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Defining Breast Implant Illness: A Systematic Review and Meta-analysis of Patient-reported Symptoms

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Background: Although no definitive scientific link has been established, public concern surrounding breast implant illness (BII) is increasing. To study this potential condition, a clear definition is necessary. This systematic review aimed to characterize BII through a meta-analysis of patient-reported symptoms.
Methods: Following Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines, a comprehensive literature search was conducted. The relative risk (RR) of the top 10 symptoms was meta-analyzed, comparing patients with and without breast implants. Additional analyses assessed whether surgical or patient-related factors influenced symptom occurrence.
Results: A total of 36 articles were included in this study, accounting for 10,519 patients. Fatigue or malaise (RR = 3.15 [2.89–3.43]), myalgia or weakness (RR = 2.96 [2.76–3.18]), and cognitive dysfunction (RR = 2.87 [2.64–3.12]) were most strongly associated with the presence of breast implants. Implants that were ruptured (RR = 1.12 [1.04–1.21], $P = 0.003$) or filled with silicone (RR = 2.11 [1.49–2.99], $P < 0.0001$) appeared more likely to lead to BII-type symptoms. In contrast, patients who underwent explantation (RR = 0.94 [0.90–0.98], $P = 0.003$) or had implants for aesthetic reasons (RR = 0.91 [0.84–0.99], $P = 0.02$) reported fewer symptoms.
Conclusions: Given increasing awareness and concern surrounding BII, it is essential for the plastic surgery community to critically examine patient outcomes. Establishing a consistent, symptom-based definition of BII and identifying key risk factors are necessary to guide future research and improve patient care. *(Plast Reconstr Surg Glob Open 2025;13:e6773; doi: 10.1097/GOX.0000000000006773; Published online 19 May 2025.)*

INTRODUCTION

Despite being some of the most widely used and studied medical devices, a certain weariness regarding the potential systemic effects of breast implants persists. More recently, coined under the umbrella term breast implant illness (BII), an array of systemic symptoms reported by patients with breast implants have been under scrutiny by the plastic surgery community.[1,2] This comes at a time when the media has been on a heightened sense of vigilance in relation to breast implants following the recent breast implant-associated anaplastic large cell lymphoma-related recalls.[3–5]

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To date, no clear scientific link has been proven, despite many theories arising in parallel.[6–9] Despite many attempts at elucidating BII,[10,11] there has yet to be a clear-cut definition of the disease, which has naturally hindered the scientific endeavors to better study this entity. This is in addition to the fact that no clear physical or laboratory findings exist to aid physicians in establishing the diagnosis. This is likely due to the nonspecific, wide range, and varying presence of symptoms experienced by patients. Nonetheless, to begin understanding a disease, there must first exist a clear understanding of its nature.

With this in mind, the goal of this systematic review is to better define BII by means of a meta-analysis of patient-reported symptoms, to ultimately determine the most prevalent symptoms as the basis of a symptom-based definition. Secondarily, the authors sought to determine

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whether certain surgical/patient factors may affect the presence and types of symptoms experienced.

MATERIALS AND METHODS

Search

In accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines[12] and validated by a medical librarian, a search of PubMed, Medline, and Embase was carried out. The search's keywords included: "breast implant illness" OR "human adjuvant disease" OR "autoimmune syndrome induced by adjuvants" OR "ASIA syndrome" OR "inflammatory syndrome induced by adjuvants" OR "silicone implant incompatibility syndrome" OR "silicone-related symptom complex" OR "siliconosis" OR "Shoenfeld's syndrome" OR ("breast" AND implant* AND symptom*). Results were screened according to strict inclusion and exclusion criteria. Studies pertaining to adults undergoing breast surgery and where patient-reported symptoms were clearly presented were included. Studies that were of low generalizability or a nonprimary source (case reports, case series < 10 patients, letter to editor, commentaries, editorials, and literature reviews), where symptoms or their prevalence were unclear, or that were not written in English were excluded. This entire process was carried out independently between 2 authors, with any discrepancies resolved by means of consensus.

Data pertaining to study characteristics, patient demographics, and prevalence of symptoms were extracted from included studies. Comparative studies were also subgrouped into 1 of 5 categories: breast implants versus controls, ruptured versus intact implants, silicone versus saline implants, augmentation versus reconstruction, and pre-/postexplantation. All studies were assessed for level of evidence according to the Oxford Centre for Evidence-Based Medicine criteria.[13] A funnel plot was created to assess for publication bias among included studies. The data collection process was also carried out independently between 2 authors, with any discrepancies resolved by means of consensus.

Statistical Analysis

First, an overall pooled analysis of reported symptoms was conducted among patients with breast implants. Percentages were calculated in terms of overall patients and overall patients specifically questioned about the symptom. Of note, in the latter group, if a cohort of patients was asked about multiple symptoms related to one of the overall symptom categories, the cohort was multiplied by that when tabulating the denominator (total patients). For example, if patients in a study were questioned for brain fog, difficulty concentrating, and memory loss, which are all under the "cognitive dysfunction" overall category, the total number of patients was multiplied by 3. Study characteristics and patient demographics were also presented descriptively. The relative risk (RR) of the top 10 symptoms was meta-analyzed, comparing patients with/without implants, utilizing the ratio of overall patients specifically questioned about the symptom.

Takeaways

Question: How can we serve our patients complaining of breast implant illness (BII) without a definition for the disease?

Findings: Based on data extracted from 10,519 patients from our 36 included studies, joint complaints, fatigue/malaise, myalgia/weakness, cognitive dysfunction, and musculoskeletal/undefined pain were the most prevalent symptoms overall and may thus serve as a basis for defining BII. Implants that were intact, filled with saline, used for aesthetic purposes, or that were explanted seemed to be less likely to cause patients to experience BII-type symptoms overall.

Meaning: BII most commonly presents with joint complaints, fatigue/malaise, myalgia/weakness, cognitive dysfunction, and musculoskeletal/undefined pain.

Second, a subgroup meta-analysis of solely comparative studies was conducted. Five categories (breast implants vs no implants, ruptured vs intact implants, silicone vs saline implants, augmentation vs reconstruction, pre/postexplantation) of patients were compared by means of forest plots in terms of experiencing symptoms overall, and in terms of experiencing the top 5 specific symptoms.

The meta-analysis was conducted on Review Manager (RevMan) v5.4 (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, 2014). A fixed effects model and the Mantel–Haenszel statistical method were utilized to determine the RR. The RR estimates with 95% confidence intervals were computed, with statistical significance set at P value less than 0.05. Heterogeneity was computed using the chi-square test and formally quantified by the I^2 statistic. Comparisons with less than 3 cohorts were not meta-analyzed, due to lack of power. As typically done in a fixed effects model, the effect size was weighted by the inverse of its associated variance.

RESULTS

Search Outcome

In total, 3391 records were identified from the 3 different databases. Following this, 1652 duplicate articles were removed, yielding 1739 records for screening. From these, 843 were excluded based on title only, whereas a further 690 were excluded based on their abstract. Following exclusion of the 12 reports not retrieved, a total of 194 articles were then assessed for eligibility based on their full text, among which 158 were excluded. Finally, a total of 36 articles were included in this study (Fig. 1).

Overall Analysis

A total of 10,519 patients were extracted from these 36 studies. Studies were most commonly conducted in the United States (n = 17) and were either mostly (n = 15) from before the year 2000, or part of a recent uptick since 2020 (n = 10). On average, included patients were 43.6 years of age (±10.8 y), had breast implants for 11.6 years

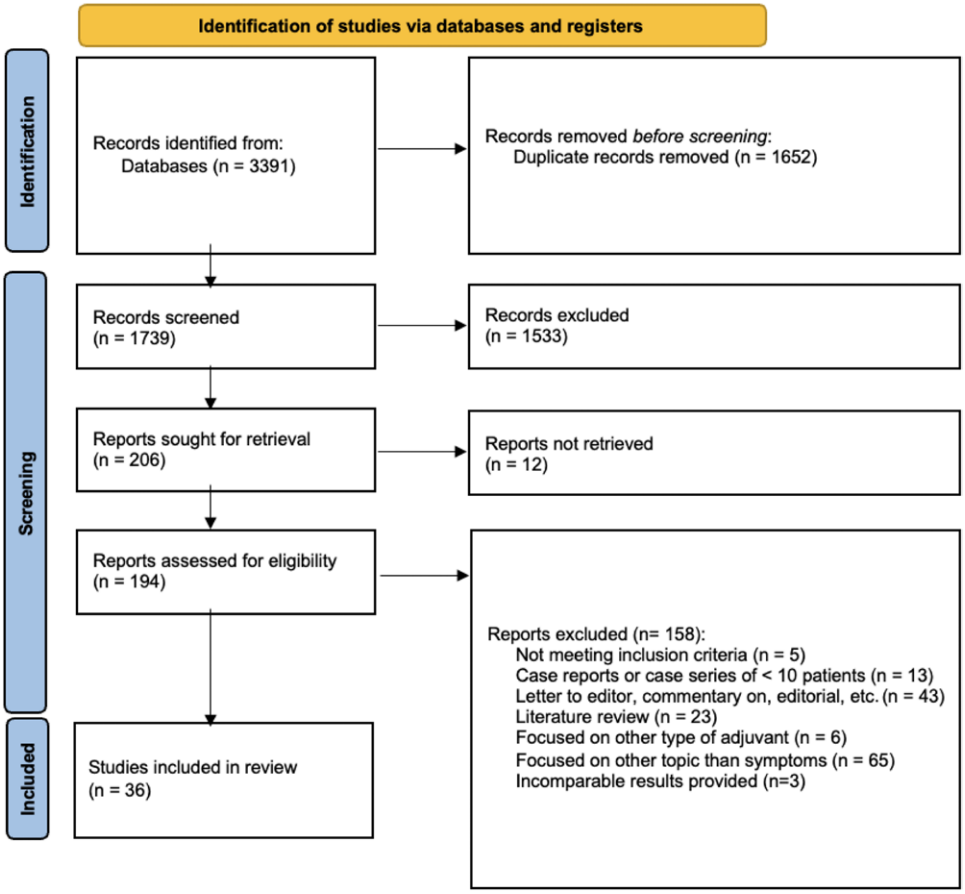

Fig. 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow chart for systematic review.

(±5.6 y), and mostly (90.5%) had silicone implants (Table 1).

A total of 27 categories of symptoms were established (Table 2). Overall, the most commonly reported symptoms were joint complaints (n = 4109, 39.1%), fatigue/malaise (n = 2862, n = 27.2%), myalgia/weakness (n = 2643, n = 25.1%), cognitive dysfunction (n = 2271, n = 21.6%), and musculoskeletal (MSK)/undefined pain (n = 1774, n = 16.9%). When weighing symptoms only among patients who were explicitly asked about said symptom, the most commonly reported symptoms were fatigue/malaise (44.5%), sleep disturbance (38.7%), dizziness/vertigo (28.4%), cognitive dysfunction (26.4%), and myalgia/weakness tied with MSK/undefined pain at 25.7% (Table 3).

A forest plot representing a meta-analysis of the top 10 reported symptoms can be seen in Figure 2, demonstrating that fatigue/malaise (RR = 3.15 [2.89–3.43]), myalgia/weakness (RR = 2.96 [2.76–3.18]), and cognitive dysfunction (RR = 2.87 [2.64–3.12]) were most strongly associated with the presence of breast implants. The top 10 symptoms were significantly associated ($P < 0.00001$) with the presence of implants.

Subgroup Analysis

In terms of the subgroup meta-analyses of comparative studies, they were divided into breast implants versus no implants (n = 12), ruptured versus intact implants (n = 4), silicone versus saline implants (n = 2), augmentation versus reconstruction (n = 2), and pre-/postexplantation (n = 2). (**See figure, Supplemental Digital Content 1**, which displays the categories of meta-analyzed comparative studies, **https://links.lww.com/PRSGO/E22**.).

In terms of the first category (implants versus no implants), breast implants were associated with a significantly increased risk of overall symptoms (RR = 1.33 [1.30–1.36], $P < 0.00001$) (Fig. 3). In addition, with regard to specific symptoms, breast implants were associated with a significantly increased risk of experiencing joint complaints (RR = 1.40 [1.32–1.50], $P < 0.00001$), fatigue and malaise (RR = 1.32 [1.18–1.48], $P < 0.00001$), myalgia and weakness (RR = 1.36 [1.25–1.49], $P < 0.00001$), cognitive dysfunction (RR = 1.51 [1.37–1.66], $P < 0.00001$), and undefined pain (RR = 1.27 [1.19–1.36], $P < 0.00001$) (Fig. 4).

In terms of the second category (ruptured versus intact implants), ruptured implants were associated with a significantly increased risk of experiencing overall symptoms (RR = 1.12 [1.04–1.21], $P = 0.003$) (Fig. 5). However, with regard to specific symptoms (joint symptoms, fatigue/malaise, myalgia/weakness, cognitive dysfunction, and cutaneous symptoms), no statistically significant association was found (Fig. 6).

Table 1. Included Study Characteristics and Patient Demographics

Author (Year)	Country	Study Type	Level of Evidence	No. Patients	Age at Study		Time with Implant		Type of Implant	
					Age, y	SD, y	Time, y	SD, y	Silicone	Saline
Barbosa et al (2021)[14]	United States	Retrospective cohort	2b	452	40	15				
Bird and Niessen (2022)[15]	Netherlands	Prospective cohort	1b	140	43.2	10.6	14.4	7.4	134	6
Brawer (1996)[16]	United States	Descriptive study	4	300	33		12.75		300	0
Breiting et al (2004)[17]	Denmark	Retrospective cohort	3b	190	52		19			
Brown et al (2001)[18]	United States	Cross-sectional analysis	4	344	51.4	8.4	16.5	3.4	344	0
Cuellar et al (1995)[19]	United States	Descriptive study	4	300	44.4				276	24
De Jong et al (2004)[20]	Netherlands	Cross-sectional analysis	4	84			19.5	6.05	84	0
Edworthy et al (1998)[21]	United States	Retrospective cohort	3b	1576	42.3				1112	352
Englert et al (2001)[22]	Australia	Retrospective cohort	2b	458					458	0
Englert et al (2004)[23]	Australia	Retrospective cohort	2b	458					458	0
Freundlich et al (1994)[24]	United States	Descriptive study	4	50	43		9.9		50	0
Fryzek et al (2001)[25]	Sweden	Retrospective cohort	2b	1369	44.3	10				
Gabriel et al (1994)[26]	United States	Retrospective cohort	2b	749	34.4	10.5	7.8	5.5		
Gaubitz et al (2002)[27]	Germany	Descriptive study	4	90	49.9	10.5	9.14	6.34	90	0
Giltay et al (1994)[28]	Netherlands	Retrospective cohort	2b	235	43				235	0
Godfrey et al (1996)[29]	United States	Retrospective cohort	3b	78						
Greenbaum et al (2023)[30]	Israel	Descriptive study	4	160	43.7				160	0
Holmich et al (2003)[31]	Denmark	Retrospective cohort	3b	238	32.6				238	0
Khoo et al (2019)[32]	Australia	Retrospective cohort	2b	30	47.9				30	0
Lee et al (2020)[9]	Australia	Prospective cohort	1b	100	44		4		92	8
Magno-Padron et al (2021)[33]	United States	Cross-sectional analysis	4	182					90	75
Maijers et al (2014)[34]	Netherlands	Descriptive study	4	80			14.5		80	0
Metzinger et al (2022)[35]	United States	Retrospective cohort	2	200	45.5					
Misere et al (2021)[36]	Netherlands	Cross-sectional analysis	4	181	54.5				168	13
Misere and Van der Hulst (2022)[37]	Netherlands	Descriptive study	4	197	52	12.1	8.57		172	13
Newby et al (2020)[38]	Australia	Retrospective cohort	3b	165	41.2	11.5	9.74	7.86	115	43
Park et al (1998)[39]	Scotland	Cross-sectional analysis	4	317	47.9				317	0
Robinson Jr et al (1995)[40]	United States	Descriptive study	4	300					300	0
Rosenberg (1996)[41]	United States	Case series	4	131					131	0
Siceloff and Blasko (1999)[42]	United States	Retrospective cohort	2b	183	49.4				183	0
Solomon (1994)[43]	United States	Descriptive study	4	176	45				171	5
Spit et al (2022)[44]	Netherlands	Descriptive study	4	467	48	12	12		467	0
Vermeulen and Scholte (2003)[45]	Netherlands	Cross-sectional analysis	4	319	49	8.6			319	0
Weinzweig et al (1998)[46]	United States	Retrospective cohort	2b	43					29	14
Weisman et al (1988)[47]	United States	Retrospective cohort	3b	125	42				125	0
Wells et al (1995)[48]	United States	Case series	4	52	45.6	8.65	11.9	6.3	44	8
Overall amount				10,519					6772	561
Overall mean				292	43.6	10.8	11.6	5.6	90.5%	7.5%

In terms of the third category (silicone versus saline implants), silicone breast implants were associated with a significantly increased risk of overall symptoms (RR = 2.11 [1.49–2.99], $P < 0.0001$). **(See figure, Supplemental Digital Content 2**, which displays the forest plot comparing patients with silicone versus saline breast implants for overall symptoms, **https://links.lww.com/PRSGO/E23**.) No meta-analyses were conducted regarding specific symptoms due to having less than 3 comparative studies available.

In terms of the fourth category (augmentation versus reconstruction), there was a decreased risk of overall symptoms in the augmentation group (RR = 0.91 [0.84–0.99], $P = 0.02$). (**See figure, Supplemental Digital Content 3**, which displays the forest plot comparing patients with breast implants for augmentation versus reconstruction for overall symptoms, **https://links.lww.com/PRSGO/E24**.) No meta-analyses were conducted regarding specific symptoms due to having less than 3 comparative studies available.

In terms of the fifth category (pre-/postexplantation), explantation was associated with a significantly decreased risk of overall symptoms (RR = 0.94 [0.90–0.98], $P = 0.003$]). (**See figure, Supplemental Digital Content 4**, which displays the forest plot comparing patients pre- versus postexplantation of their breast implants for overall symptoms, **https://links.lww.com/PRSGO/E25**.) No meta-analyses were conducted regarding specific symptoms due to having less than 3 comparative studies available.

Study Bias

The majority of studies were of Oxford Centre for Evidence-Based Medicine level 4 (n = 18), and all were level 4 or higher. To assess for publication bias, funnel

Table 2. Categories of BII Symptoms

1. Cognitive dysfunction
   - Brain fog
   - Difficulty concentrating
   - Memory loss
   - Difficulty finding words
2. Headache/migraine
3. Dizziness/vertigo
4. Fatigue/malaise
5. Psychological disorders
   - Depression
   - Anxiety
6. Sleep disturbance
7. Joint complaints
   - Arthralgia
   - Joint stiffness
   - Joint swelling
8. Myalgia/weakness
9. Adenopathy
   - Painful/tender lymph nodes
   - Swollen lymph nodes
10. Paresthesia
    - Numbness
    - Tingling in the extremities
    - Pins and needles
    - Burning in the extremities
11. MSK/undefined pain
    - Back pain
    - Neck pain
    - Shoulder pain
    - Knee pain
    - Other pain
12. Hair loss/alopecia/hair changes
13. Cutaneous complaints
    - Dermatologic symptoms
    - Dry skin
    - Skin rash
    - Photosensitivity
    - Skin disease/abnormality
    - Skin tightness
    - Pruritus
14. Raynaud phenomenon
15. Mucosal complaints/sicca symptoms
    - Eye symptoms
      - Dry eyes
      - Itchy eyes
      - Teary eyes
      - Puffy eyes
      - Burning eyes
    - Mouth symptoms
      - Dry mouth
      - Mouth ulcers
16. Changes in vision
    - Altered vision
    - Double vision
    - Tunnel vision
17. Swelling/edema
18. Nonspecific constitutional symptoms
    - Fever
    - Night sweats
    - Sweating
    - Weight change
19. Flu-like symptoms
    - Sore throat
    - Hoarseness
    - Cough
    - Sputum
    - Sinusitis
20. Change in hearing
    - Hearing loss
    - Tinnitus
    - Muffled hearing
    - Altered speech perception
21. Chest complaints
    - Palpitations
    - Angina
    - Pleuritic chest pain
    - Other chest pain
22. Dyspnea/wheezing
23. G-I symptoms
    - Nausea/vomiting
    - Diarrhea
    - Constipation
    - Dysphagia
    - Food intolerance
    - GERD
    - Abdominal pain
24. Urinary symptoms
    - Change in bladder habits
    - Dysuria
    - Frothy urine
    - Red urine
25. Breast complaints
    - Breast pain
    - Breast lumps/mass
    - Breast tenderness
26. Recurrent infections
27. Hormonal and sexual changes
    - Decreased libido
    - Dry vagina
    - Vaginal discharge
    - Vaginitis
    - Early menopause
    - Pain with intercourse
    - Hormonal imbalance

GERD, gastroesophageal reflux disease); G-I, gastrointestinal; MSK, musculoskeletal.

plots were created. Overall, none demonstrated asymmetry or publication bias. (**See figure, Supplemental Digital Content 5**, which displays the funnel plots for each meta-analysis, **https://links.lww.com/PRSGO/E26**.)

DISCUSSION

Given the persistent weariness surrounding breast implants, namely attributed to the recently growing concerns related to BII,[3] it is our duty as plastic surgeons to duly investigate such claims. To study this potential disease, we must first arrive at its proper definition. Based on data extracted from 10,519 patients from our 36 included studies, joint complaints, fatigue/malaise, myalgia/weakness, cognitive dysfunction, and MSK/undefined pain were the most prevalent symptoms overall and may serve as a basis for BII's symptom-based definition. In addition, fatigue/malaise, myalgia/weakness, and cognitive dysfunction were most strongly associated with the presence of breast implants. Results from our meta-analysis suggest that the presence of implants is significantly correlated with the presence of BII-type symptoms. Implants that were intact, filled with saline, used for aesthetic purposes, or that were explanted seemed to be less likely to cause patients to experience BII-type symptoms overall. To the best of our knowledge, this is the first meta-analysis of patient-reported symptoms relating to BII, providing higher level evidence to the BII literature.

Many authors have previously attempted to better define this entity. In a recent analysis of the Food and Drug Administration (FDA) Manufacturer and User Facility Device Experience database, Taskindoust et al[10] synthesized the results of 751 BII-related reports. They determined that fatigue/weakness (43.7%), numbness/tingling (33.2%), and brain fog/memory loss (32.9%) were the overall most commonly reported symptoms. These were present among patients with both silicone (61%) and saline-filled (39%) implants. Similarly, in a 3-tier Delphi study made up of a total of 27 patients, researchers, surgeons, and regulators, the top 3 agreed-upon symptoms for BII were fatigue, brain fog, and joint pain.[49] Both of these results are generally in line with the results from our meta-analysis.

Some authors have attempted to define BII according to associations to more formal medical diagnoses, rather than symptoms. For example, in a cross-sectional analysis comparing 24,651 women with breast implants to 98,604 controls, Watad et al[50] show that the Sjögren syndrome, systemic sclerosis, and sarcoidosis were significantly more prevalent among patients with silicone breast implants. Further, a systematic review pooling 32 studies found associations between silicone implants and rheumatoid arthritis, Sjogren syndrome, and Raynaud phenomenon.[51] In a similar vein, an analysis of the FDA's postapproval studies related to breast implants encompassing more than

Table 3. Symptoms and Their Frequency

Rank	Symptom	n	% of Total	% of Total Patients Who Were Questioned for This Symptom
1	Joint complaints	4109	39.06	23.40
2	Fatigue/malaise	2862	27.21	44.52
3	Myalgia/weakness	2643	25.13	25.74
4	Cognitive dysfunction	2271	21.59	26.37
5	MSK/undefined pain	1774	16.86	25.68
6	Nonspecific constitutional symptoms	1743	16.57	19.16
7	Cutaneous complaints	1688	16.04	12.09
8	Mucosal complaints	1562	14.85	11.05
9	Paresthesia	1359	12.91	22.29
10	G-I complaints	1140	10.84	12.45
11	Headache/migraine	1073	10.20	18.25
12	Hair loss	824	7.83	15.92
13	Sleep disturbance	748	7.11	38.66
14	Psychological symptoms	709	6.74	20.41
15	Breast complaints	632	6.01	22.19
16	Flu-like symptoms	607	5.77	15.14
17	Chest complaints	579	5.50	18.54
18	Dyspnea	496	4.72	16.80
19	Adenopathy	463	4.40	19.61
20	Hormonal and sexual changes	441	4.19	22.67
21	Raynaud phenomenon	367	3.49	12.79
22	Dizziness/vertigo	325	3.09	28.43
23	Change in hearing	279	2.65	18.75
24	Change in vision	211	2.01	12.43
25	Urinary symptoms	148	1.41	9.36
26	Recurrent infections	125	1.19	12.17
27	Swelling/edema	45	0.43	6.82

G-I, gastrointestinal.

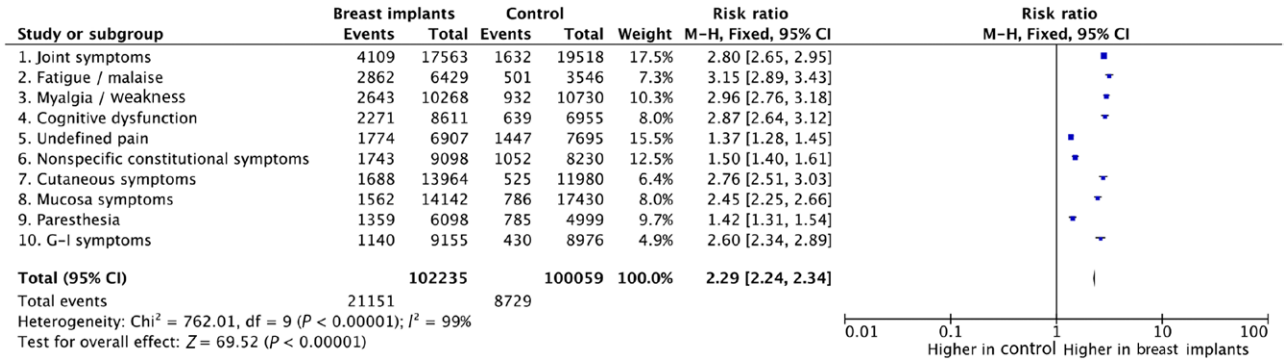

Fig. 2. Meta-analysis of the association of the top 10 reported symptoms with breast implants overall. CI, confidence interval; M–H, Mantel–Haenszel.

100,000 patients demonstrated that the Sjogren disease, scleroderma, and rheumatoid arthritis were present at significantly higher rates among patients with silicone implants compared with the general population.[52] The majority of such studies have largely focused on silicone implants, a trend which is supported by the increased risk of experiencing BII-type symptoms with silicone implants when compared with saline, as demonstrated by our meta-analysis. Nonetheless, some recent studies seem to promote that BII is equally present among patients with saline-filled implants[10] or that the issue arises from the capsule rather than the actual implant,[53] making saline implants a potential perpetrator as well. In fact, in the recent Aesthetic Surgery Education and Research Foundation studies by Glicksman et al,[54] saline implants consisted of a large part of their BII cohort, although implant fill may not impact BII-type symptoms.

Despite the increase in recent studies, this is not a new phenomenon. Dating back as far as 1964,[55] a link between breast implants and systemic manifestations has been postulated. In fact, reports of BII-type symptoms in the FDA Manufacturer and User Facility Device Experience database dating back as far as 1981 can be found.[10] Terms such as human adjuvant disease, autoimmune syndrome induced by adjuvants (ASIA syndrome), inflammatory syndrome induced by

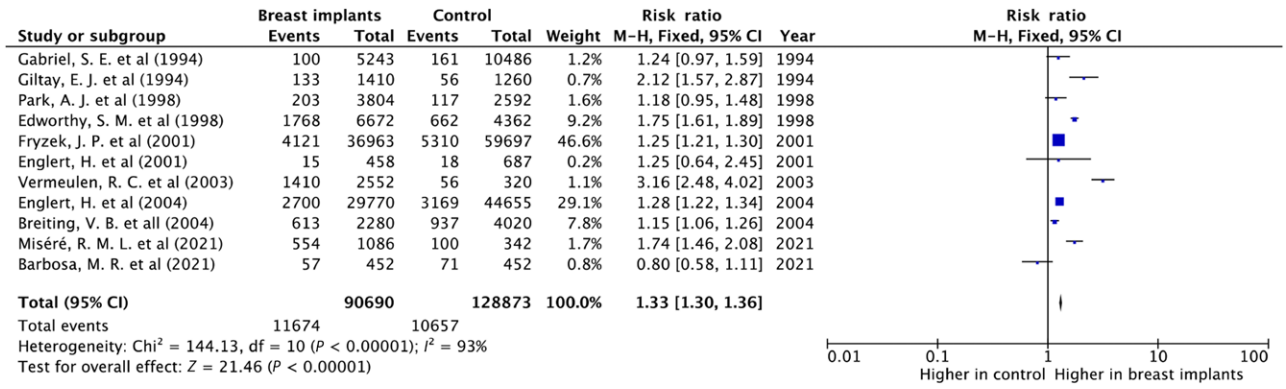

Fig. 3. Forest plot comparing patients with vs without breast implants for overall symptoms. CI, confidence interval; M–H, Mantel–Haenszel.

adjuvants, silicone implant incompatibility syndrome, silicone-related symptom complex, siliconosis, and the Shoenfeld syndrome have been used to classify this disease over the years, to name a few.[56] Initially, a link between the silicone nature of implants and rheumatic symptoms clusters was of interest, which failed to be proven.[57] Nonetheless, "BII" has now become the most widely accepted term to define this entity characterized by nonspecific, subjective, systemic symptoms following breast implants.

Although criticism regarding the use of patient-reported symptoms for this review may be valid, notably, when focusing on the subjective and unverified nature of these reports, the authors believe this is the most appropriate approach for the stated goal of this review. As demonstrated by the vast heterogeneity of symptoms in the literature, BII is arguably subjective in nature and is thus likely best studied as such. This is strengthened by the fact that, therefore, most studies are in fact self-reported or survey-based. In addition, as our goal would be to define BII as its own entity, this would best be done through symptoms rather than associations with predefined diseases. Whether it is, in fact, its own entity rather than a constellation of autoimmune or rheumatic diseases, only time will tell. Nevertheless, adopting a patient-centered approach based on individual symptoms seems most appropriate based on our endeavors and the current state of the literature.

Limitations and Future Directions

Despite its strengths, our meta-analysis carries its own set of limitations. There is, first, an inherent challenge in studying subjective outcomes in an objective manner and quantifying those results, which leads to challengeable external validity. In the same train of thought, the retrospective designs of many of our primary studies may hinder the true validity of our conclusions. Furthermore, although excluding studies with less than 10 patients is not grounded in any scientific basis and may further bias our results, this was done to improve the generalizability of our results. As well, it is important to note that there is an inherent bias in using such search terms as results will tend to naturally show stronger associations. Nevertheless, given the primary goal was to synthesize symptoms of BII in the manner of a systematic review, this was the most appropriate way to do so and was temporized by the use of solely comparative studies, a meta-analysis, and looking into publication bias is a means to limit such. In addition, many of the subgroups compared lacked a meaningful number of comparative studies, affecting the power of our analyses. Despite some authors demonstrating favorable results in terms of ridding patients of BII-type symptoms thanks to explantation, the literature is heterogeneous in terms of long-term outcomes, and even in terms of intricacies of the procedure (eg, the necessity of en bloc capsulectomy).[15,58–60] Furthermore, an analysis stratified between smooth versus textured implants would have been of interest. Unfortunately, no more than 3 studies[9,33,38] included details pertaining to such in their methodology. The same can be said about which type of silicone gel was used, as, in theory, older implants are more at risk of inflammation through their higher risk of gel bleed and rupture. Stratifying our analysis based on patients who had breast cancer (chemotherapy/radiation, time to diagnosis/treatment) and breast implant–related mechanical issues (capsular contracture, implants too large, radiation injury) would have also added an interesting dimension, given both of these can cause systemic symptoms in patients similar to some stated by BII patients. It would also allow for a better comparison between groups, eliminating such confounding factors. However, such a granular stratification was limited by the primary studies utilized and the data that was able to be collected. Future, prospective observational cohorts are needed to objectively study BII among patients, especially with comparative study designs and when studying potential treatment options.

CONCLUSIONS

In the face of increasing public awareness surrounding BII, a clear symptom-based definition of the disease must be established. It is with the hope that a better understanding of the phenomenon that is BII may be facilitated through the results presented in our study. The most common symptoms determined from the present meta-analysis may become the basis for structured questionnaires and aid in the standardization of BII-related

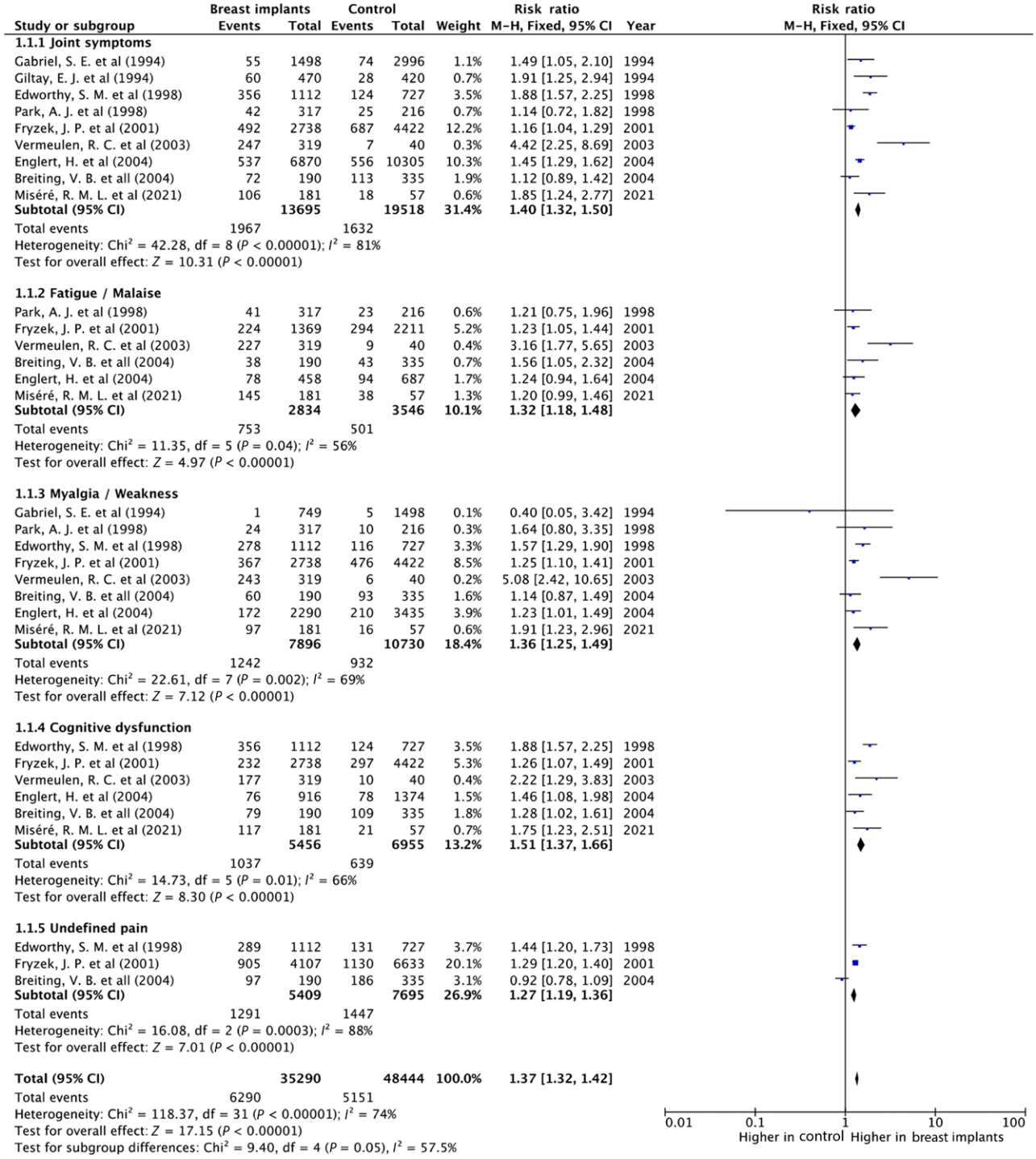

Fig. 4. Forest plots comparing patients with vs without breast implants for specific symptoms. CI, confidence interval; M–H, Mantel–Haenszel.

research. Ultimately, in the spirit of increasing evidence-based practice in plastic surgery, the authors hope this study will allow plastic surgeons to better serve their patients, address their concerns, and provide informed consent when discussing breast implants and their potential consequences. Although this study does not necessarily prove anything new, it confirms what many individual studies have shown over the years, that is, which symptoms are most commonly associated with BII, with higher level evidence.

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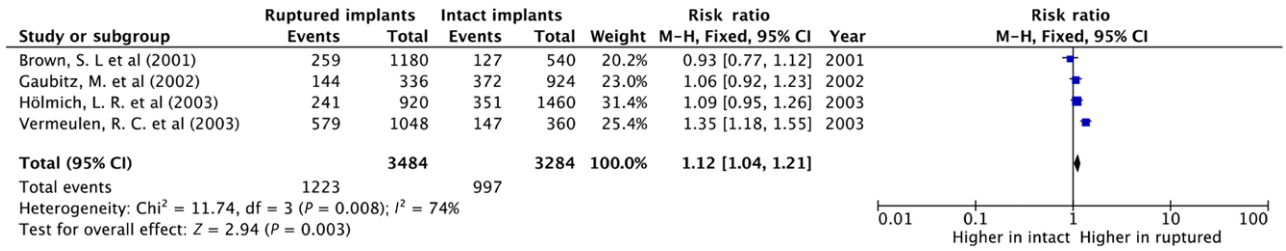

Fig. 5. Forest plot comparing patients with ruptured vs intact breast implants for overall symptoms. CI, confidence interval; M–H, Mantel–Haenszel.

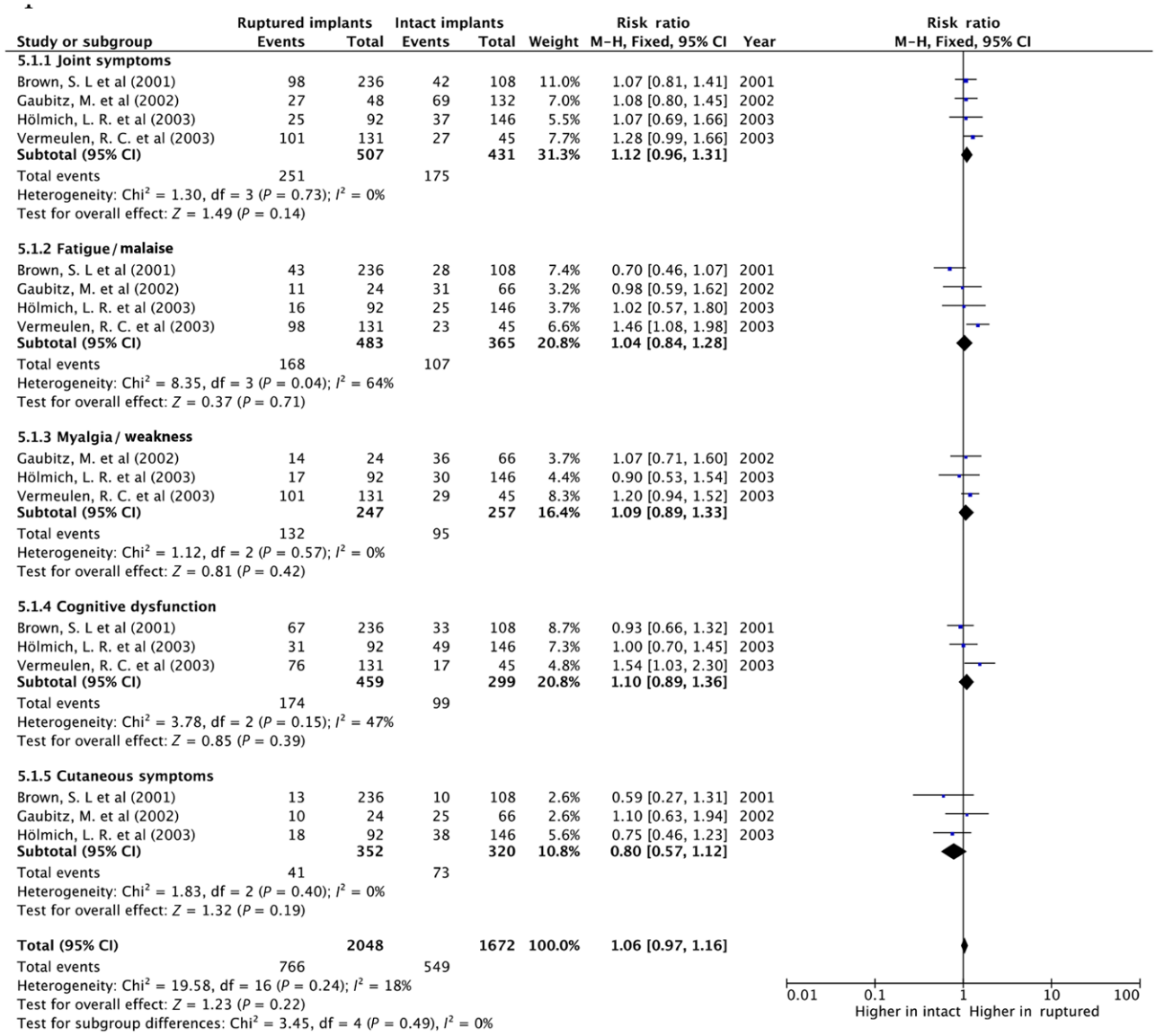

Fig. 6. Forest plots comparing patients with ruptured vs intact breast implants for specific symptoms.

DISCLOSURE

The authors have no financial interest to declare in relation to the content of this article.

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