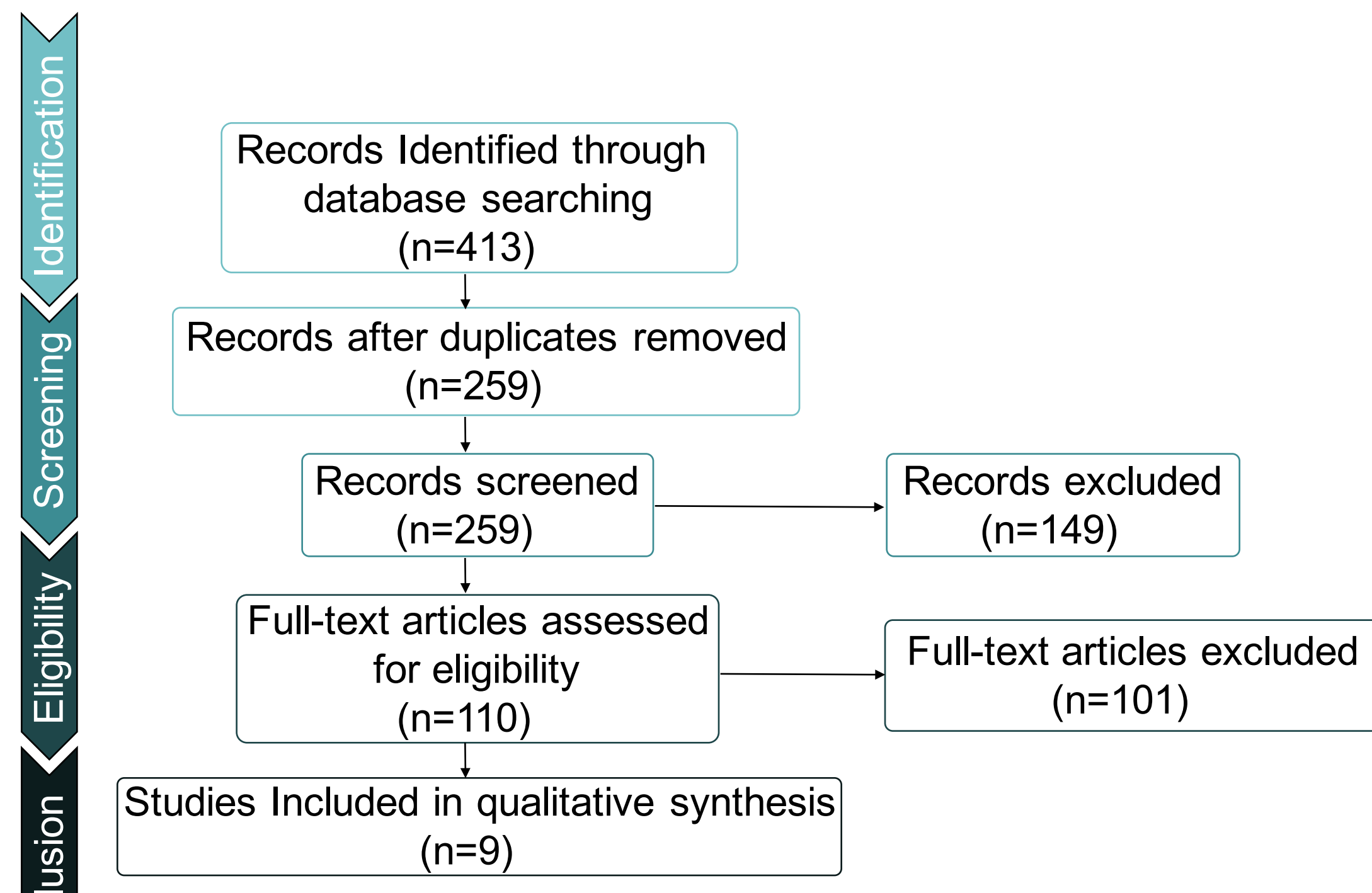


Figure 1. PRISMA flowchart of structured review

## RESULTS

Article	Author (Year)	Study Design	Country	Sample Size	Age	Methods	Results Risk (95% CI)
1	Lahiri et al. (2014)	Population-based prospective cohort	UK	137 772	40-79	Self-administered questionnaire regarding demographic, health, and lifestyle factors Blood samples for ACPA and RF status	RA Breastfeeding HR 0.71 (0.49-1.03)
2	Karlson et al. (2004)	Prospective Cohort	USA	121 700	30-55	Biennial mailed questionnaire regarding diseases, lifestyle, and health practices Medical Records screened to confirm RA diagnosis	≤3 months RR 1.0 (0.8-1.2) 4-11 months RR 0.9 (0.7-1.1) 12-23 months RR 0.8 (0.6-1.0) ≥24 months <b>RR 0.5 (0.3-0.8)</b>
3	Pikwer et al. (2009)	Case-control	Sweden	680	44-74	Self-administered questionnaire on lifestyle factors, reproductive factors, and health status	1-12 months OR 0.74 (0.45-1.20) ≥13 months <b>OR 0.46 (0.24-0.91)</b>
4	Adab et al. (2014)	Cohort	UK	7349	≥50	Comprehensive structured interview and examination Questionnaire on socioeconomic status, family and personal disease histories and lifestyle habits	1-11 months OR 0.81 (0.51-1.31) 12-35 months <b>OR 0.62 (0.42-0.91)</b> ≥36 months <b>OR 0.54 (0.36-0.82)</b>
5	Shishavan et al. (2016)	Hospital-based Case-control	Iran	469	26-64	Interviewer administered questionnaires related to reproductive events prior to developing RA	≤3 months OR 0.16 (0.01-1.88) 4-11 months <b>OR 0.04 (0.01-0.44)</b> 12-23 months <b>OR 0.06 (0.01-0.65)</b> ≤24 months <b>OR 0.06 (0.01-0.59)</b>
6	Brennan et al. (1994)	Case-control	UK	336		Mailed questionnaire on details of pregnancy and breastfeeding, age, marital status, SES status, and OC use. Clinical details of diagnosis (RF status) from rheumatologist or GP	1 <sup>st</sup> pregnancy <b>OR 5.4 (2.5-11.4)</b> • Seropositive erosive <b>RA 8.0 (2.7-23.5)</b> • Seronegative erosive <b>RA 4.6 (1.5-13.6)</b> • Seropositive nonerosive RA 2.0 (0.5-7.6) 2 <sup>nd</sup> pregnancy OR 2.0 (0.8-5.0) 3 <sup>rd</sup> pregnancy OR 0.6 (0.2-2.2)
7	Berglin et al. (2010)	Case-control	Sweden	350	20.1-68.4	Questionnaire concerning previous exposures until disease onset including hormonal and reproductive factors, and smoking habits Blood samples to determine ACPA	4-8 months <b>OR 4.0 (1.32-11.98)</b> 9-16 months <b>OR 3.2 (1.08-9.73)</b> ≥17 months <b>OR 5.7 (1.83-17.95)</b>
8	Merlino et al. (2003)	Prospective Cohort	US	31 336	55-59	Baseline questionnaire on demographic data, weight history, reproductive history, lifestyle factors, and history of various medical conditions Four mailed follow up questionnaires	No association for number of children breastfed and risk of RA Information on duration of breastfeeding was unavailable
9	Orellana et al. (2017)	Population-based case-control	Sweden	6892	≥18	Questionnaire on lifestyle and environmental exposures Blood samples to determine ACPA status	7-12 months OR 0.93 (0.75-1.14) ≥13 months <b>OR 0.77 (0.63-0.94)</b> *No longer significant when adjusted for smoking and alcohol consumption

Table 1. Results of structured literature review.

## DISCUSSION

- Of the nine included studies, five found breastfeeding to be protective against the development of rheumatoid arthritis. Two studies suggested breastfeeding increased the risk of RA and two other studies did not determine an association.
- There was a lack of consensus as to the duration of breastfeeding required to elicit a reduced risk. However, there appears to be a dose-dependent relationship between breastfeeding and RA with long-term effects.
- Limitations of the reviewed articles include; selection bias, recall bias, small sample size in studies indicating an increased risk.
- Limitations of the structured review include;
  - Restriction to peer-reviewed articles published in English accessible through PubMed and SCOPUS databases
  - Difficulty comparing articles due to differences between studies in regards to; definition of RA, categorization of the duration of breastfeeding, and confounders adjusted for.



## CONCLUSION

The results from the literature review are inconsistent. As such, it is not possible to conclusively determine whether breastfeeding reduces the risk of developing rheumatoid arthritis. However, after assessing the quality of the studies, it appears as though long durations of breastfeeding, specifically over 12 months, is protective against the development of RA. As such, more research is needed to fully elucidate the association.

In addition, studies that found an increased risk of RA suggest the proinflammatory nature of prolactin as a possible mechanism while studies that found a protective effect of breastfeeding suggest progesterone and cortisol are involved in reducing risk. Therefore, further research into the etiology of rheumatoid arthritis and the mechanism involved in the association between breastfeeding and risk of developing rheumatoid arthritis is needed.

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