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# The effects of intermittent fasting on anthropometric indices, glycemic profile, chemotherapy-related toxicity, and subjective perception in gynecological and breast cancer patients: a systematic review and meta-analysis

Xiaoxia Liu[1], Qiucen Meng[1], Wenqi Fan[1], Lianzhen Ning[1] and Lina Ge[1*]

## Abstract

**Background** Mounting evidence supports the health benefits of intermittent fasting (IF) in general. This study evaluates its impact on patients with gynecological or breast cancer specifically.

**Methods** A thorough search for studies comparing IF with either nonintervention diets or calorie restriction (CR) in patients with either gynecological or breast cancer and published prior to October 5, 2024 was carried out on the PubMed, Web of Science, Cochrane Library, Scopus, Embase, China National Knowledge Infrastructure (CNKI), and Chinese Biomedical Literature databases (CBM). Extracted data included but not limited to body mass index (BMI), body weight, waist circumference (WC), fasting glucose, insulin levels, chemotherapy-related toxicity, and subjective perceptions.

**Results** A total of 625 subjects were included across 7 randomized controlled trials, and 2 nonrandomized trials. Meta-analysis revealed that IF significantly reduced body weight (Effect Size [ES]: -0.611; 95% Confidence Interval [CI]: -0.886 to -0.356; $p < 0.001$; $I^2 = 0\%$), blood glucose levels (standardized mean difference [SMD]: -0.347 mmol/L; 95% CI: -0.533 to -0.140; $p < 0.001$), and insulin concentrations (SMD: -0.395 mU/L; 95% CI: -0.674 to -0.116; $p = 0.005$). Sensitivity analysis indicated that the overall effect sizes were stable. However, it remains uncertain whether IF increases chemotherapy-related adverse effects (relative risk [RR]: 1.038; 95% CI: 0.844 to 1.278; $p = 0.723$). Furthermore, three studies indicated that IF reduced fatigue and two studies indicated that IF improved quality of life.

**Conclusion** This systematic review and meta-analysis suggests that IF has a beneficial effect on reducing body weight, blood glucose, and insulin concentrations in gynecological and breast cancer patients. IF may also reduce

*Correspondence:
Lina Ge
liuxx19970428@163.com

Full list of author information is available at the end of the article

fatigue and improve quality of life. However, the effect on chemotherapy-related adverse effects is uncertain. Further high-quality studies with long-term follow-ups are needed to confirm these findings.

**Keywords** Gynecological cancer, Breast cancer, Intermittent fasting, Time-restricted eating, Short-term fasting

## Introduction

Despite significant advancements in oncology, cancer remains a leading cause of death among adults aged 30 to 70 years. The Global Cancer Statistics indicate that there were 20 million new cancer cases and approximately 10 million cancer-related deaths worldwide in 2022 [1]. Specifically, there were 2,308,897 new cases of breast cancer, 661,021 new cases of cervical cancer, 420,242 new cases of endometrial cancer, and 324,398 new cases of ovarian cancer among women, and cervical and breast cancer have been found to be the leading cancer-related causes of death among women [2].

Bray et al. [1] found that approximately 42.0% of new malignancies in individuals aged 30 and older are associated with potentially modifiable risk factors. For example, excess body weight accounted for the second largest population attributable fraction (PAF) at 7.8%, and being overweight was responsible for 10.9% of all malignancies in women. Breast and uterine body cancers among women have also been found to be associated with being overweight [3]. A positive association between adult body mass index (BMI) and the risk of gynecological and breast cancers has been observed in a number of studies [4–7]. Furthermore, mounting evidence indicates that obesity is associated with an increased risk of cancer development, recurrence, and death [8, 9].

Dietary patterns may be a key nonpharmacological intervention for enhancing cancer treatment and improving overall patient outcomes. Intermittent Fasting (IF) was the most commonly cited nonstandard dietary pattern for Americans aged 18 to 80 as of 2020 [10]. IF, which is characterized by alternating periods of consumption and extended abstention from food, has garnered significant attention in recent years due to its potential health benefits and positive contributions to longevity [11]. IF can be categorized into five types: zero-calorie, alternate-day fasting (ADF); modified alternate-day fasting (MADF); twice-weekly fasting (TWF); time-restricted eating (TRE); and periodic or short-term fasting (FST) [12] (Table 1).

Recent meta-analyses have highlighted the potential health benefits of IF, particularly in relation to being overweight, type 2 diabetes, and cardiovascular disease, that stem from weight loss and enhanced metabolic health [13–17]. Calorie restriction (CR), when free from malnutrition, has been found to be the most effective intervention for cancer prevention in rodents and primates [18, 19]. In humans, IF promotes anticancer adaptations by reducing the synthesis of growth factors, pro-inflammatory cytokines, and anabolic hormones, as well as decreasing oxidative stress and free radical-induced DNA damage [8, 20, 21]. Several randomized clinical trials have demonstrated that ADF or the 5:2 diet positively impacts certain cancer risk factors, including reductions in fasting blood glucose, insulin, and leptin levels, as well as increases in lipocalin [22–25].

Kleckner et al. [26] conducted a TRE intervention in breast and endometrial cancer patients and found that TRE alleviated fatigue in breast and endometrial cancer patients. Similarly, Vega et al. [22] demonstrated that TRE reduced body weight and waist circumference, and improved blood glucose levels in breast cancer patients. In another study, Bauersfeld et al. [24] showed that FST improved the quality of life in patients with breast and ovarian cancers. However, some studies have presented inconsistent results. For instance, Harvie et al. [27] reported that TWF did not have a significant effect on weight loss in breast cancer, and Groot et al. [28] found that FST did not significantly improve chemotherapy-related toxicity in breast cancer patients. Thus, the effects of IF on weight, metabolism, and chemotherapy toxicity in gynecological and breast cancers remain unclear, and there are limited systematic evaluations and meta-analyses to assess its benefits and risks comprehensively in patients with these cancers. Only Ferro et al. [29] have previously conducted a meta-analysis in 2023 on the effect of IF on the side effects of chemotherapy in cancer patients. To the best of our knowledge, no meta-analysis or systematic review has yet been conducted on the effects of IF on body weight, metabolic health, and quality of life in patients with gynecological or breast cancers.

Specifically, our present study explore the potential of IF as a nonpharmacological intervention for gynecological and breast cancer patients by evaluating its effects on anthropometric measures, metabolic outcomes, chemotherapy-related toxicities, and subjective health indicators, with the ultimate goal of informing clinical decision-making.

## Methods

A comprehensive systematic review and meta-analysis was conducted to evaluate the effects of IF methods in patients with gynecological or breast cancers. The systematic review followed the 2020 guidelines of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA), and the synthesis protocol has been registered with PROSPERO (CRD42024605963).

**Table 1** Different types of IF

| Type | Definition |
|---|---|
| Zero-calorie, alternate-day fasting (ADF) | Individuals consume no calories every other day. On fasting days, only noncaloric beverages, such as water, unsweetened tea, and black coffee, are permitted, with no intake of food or any other calories. |
| Modified alternate-day fasting (MADF) | Individuals cycle between periods of free eating and fasting during which intake of calories varied from 0 to 40% of daily requirements, or from 0 to approximately 600 kcal, three to five days each week. |
| Twice-per-week fasting (TWF) | Individuals fast for two days per week, restricting caloric intake from 0 to 40% of daily requirements, or between 0 and approximately 600 kcal per day, followed by five days of unrestricted eating. |
| Time-restricted eating (TRE) | Individuals fast for 12–24 h per day. |
| Periodic fasting/ short-term fasting (FST) | Individuals undergo infrequent but prolonged fasting intervals, such as a 2- to 5-day pure water fast or a 4- to 7-day |

### Search methods

Seven electronic databases were searched: the Cochrane Central Register of Controlled Trials, Embase, PubMed, Scopus, Web of Science, China Knowledge Network (CNKI), and the China Biomedical Literature Database (CBM). The timeframe for the search extended from the inception of each database to October 5, 2024. L.X.X. and M.Q.C. conducted the search, utilizing terms related to cancer (e.g., cancer*, neoplasm*, tumor*) combined with those pertaining to IF (e.g., IF, periodic fasting, alternate-day fasting, modified alternate-day fasting, time-restricted feeding, Ramadan fasting). No language restrictions were applied. Furthermore, reference lists from acquired papers, prior meta-analyses, and reviews were examined to locate other pertinent studies. The detailed search terms used in the review are presented in Supplementary Material 2. After the initial literature screening, relevant articles were selected using specific keywords.

### Eligibility criteria

The Population, Intervention, Comparison, Outcome, and Study Design (PICOS) framework was utilized to define the inclusion criteria for this systematic review. L.X.X, M.Q.C, and N.L.Z. were responsible for screening articles based on titles and abstracts. For the full-text screening, L.X.X, M.Q.C, F.W.Q, N.L.Z, and G.L.N. were responsible for reviewing and assessing the articles.

### Inclusion criteria

- Population: Individuals aged 18 or older diagnosed with gynecological (cervical, endometrial, ovarian) or breast cancer during or after treatment (e.g. chemotherapy, surgery).
- Intervention: The intervention must have undergone any type of IF protocol.
- Comparison: The control group must have adhered to a no dietary intervention protocol, as well as those following CR. The nonintervention diet must have consisted of subjects' regular dietary intake, and CR must have entailed sustained caloric reduction.
- Outcome: At least one outcome of interest had to be included. These were: body weight, BMI, waist circumference, blood glucose levels, insulin levels, chemotherapy-related toxicity, and subjective perceptions (e.g., fatigue, quality of life). Methods of collection included the following: subjective outcomes had to have been reported by patients based on validated instruments; anthropometric outcomes had to have come from patient reports, medical records, questionnaire data surveys, or other appropriate methods; metabolic outcomes had to have been derived from laboratory assessments; chemotherapy toxicity had to have been assessed using common clinical scoring criteria such as CTCAE (Common Terminology Criteria for Adverse Events), and patient self-reported symptoms had to have been collected by standardized questionnaires or interviews.
- Study design: Eligible study designs included randomized controlled trials (RCTs) and nonrandomized experimental studies.

### Exclusion criteria

- Population: Studies in humans less than 18 years of age, as well as animal studies were excluded.
- Intervention: Studies that discussed the effects of IF on the risk of developing breast or gynecological cancers were excluded.
- Comparison: Control group interventions that included IF components were excluded.
- Outcome: Studies that did not report outcome of interest were excluded.
- Study design: Editorials, letters, reviews, commentary pieces, and other nonresearch articles, animal or cell-based studies, qualitative research, and case reports were excluded.
- Full-text articles that were not made available after contacting the author were also excluded.

### Study selection

We used a citation management system (Endnote20, Michael O. McCracken) to manage records during the screening and study selection phases. After duplicates were removed, two reviewers (L.X.X. and M.Q.C.)

independently evaluated the titles and abstracts based on the inclusion criteria, with any discrepancies resolved through discussion with a third reviewer (N.L.Z). Abstracts with unclear or ambiguous information were retained for full-text review. L.X.X, M.Q.C, F.W.Q. reviewed the full text of each article. G.L.N. conducted an independent review of each article to determine whether it should be included or excluded. Any disagreements on any of these steps were resolved through discussion and participation by another researcher (N.L.Z.).

### Data collection process

A standardized, computerized data extraction form was developed in accordance with the PRISMA guidelines. The extracted data included: (1) study characteristics (e.g., author, year, country of origin, study design, and sample size); (2) participant details (e.g., medical history and demographics); (3) duration of intervention and follow-up; (4) data for both intervention and control groups; and (5) primary outcomes. Subjective perception outcomes, such as fatigue and quality of life, were assessed using validated self-reported tools referenced in the included studies (including, but not limited to, the Functional Assessment of Chronic Illness Therapy-Fatigue [FACIT-F] and Brief Fatigue Inventory [BFI] scales). In contrast to objective anthropometric and metabolic outcomes, subjective perception outcomes were based on self-reported measures, which may have introduced variability due to differences in the measurement tools and reporting methods used across studies. This potential problem was carefully considered during the interpretation process. Data extraction from full-text publications was conducted by L.X.X. and M.Q.C., with L.X.X. checking the accuracy of the extracted data.

### Quality assessment and risk of bias

The quality of the included RCTs was assessed using the Cochrane Risk of Bias 2 (RoB2) tool [30] and the JBI Critical Appraisal Tool [31] and covered domains such as randomization, deviations from intended interventions, and outcome measurement. Nonrandomized trials were evaluated with the Risk of Bias in Nonrandomized Studies of Interventions (ROBINS-I) tool [32], which assesses risk across seven domains, including confounding and missing data. Quality assessments were conducted independently by L.X.X. and M.Q.C., and discrepancies were resolved through discussion with G.L.N.

### Synthesis methods

The units for fasting glucose and insulin were standardized to mmol/L and mU/L, respectively.

### Data analysis

Descriptive summaries of the study, participant, and intervention features, as well as the qualitative assessments, were created. In this meta-analysis, we used the mean and standard deviation (SD) of post-test and follow-up measurements at each time point to calculate the effect sizes in each study, but body weight changes were synthesized using effect size (ES) as the summary measure. This approach was chosen because several of the included studies provided only the effect size and the corresponding 95% confidence interval (CI) rather than raw mean differences or standard deviations. The use of ES thus allowed for the combination of results across studies with differing outcome measures and units and provided a standardized summary measure that facilitated the comparison and pooling of data. For the pooling of blood glucose and insulin levels, since some studies provided data as medians with interquartile ranges, the means and standard deviations for this part of the study were estimated according to the equations outlined in the Cochrane Handbook, and the intervention effect was expressed as Cohen's d. Standardized mean difference (SMD) and 95% CI were calculated for the post-intervention outcomes between groups [33, 34]. A Cohen's d greater than 0.8 indicated a large effect, between 0.5 and 0.8 indicated a medium effect, and between 0.2 and 0.5 indicated a small effect [22].

The risk ratio (RR) for dichotomous outcomes was calculated using the Mantel-Haenszel method. A random-effects model was employed when heterogeneity was greater than 50%, and a fixed-effects model was applied when heterogeneity was less than or equal to 50%. Leave-one-out sensitivity analyses were performed for all combined effect sizes, but additional subgroup analyses were not conducted due to the limited number of studies for each outcome indicator. When an outcome indicator occurred in no more than two studies, descriptive analysis was performed for that outcome indicator only, and effect sizes were not combined. Endpoint publication bias of studies was assessed using the Egger's test, with significant publication bias defined as $p < 0.05$. Finally, a two-tailed $P < 0.05$ was the threshold used to indicate a statistically significant test result. All of the above analysis was carried out using Stata (version 16.0; StataCorp LLC, College Station, TX, USA).

## Results

Following the search and removal of duplicates, 1,529 articles remained for final assessment. Of these, 1,450 articles were excluded after reading the title and abstract, leaving a total of 79 articles to be read in full, and one article for which the original text was not available. A thorough review of the full text of the available 78 articles resulted in the exclusion of 69 of them. A total of 9

articles [22–24, 26–28, 35–37] were left to be included in the systematic review. 6 studies [22, 23, 27, 28, 35, 36] were selected for the meta-analysis, with publication dates ranging from 2015 to 2024. The detailed search process, along with reasons for exclusion, is presented in a flowchart in Fig. 1, and the attributes of the studies incorporated in the systematic review are encapsulated in Table 1 of Supplementary File 2. There were seven RCTs [23, 24, 27, 28, 35–37], and two nonrandomized experimental studies [22, 26]. A total of 625 participants were included.

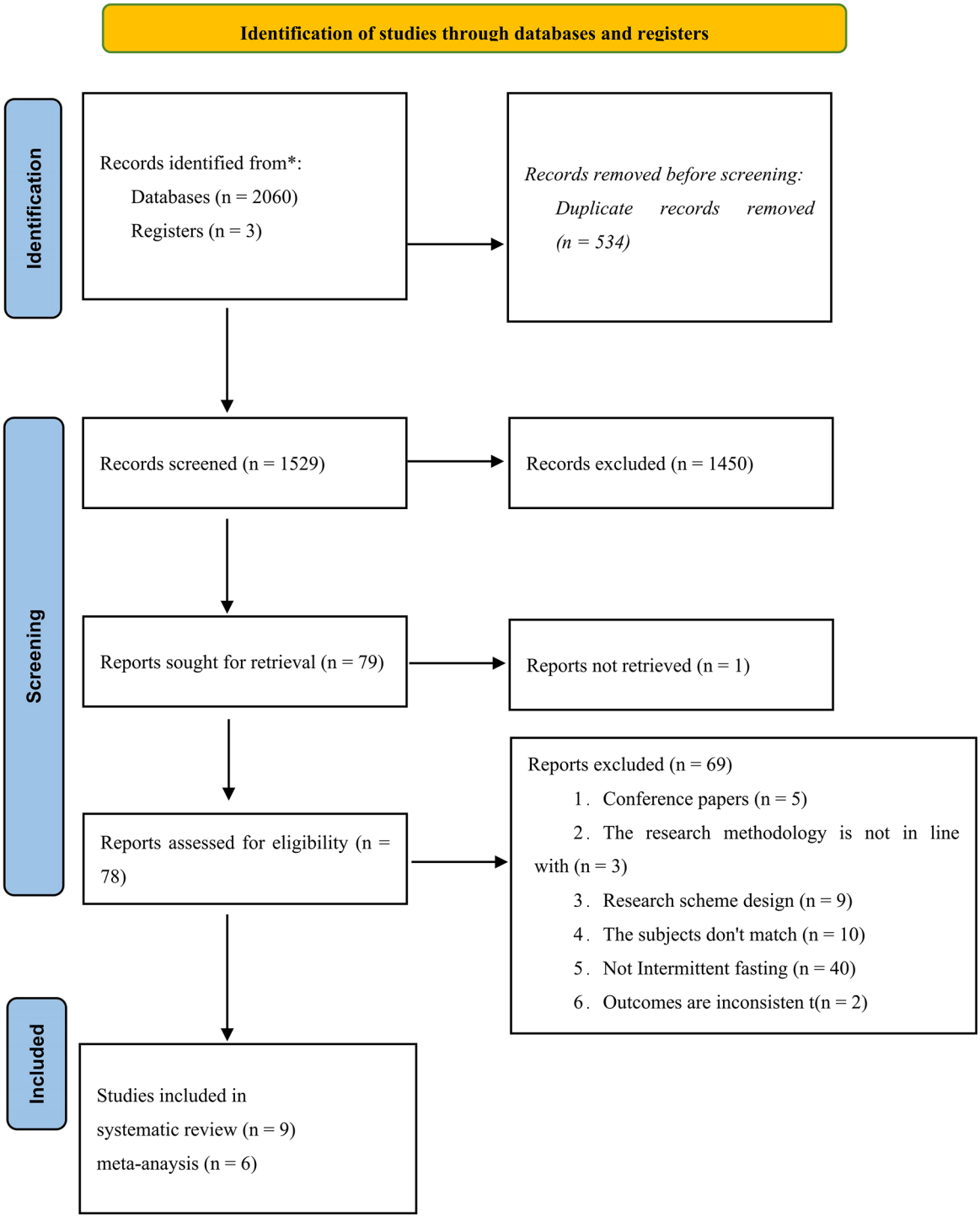


**Fig. 1** PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flowchart of the study selection process

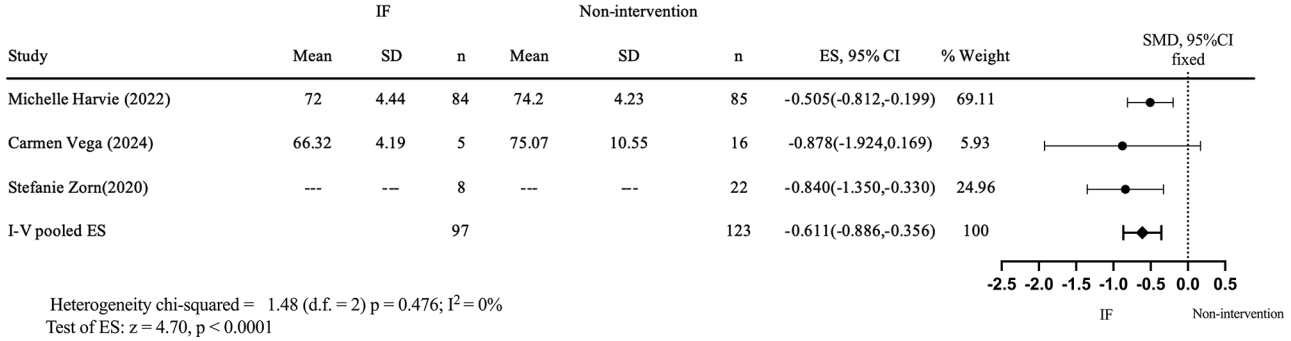


**Fig. 2** Forest plots illustrating the aggregated effects of IF on body weight

**Table 2** Egger's test results for each outcome indicator

| Outcome | Intercept (B) | Standard Error (SE) | 95% CI | *P*-value |
|---|---|---|---|---|
| Body weight | -0.14 | 1.01 | -14.15, 11.45 | 0.41 |
| Glucose | -1.31 | 1.37 | -5.66, 3.05 | 0.41 |
| Insulin | 0.76 | 0.85 | -2.89, 4.40 | 0.46 |
| Toxicity | -0.10 | 0.66 | -2.93, 2.73 | 0.89 |

The studies included three main modes of fasting: TWF (1/9) [27], TRE (3/9) [22, 23, 26] and FST (5/9) [24, 28, 35–37]. The control group dietary patterns consisted of noninterventional diets and CR. Studies included in the analysis had a minimum follow-up duration of 2 weeks [26], with the longest follow-up being 6 chemotherapy cycles [24, 27, 35] and a median follow-up of 4 chemotherapy cycles. Patients' adherence to IF ranged from 33.8 to 100% [22, 23, 28], and the outcome indicators in the included studies were weight [22, 24, 26, 27, 36], BMI [26, 27, 36, 37], waist circumference [22, 27], quality of life [24, 26, 28, 36, 37], metabolic parameters [22, 23, 27, 28, 35], and toxic response to chemotherapy [23, 27, 28, 35]. Participants hailed from the United Kingdom (1/9) [27], the United States (1/9) [26], Chile (1/9) [22], Egypt (1/9) [23], Germany (2/9) [24, 36], and the Netherlands (3/9) [28, 35, 37].

### Quality assessment and risk of bias of the included studies

The details of the evaluation of study quality and risk of bias for the included articles are provided in Supplementary Tables 2, 3, and 4 along with Figs. 1 and 2. Most of the randomized controlled trials (RCTs) (Supplementary Figs. 1 and 2) demonstrated a minimal risk of bias in sequence generation and allocation concealment. Only one study [36] exhibited a significant risk related to sequence generation. Due to the characteristics of the food interventions, participant blinding was impracticable. Consequently, all seven RCTs were assessed as having a high risk of bias concerning blinding. Regarding other sources of bias, two studies [35, 36] were rated as having an unclear risk, and the remaining five [23, 24, 27, 28, 37] were rated as low risk. Among the nonrandomized experimental studies (Supplementary Table 3), two studies [22, 26] had high and moderate risk of bias in terms of confounding bias and participant selection bias, respectively. Notably, these two studies were otherwise at lower risk of bias. Egger's test revealed that none of the studies included in the meta-analysis were likely to have publication bias ($P > 0.05$) (Table 2).

### The effects of IF on anthropometric outcomes

Figure 2 summarizes the effects of IF on body weight and BMI among patients with gynecological or breast cancer. The pooled analysis indicated that IF was effective in reducing body weight compared to controls (ES, -0.611; 95% CI, -0.886, -0.356; $p < 0.001$; $I^2 = 0\%$). We note that one study [24] used a crossover experimental design but did not indicate the change in body weight of groups A and B at the crossover point and was therefore not included in the our meta-analysis. This study reported a reduction in patient weight following the intervention. In group A, the average body weight was 73 kg (SD = 26.1) at baseline and 72.3 kg (SD = 25.8) at the conclusion of the trial, and in group B the respective values were 67.9 kg (SD = 23.7) and 68.5 kg (SD = 24.2).

Harvie et al. [27] and Lugtenberg et al. [37] investigated the effects of IF on BMI. Harvie et al.'s study demonstrated that TWF led to a reduction in BMI in both normal-weight and overweight patients with early-stage breast cancer. In contrast, Lugtenberg et al.'s study [37] found that FST had no significant impact on BMI reduction in breast cancer patients. Supplementary Fig. 3 gives an idea of the sensitivity analysis of body weight by showing that the pooled effect sizes are robust. Similarly, both Harvie et al. [27] and Vega et al. [22] studied the effects of IF on waist circumference in breast cancer patients. However, we could not summarize the effect sizes for waist circumference as these were the only 2 studies. Harvie et al.'s study [27] demonstrated that IF had no effect on waist circumference in breast cancer patients, whereas Vega et al.'s study [22] showed that IF reduced

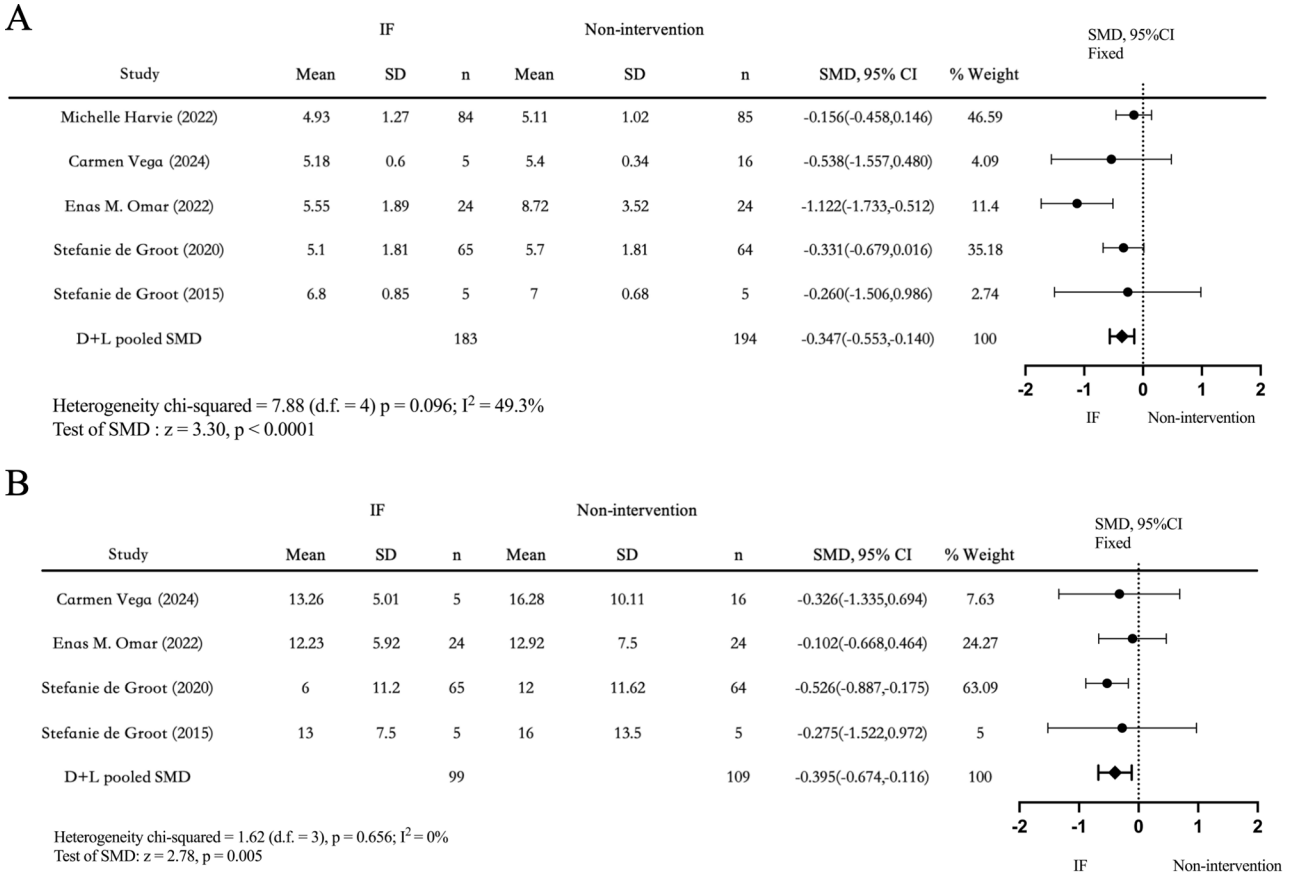


**Fig. 3** Forest plots depicting the aggregated effects of IF on blood glucose levels (**A**) and insulin levels (**B**)

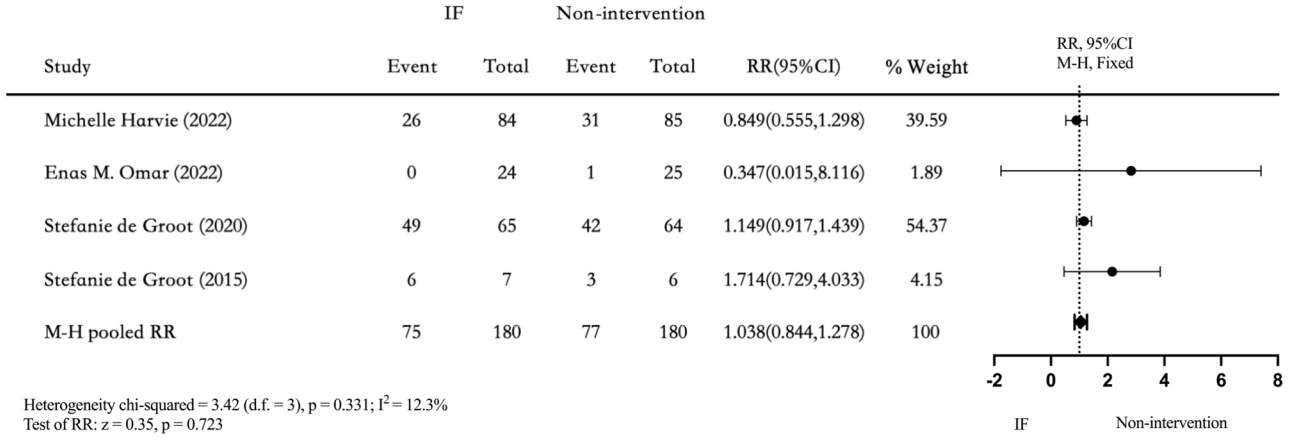


**Fig. 4** Forest plot showing pooled data on chemotherapy toxicities greater than grade 2 in IF vs. controls

waist circumference in breast cancer patients with a BMI over 24.

### The effects of IF on glycemic metabolism

Figure 3 depicts the effects of IF on blood glucose parameters. From the figure we can see that IF led to a substantial reduction in blood glucose levels, with a SMD of -0.347 mmol/L (95% CI: -0.553 to -0.140, $p < 0.0001$) and moderate heterogeneity ($I^2 = 49.3\%$). The SMD in serum insulin levels was – 0.395 mU/L (95% CI: -0.674 to -0.116, $p = 0.005$) and exhibited low heterogeneity ($I^2 = 0\%$). The sensitivity analyses, as shown in supplementary Fig. 4, indicate that the pooled effect sizes for both glucose and serum insulin are robust.

### The impact of IF on chemotherapy-induced toxicity

Figure 4 summarizes the effects of IF on chemotherapy-related toxicity in patients with gynecological or breast cancer. The pooled analysis shows no significant difference in the risk of experiencing a chemotherapy toxicity event greater than grade 2 between the IF and non-IF groups (RR: 1.038; 95% CI: 0.844, 1.278; $p = 0.723$), and heterogeneity was low ($I^2$ = 12.3%). Studies by Zorn et al. [36] (-0.16 ± 0.06; 95% CI: -0.28 to -0.03, $p = 0.013$) and Omar et al. [23] ($p = 0.004$) both suggested that patients with an mSTF cycle had a significantly lower frequency of grade I/II stomatitis compared to normocaloric diet (NC) cycles. Once again, he sensitivity analyses indicated that the pooled effect size was consistent and robust (Supplementary Fig. 5).

### The effects of IF on patients' subjective perception

Although 5 (55.6%) of the included studies examined the effects of IF on the subjective state of patients [24, 26, 28, 36, 37] 1 was a single-arm experiment [26], and 2 were crossover experimental studies [24, 36], which did not allow for data extraction sufficient to summarize the effect sizes of interest. Therefore, a descriptive analysis was instead conducted on the effects of IF on the subjective state of patients. Kleckner et al. [26] conducted a descriptive analysis of IF's effects on the subjective state of patients through a single-arm experiment that assessed fatigue in patients with gynecological or breast cancer and found that the total FACIT-F score increased by 9.3 ± 13.3 points following the intervention, indicating significant improvements in fatigue ($p < 0.001$, ES = 0.50). Additionally, the BFI scores also showed a reduction in fatigue, with a decrease of 1.0 ± 1.7 points ($p < 0.001$, ES = -0.58), further supporting the beneficial effects of IF on patients' fatigue levels. Bauersfeld et al. 's [24] study on the effects of short-term fasting in gynecological cancer patients found that in group A, chemotherapy-induced fatigue, as measured by the total FACIT-F score, decreased by 10.4 ± 5.3 points during fasting cycles and by 27.0 ± 6.3 points during nonfasting cycles. In contrast, group B experienced a mean decline of 14.1 ± 5.6 points during nonfasting cycles and 11.0 ± 5.6 points during fasting cycles. However, Zorn et al.'s study [36] indicated that short-term fasting did not significantly improve quality of life for cancer patients. For breast cancer patients, participants adhering to fasting mimicking diets (FMD) had higher scores for mood, physical, role, cognitive, and social functioning, and lower scores for fatigue, nausea, and insomnia symptoms compared to nonadherents and those on conventional diets [28, 37].

## Discussion

To our knowledge, this review is the first to assess the effects of IF in patients with gynecological or breast cancer comprehensively. Our analysis provides moderate- to high-quality evidence that suggests that IF has a beneficial impact on body weight, glucose, and insulin levels in these patients, without increasing chemotherapy-related toxicity, and the results demonstrate low heterogeneity. Moreover, IF may also improve BMI and subjective outcomes. We conducted several sensitivity analyses that validated the robustness of the findings on anthropometric outcomes, glucose metabolism, and chemotherapy-related toxicity.

No publication bias was detected, and the pooled data indicated that IF effectively reduced body weight in patients with gynecological or breast cancer [23, 27, 36]. This result means that IF may be an effective non-pharmacological intervention for weight management in these populations. This is noteworthy, as obesity is a major risk factor for gynecological and breast cancers [38]. For instance, Chlebowski et al. [39] conducted a randomized clinical trial involving 48,835 breast cancer patients found that weight control could help reduce the recurrence rate, lower the risk of developing a second cancer, and improve overall survival. Weight loss in cancer patients is associated with improved metabolic status, reduced risk of comorbidities, and potentially better treatment outcomes, emphasizing the potential clinical value of incorporating IF into supportive care.

Our findings are consistent with previous findings in other populations as well. For example, a systematic review by Patikorn et al. [40] reported that, following two months of IF, fasting resulted in weight loss among both healthy adults and overweight and obese, as well as those with nonalcoholic fatty liver disease. Several preclinical studies have also reported that IF modulates energy metabolism and reduces fat accumulation, which may benefit cancer patients at risk of metabolic disorders due to chemotherapy or hormone therapy [18, 41]. In addition, we found that IF may lead to a reduction in WHR, which is important for the overall health of patients with gynecological and breast cancers, as abdominal (visceral) obesity, irrespective of body weight or BMI, is considered a major health risk factor [42, 43].

Our findings also align with previous research conducted in noncancer populations that the benefits of IF for metabolic regulation, particularly in relation to fasting blood glucose and insulin levels. Numerous studies have demonstrated that IF enhances fasting blood glucose levels and decreases insulin resistance [16, 44, 45]. Interestingly, however, Sun et al. [46] found no significant changes in fasting glucose levels within the IF group, and this has led to some uncertainty in the relationship between IF and blood glucose levels. Factors such as the

duration of fasting, variations in demographic characteristics, and differences in patients' metabolic profiles may contribute to variability in the effect of IF on blood glucose levels. Consequently, further research is warranted to clarify the effect of IF on blood glucose.

Additionally, our meta-analysis provided aggregated evidence, free from publication bias, indicating a beneficial impact of IF on insulin levels. This result also aligns with previous studies demonstrating that IF regimens lead to a modest reduction in fasting insulin concentrations [47]. The effect of IF on insulin levels is the result of a combination of mechanisms, including improved insulin sensitivity, promotion of lipolysis, metabolic switching, increased glucagon secretion, activation of cellular autophagy, and reduced inflammation and oxidative stress [48], and each of these mechanisms is an important for cancer progression and treatment outcomes [49]. Studies by Ferroni et al. [50] and Monzavi-Karbassi et al. [51] on nondiabetic breast cancer patients have demonstrated that higher blood glucose and insulin levels are connected with a poor prognosis. Thus, the observed reductions in blood glucose and insulin levels suggest that IF may be able to mitigate these risks.

Our systematic review did not find a significant effect of IF in reducing chemotherapy-related side effects, which aligns with the findings of Ferro et al. [29]. Notably, in the study by Groot et al. [28, 35] patients in the IF group were not treated with dexamethasone prior to chemotherapy, even though there was no statistically significant difference in toxicity response between the IF and regular diet groups, suggesting that IF may have eliminated the need for dexamethasone for preventing chemotherapy side effects. Importantly, patients who received IF along with chemotherapy had less DNA damage in T lymphocytes compared to those receiving chemotherapy with a normal diet, suggesting that IF protects these cells from chemotherapy-induced DNA damage [28]. Therefore, IF may have the potential to attenuate chemotherapy-related side effects, and future studies should further explore different IF types, using longer durations and larger sample sizes, in diverse cancer populations.

Some of the studies included in our systematic review suggest that IF may benefit the subjective perception of gynecological and breast cancer patients [24, 26, 28, 36, 37]. This includes quality of life, treatment functioning, disease perception, treatment burden, and fatigue. Our findings are consistent with those of other experimental and animal studies [24, 52], and they emphasize the potential role of IF in improving the overall health of cancer patients, not just the metabolic and physical health benefits. In general, patients with breast and endometrial cancers gain weight during chemotherapy, which usually persists for several years after treatment ends [38, 53]. Weight gain can lead to poor quality of life, physiological stress, and body image concerns. IF may also have a positive impact on mental health by promoting hormone balance and reducing inflammatory markers (often associated with mental fatigue and depression) in addition to controlling patients' weight and thereby improving their overall subjective well-being [54, 55].

Compared to other dietary interventions (e.g., continuous calorie restriction), IF offers a more flexible approach that may be more acceptable and sustainable for patients. Adherence frequently remains suboptimal due to the long-term nature of IF as a lifestyle intervention. In Groot et al.'s trial [28], fewer than 33% of patients adhered to the IF regimen throughout all chemotherapy cycles. Likewise, research by Zorn et al. [36] revealed that just 50% of participants expressed a readiness to fast again after treatment. Improving patient awareness, comprehension, and involvement may therefore be essential for increasing adherence to IF treatment procedures [56]. Understanding what are seen as benefits and obstacles to IF adherence may promote compliance and improve therapeutic results [57].

Crucially, however, the use of IF should be carefully tailored to the needs of each patient, especially those receiving intensive cancer therapy. Although IF can help with hyperglycemia, hyperinsulinemia, and fatigue, careful monitoring is essential to avoid potential risks such as hypoglycemia, particularly in patients receiving treatment regimens that affect appetite and nutrient intake [58]. Collaboration between oncologists, dietitians, and other healthcare professionals is thus essential to ensure the safe and effective implementation of IF.

Our study features several strengths. To begin, we adhered to strict inclusion criteria, systematically searched all relevant studies that met our predefined criteria, and followed the PRISMA guidelines for reporting systematic reviews and meta-analyses. We also employed rigorous quality assessment tools, including RoB2 for RCTs, and ROBINS-I for nonrandomized studies. A comprehensive literature search across seven major databases, supplemented by reference tracking, ensured the inclusion of high-quality and relevant studies. However, although randomized controlled trials generally offer more reliable evidence, our inclusion of nonrandomized trials may limit the external validity of our findings. Notably, this review is the first to assess the effects of IF in gynecological and breast cancer systematically. Our findings provide clinically significant insights into the potential of IF as a nonpharmacological intervention for weight management and metabolic improvement in cancer patients. Additionally, the use of sensitivity analysis to validate the robustness of the combined effect size further strengthens the reliability of our results.

The study is not without limitations, however. First, the heterogeneity of cancer types and treatment regimens

in the included studies present a significant limitation in interpreting the results of our systematic review and meta-analysis. For instance, cancers such as breast, ovarian, and endometrial differ in their biological pathways and metabolic profiles, which may influence their response to IF interventions. Second, treatment regimens such as chemotherapy, hormone therapy, and radiotherapy interact with metabolic pathways in distinct ways, potentially altering the effects of IF. These variations across cancer types and treatments complicate direct comparisons and may contribute to differences in observed outcomes. Third relatively small sample sizes and lack of subgroup analysis further restrict the study's ability to assess the specific effects of IF on different cancer types or treatments.

Future research should focus on including larger, more homogeneous populations and stratifying analyses by cancer type and treatment regimen. Furthermore, exploring the impact of various IF regimens on patients, alongside standardization of IF protocols, could improve the comparability and robustness of the findings in future meta-analyses.

## Conclusions

IF is effective in managing body weight and blood glucose levels without exacerbating the toxic effects of chemotherapy, making it a viable nonpharmacological intervention for weight control in patients overweight or obese patients with gynecological or breast cancer. However, improving adherence to this intervention is crucial to support further research and development in this field. Given the limitations of this meta-analysis, including methodological shortcomings such as the inclusion of multiple study designs with small sample sizes, our findings should be interpreted cautiously. High-quality, adequately powered randomized controlled trials are necessary to explore specific IF regimens in different subgroups of cancer patients and cancer survivors.

### Abbreviations

| | |
|---|---|
| IF | Intermittent fasting |
| CNKI | China National Knowledge Infrastructure |
| CBM | Chinese Biomedical Literature Database |
| CR | Calorie restriction |
| BMI | Body mass index |
| RCT | Randomized controlled trials |
| ES | Effect Size |
| SMD | Standardized mean difference |
| SD | Standard deviation |
| MD | Mean difference |
| RR | Relative risk |
| CI | Confidence interval |
| ADF | Zero-calorie alternate-day fasting |
| MADF | Modified alternate-day fasting |
| TWF | Twice-weekly fasting |
| TRE | Time-restricted eating |
| FST | Periodic or short-term fasting |
| PRISMA | Preferred Reporting Items for Systematic Reviews and Meta-Analyses |
| CTCAE | Common Terminology Criteria for Adverse Events |
| FACIT-F | Functional Assessment of Chronic Illness Therapy-Fatigue |
| BFI | Brief Fatigue Inventory |
| RoB2 | Risk of Bias 2 |
| NOS | Newcastle-Ottawa Scale |
| ROBINS-I | Risk of Bias in Non-randomized Studies of Interventions |
| FMD | Fasting mimicking diets |
| NC | Normocaloric diet |

## Supplementary Information

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Supplementary Material 1

Supplementary Material 2

Supplementary Material 3

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### Author contributions

L.X.X: Conceptualisation, Methodology, Data management, Formal analysis, Visualisation, Writing - original draft preparation; M.Q.C: Methodology, Data management, Formal analysis, Validation; F.W.Q: Data management, Formal analysis, Validation; N.L.Z: Data management; G.L.N: Validation, Resources, Project Management, Oversight, Funding Acquisition, Writing - Review and Editing. All authors have read and agreed to the published version of the manuscript.

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### Data availability

Original contributions presented in the study are included in the article and further enquiries can be directed to the corresponding author.

## Declarations

### Ethics approval and consent to participate

Not applicable.

### Informed consent

None.

### Consent for publication

Not applicable.

### Competing interests

The authors declare no competing interests.

### Author details

[1]Department of Obstetrics and Gynecology, Shengjing Hospital of China Medical University, Shenyang 110004, China

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## Publisher's note