WEP Warwick Evans Publishing

International Journal of Public Health and Medical Research

ISSN: 3006-7707 (Print), ISSN: 3006-3752 (Online) | Volume 6, Number 6, Year 2026
DOI: https://doi.org/10.62051/ijphmr.v6n6.06
Journal homepage: https://wepub.org/index.php/IJPHMR/index

The Risk Factors for Benign Breast Diseases: A Literature Review

Jiawen He

Melbourne School of Population and Global Health, University of Melbourne, Melbourne, Australia

ABSTRACT

Benign breast diseases (BBDs) are a group of heterogeneous, non-malignant breast conditions that affect many women around the world. It is associated with the risk of breast cancer. However, the evidence of the risk factors for BBDs is inconsistent. This review aimed to synthesize the existing evidence on the risk factors of overall BBD and its subtypes, including non-proliferative diseases, proliferative diseases (proliferative diseases without atypia and atypical hyperplasia). A comprehensive search was conducted in the Embase database for studies that evaluate the associations between various risk factors and BBDs. Twenty-one eligible articles were included. Due to the high heterogeneity of the included articles, this study adopted a narrative synthesis approach. The results showed that multiple dietary and lifestyle factors were associated with the risk of overall BBD, including alcohol consumption, tanning bed use, body mass index, height, family fat, vegetable protein, fiber, nuts, etc. For non-proliferative diseases, alcohol consumption was associated with an increased risk, while the intake of vitamin E and dietary fiber may have negative association. For proliferative BBD, vitamin E and fiber both showed a negative association, while alcohol consumption was associated with an increased risk. Caffeine intake may increase the risk of atypical hyperplasia. In summary, this review indicates that the risk factors may vary across subtypes of BBD, although the evidence for certain BBD subtypes remains limited. Therefore, BBD should not be treated as a single disease entity in future studies. Subtype-specific investigations are recommended to better clarify the etiology of BBDs.

KEYWORDS

Benign breast disease; Risk factors; Proliferative breast disease; Atypical hyperplasia; Lifestyle factors

1. INTRODUCTION

Benign breast diseases (BBDs) are common non-malignant lesions that primarily affect women of reproductive age [1]. In the United States, approximately one million women are diagnosed with this disease each year [2]; however, the true number is likely higher, as many cases are asymptomatic and therefore remain undiagnosed [3]. Although BBDs are not cancerous, their high prevalence can impose serious psychological distress and negatively affect quality of life [4]. Most importantly, certain subtypes of BBDs are associated with an increased risk of subsequent breast cancer, underscoring their public health implications [5].

According to the Dupont and Page classification system [6]. BBDs can be divided into non-proliferative diseases, proliferative diseases without atypia, and atypical hyperplasia. Non-proliferative diseases are simple lesions; the cells of breast tissue do not show abnormal growth. The cells of breast tissue among proliferative diseases without atypia grow actively, but their structure still looks normal. However, the cells of atypical hyperplasia not only grow abnormally but also have abnormal structures and shapes. This classification reflects the progressive spectrum of epithelial

hyperplasia and dysplasia in BBDs [7]. The risk of breast cancer varies significantly across subtypes: women with proliferative diseases without atypia have approximately twice the risk of developing breast cancer compared to those with non-proliferative diseases, while atypical hyperplasia increases the risk by four times [8]. Moreover, compared with healthy women, people with non-proliferative BBD had an approximately 1.17 times higher risk of developing breast cancer. Among women with proliferative disease without atypia, the risk of breast cancer is significantly increased, approximately 1.76 times [7]. Therefore, different mechanisms may underlie the subtypes of BBDs.

Many studies have evaluated the risk factors of BBD, but there are inconsistencies among the research findings. For example, a study in Canada found that the use of oral contraceptives was associated with a reduced risk of BBD [9]. However, another study did not observe a significant association between them [10]. This likely stemmed from variations in research study design, exposure definition, sample population and covariate adjustment [11]. More importantly, most of these studies examined BBDs as a single entity without distinguishing among different subtypes [12]. However, the results of the same risk factor may vary among different subtypes of BBD. One study reported that there was no significant association between smoking and proliferative BBD [13], while other studies have found that there was a negative correlation between smoking and the overall risk of BBD [14]. The lack of synthesized stratified evidence limits our understanding of how various factors affect different BBD subtypes.

Therefore, this review aimed to complement the current evidence by systematically integrating population-based studies to classify risk factors by BBD subtypes and assess the consistency of findings. The research question is what the risk factors are associated with the benign breast diseases and its different subtypes.

2. METHODS

I retrieved peer-reviewed research articles reporting the risk associations between BBD and potential factors, after applying the search strategy, from the Embase database via the Ovid platform. The titles and abstracts of the search results were screened, followed by full-text screening according to predefined inclusion and exclusion criteria to identify eligible studies. The screening was completed through the Covidence platform.

2.1. Search Strategy

The search strategy included the following keywords: ("benign breast disease*" or "benign breast tumour*" or "benign breast lesion*") and (risk* or association* or relationship* or etiology).

Inclusion and exclusion criteria

Studies that met the following inclusion criteria were included: (1) The article was published between March 1984 to June 2022; (2) The article was published in English; (3) The research article was original and peer-reviewed. (4) To reduce population-related heterogeneity, this review was restricted to studies conducted among White women; (5) The study reported metrics for the association between BBD risk and factors using risk ratio (RR), odds ratio (OR), or hazard ratio (HR); (6) The study design was case-control, cohort, or cross-sectional.

Articles were excluded if they: (1) only studied male participants or non-White populations; (2) did not report the relationships between any exposures and BBD; (3) did not report relevant metrics; (4) were non-original research article (such as reviews); (5) were based on hospital or clinics rather than population; (6) were non-English publications or not available for full texts.

2.2. Data Extraction

I generated a data extraction table to identify the key information included in the articles. The following information was extracted for each included study: author, year of publication, country/region, study design, study setting, follow-up time, outcome definition, sample size, follow-up time, diagnostic method, classification of BBD, risk factors, effect estimates, standardization of effect estimates, and match and variable adjustment.

2.3. Data Analysis

A meta-analysis was not feasible in this study; instead, I summarized the findings through narrative synthesis by overall BBDs and the subtypes of BBDs; for the overall BBDs, all the 21 studies were taken into account. A p value less than 0.05 was considered nominally significant. All analyses and plot generation were conducted using R (Version 4.3.3).

3. RESULTS

3.1. Study Selection

Initially, a total of 2,838 articles were identified, among which 22 duplicate articles were excluded. The remaining 2,816 articles entered the title and abstract screening. Subsequently, I conducted a full-text screening on 183 articles, among which 162 were excluded for the following reasons: duplicate articles (n = 2), non-White participants (n = 2), non-English articles (n = 12), BBDs were treated as exposures instead of outcomes (n = 20), no full-text available (n = 22), inappropriate research design (such as case report) (n = 57), not original research articles (n = 4), not population-based research (n = 31), the outcome was not BBD (n = 12). Finally, 21 eligible studies were included in the subsequent analysis (Figure 1).

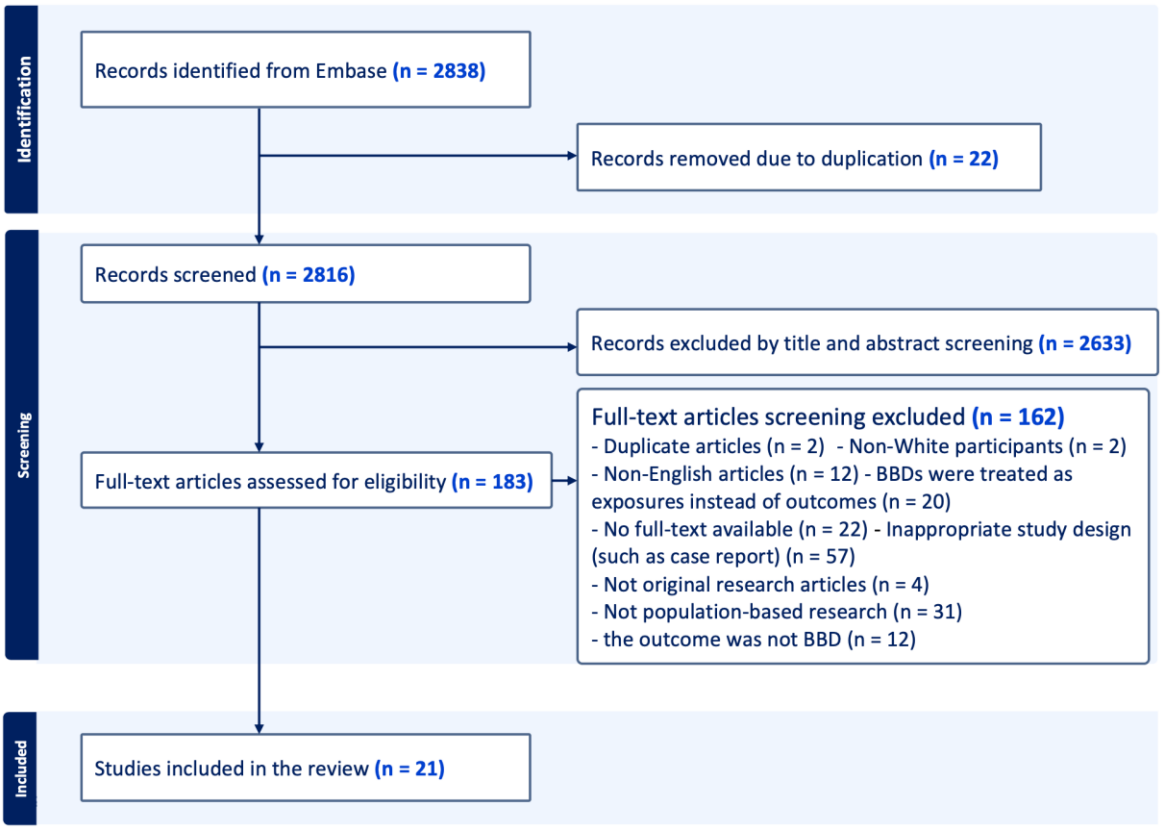

Figure 1. Flow diagram for study selection

3.2. Study Characteristics

Table 1 shows the characteristics of the 21 included articles. One study was conducted in Denmark, and the rest were in the United States. The research designs comprised 20 cohort studies and one case-control study, all of which were population-based. Among the 20 cohort studies, 11 studies used data from the Growing Up Today Study, and 8 from the Nurses' Health Study II. Among the included studies, 15 studies examined the risk factors for BBD regardless of subtypes, 2 studies focused on non-proliferative diseases, 7 studies investigated proliferative diseases, and 1 study analysed both proliferative diseases without atypia and atypical hyperplasia. The outcome, diagnosis of BBD, was primarily determined through biopsy or histopathological confirmation, while one study was self-reported. The risk factors for BBDs mainly included reproductive factors, hormonal factors, family history of BBDs/breast cancer, dietary factors, lifestyle factors, and anthropometric factors; more details can be found in Table 1.

Table 1. Characteristics of the 21 included studies

Study	Study design	Sample size	Dataset	Region	Classification of benign breast diseases	Risk factors
Berkey et al., (2017)	Cohort	7,100	Growing Up Today Study	The United States	All BBD	BMI, height, gestational weight gain, peak height velocity
Boeke et al., (2014)	Cohort	6,593	Growing Up Today Study	The United States	All BBD	α-carotene, β-carotene, lutein/zeaxanthin, lycopene, β-cryptoxanthin, Vitamin A, Carrots
Boeke et al., (2015)	Cohort	6,593	Growing Up Today Study	The United States	All BBD	Vitamin D, sunscreen use, sunburns in the past year, tanning bed use, skin color, UV index in state of residence
Su et al., (2012)	Cohort	29,480	Nurses' Health Study II	The United States	Proliferative BBD	Vitamin D, calcium, dairy protein, total dairy, total milk
Byrne et al., (2002)	Cohort	75,826	Nurses' Health Study II	The United States	All BBD, proliferative BBD, non-proliferative BBD	Alcohol consumption, alcohol consumption at ages 15-17 years, alcohol consumption at ages 18-22 years
Webb et al., (2004)	Cohort	58,628	Nurses' Health Study II	The United States	Non-proliferative BBD, proliferative BBD without atypia, atypical hyperplasia	Total energy, total fat, animal fat, vegetable fat, saturated fat, monounsaturated fat, polyunsaturated fat, fiber, vitamin A, vitamin C, vitamin E, retinol, carotene, folate, caffeine (mg), use of vitamin supplements
Berkey et al, (2013)	Cohort	6,860	Growing Up Today Study	The United States	All BBD	total dairy,milk, yogurt, cheese, dairy protein, dairy fat
Berkey et al., (2019)	Cohort	7,144	Growing Up Today Study	The United States	All BBD	Animal (non-dairy) protein, animal (non-dairy) fat, peanut butter and nuts, maternal benign breast diseases, maternal breast cancer, gestational weight gain, BMI, height, peak height velocity
Aarestrup et al., (2022)	Cohort	171,272	-	Denmark	All BBD	Childhood BMI
Goldberg et al., (2019)	Cohort	1121	-	The United States	All BBD	Maternal pre-pregnancy BMI, gestational weight gain, birth weight
Su et al., (2010)	Cohort	29,480	Nurses' Health Study II	The United States	Proliferative BBD	Fiber, peanuts, peanut butter, peanuts and peanut butter, total nuts.
Liu et al., (2012)	Cohort	29,117	Nurses' Health Study II	The United States	Proliferative BBD	Alcohol intake, total folate intake, dietary folate intake
Su et al., (2015)	Cohort	29,480	Nurses' Health Study II	The United States	Proliferative BBD	Total fat, animal fat, vegetable fat, saturated fat, monounsaturated fat, polyunsaturated fat, trans-unsaturated fat, retinol activity equivalents, vitamin E, vitamin E from food only, α-Carotene, β-Carotene, β-Cryptoxanthin, lycopene, lutein and zeaxanthin
Jung et al., (2011)	Cohort	40,318	Nurses' Health Study II	The United States	All BBD, Proliferative BBD	Strenuous activity, moderate activity, walking, total activity
Berkey et al., (2015)	Cohort	7,100	Growing Up Today Study	The United States	All BBD	Pregnancy weight gain, birth weight, mother pre-pregnancy BMI
Berkey et al., (2011)	Cohort	6,899	Growing Up Today Study	The United States	All BBD	Age at menarche, adult height, childhood BMI, adult BMI, peek height growth velocity
Odenheimer et al., (1984)	Case-control	180 (90/90)	-	The United States	All BBD	Years of oral contraceptive use, No. of children, age at menarche
Berkey et al., (2013)	Cohort	7,222	Growing Up Today Study	The United States	All BBD	Vegetable protein, vegetable fat, peanut butter, nuts, beans, lentils, soybeans, corn
Berkey et al., (2012)	Cohort	6,888	Growing Up Today Study	The United States	All BBD	The breast cancer history of mother, the benign breast disease history of mother, the breast cancer history of aunt or grandmother, adolescent alcohol, menarche age, adult height, childhood BMI, young adult BMI, adolescent waist circumference
Baer et al., (2003)	Cohort	29,494	Nurses' Health Study II	The United States	Proliferative BBD	Total fat, animal fat, vegetable fat, saturated fat, monounsaturated fat, polyunsaturated fat, trans-unsaturated fat, vitamin C (including supplements), vitamin E (including supplements), vitamin A (including supplements), retinol, total carotenoids, α-Carotene, β-Carotene, β-Cryptoxanthin, Lycopene, lutein and zeaxanthin, folate, fiber, fruits, vegetables, fruits and vegetables combined
Berkey et al., (2020)	Cohort	7,144	Growing Up Today Study	The United States	All BBD	Alcohol intake, peanut butter and nut intake, dietary fiber intake

Footnote: BMI: body mass index, BBD: benign breast disease

3.3. Risk Factors for BBDs

3.3.1. BBDs Regardless of the Subtypes

(1) Reproductive factors

Three studies evaluated the association between age at menarche and the risk of BBD[15, 16, 17]. They all found no significant association between age at menarche and the risk ($p>0.05$). One study assessed the BBD relationship with the number of children; no evidence for a statistically significant association was observed ($p=0.55$) [15]. Detailed results were shown in Appendix Figure S1.

(2) Hormonal factors

One study reported no evidence for an association between years of contraceptive use and the BBD risk ($p\geq0.05$) [15]. Detailed results were presented in Appendix Figure S2.

(3) Family history of BBD or breast cancer

Two studies examined the risk of family history of breast cancer and BBD, respectively [17, 18]. One study reported that having a first-degree family history (breast cancer and BBD history of mother) was significantly associated with a higher risk of developing BBD ($p<0.01$) [18]. Specifically, the OR for BBD among women whose mothers had a history of BBD was 1.84 (95% CI: 1.31-2.58), and the OR for those whose mothers had a history of breast cancer was 2.20 (95% CI: 1.35-3.58). In contrast, another study found no significant association between BBD risk and first-degree family history ($p>0.095$) [17]. This study additionally examined the association of second-degree family history [17]. It shows that women whose aunts were diagnosed with breast cancer had a significantly increased risk of BBD (OR: 2.34, 95% CI:1.22-4.49, $p=0.022$), whereas having grandmothers with breast cancer was not associated with BBD risk ($p>0.05$). Detailed results were presented in Appendix Figure S3.

(4) Lifestyle factors

Alcohol intake

Two studies assessed the association between alcohol consumption during the age of 18 to 22 years and the risk of BBD [19, 20]. They both reported that more alcohol consumption was associated with an increased risk of BBD regardless of subtypes (OR: 1.14-1.15, $p< 0.03$). Three studies evaluated the relationship with alcohol consumption in adolescents [17, 19, 21]. One study observed that adolescent alcohol intake had a significant association with the risk of BBD in adolescent (OR:1.75, 95% CI: 1.20-2.56, $p=0.004$) [21], while the other two studies did not find it statistically significant ($p>0.57$) [17, 19]. Detailed results were presented in Appendix Figure S4.

Sun exposure

One study evaluated the relationship between sun exposure and the risk of BBD [22]. It shows that tanning bed use significantly increased the risk of BBD (OR: 1.69, 95 CI: 1.03-2.77, $p<0.05$), compared with not using tanning bed, but there was no significant association between other exposures (sunscreen, sunburns in the past year, skin color, UV index in state of residence) and the risk of BBD ($p>0.10$). Detailed results were presented in Appendix Figure S4.

(5) Physical activity

Only one study investigated the relationship between different levels of physical activity and the risk of BBD [23]. It reported that strenuous, moderate, and total activity decreased the risk and walking activity was not significantly related to the risk ($p>0.06$). Detailed results were presented in Appendix Figure S5.

(6) Anthropometric measures

Five studies assessed the relationship between BMI in childhood and the risk of BBD in adults [16, 17, 18, 24, 25]. Four studies reported that higher BMI in childhood significantly decreased the risk (OR: 0.44, 95% CI: 0.22-0.88; OR: 0.93, 95%CI: 0.87-0.99; OR: 0.91, 95%CI: 0.84-0.99; OR: 0.88 (0.77-1.00), $p<0.05$) [16, 17, 24, 25]. One study pointed out that there was no association between the BMI and the risk of BBD ($p=0.078$) [18]. Three studies evaluated the relationship between adult BMI and BBD risk [16, 17, 26]. One study showed that higher adult BMI decreased the risk (OR: 0.91, 95% CI: 0.82-1.00, $p<0.05$) [17]. The other two studies observed a non-significant relationship ($p>0.05$) [16, 26].

Three studies assessed the association between peak height velocity and the risk of BBD [16, 18, 24]. Two studies showed that high peak height velocity was significantly associated with the increased risk (OR: 2.20-2.31, $p<0.05$) [18, 24]. One study reported a non-significant relationship ($p=0.37$) [16]. One study showed that higher adolescent waist circumference significantly decreased risk of BBD ($p=0.02$) [17]. Detailed results were presented in Appendix Figure S6.

(7) Dietary factors

Fat and protein

One study evaluated the association between non-dairy animal fat and the risk of BBD and reported a positive association (OR: 2.27, 95% CI: 1.17-4.42, $p= 0.04$) [18]. Two studies assessed the relationship of animal fat with the risk [27, 28], with only one showing a statistically significant association (OR: 1.55, 95% CI: 1.52-2.09, $p=0.03$) [27]. Of the two studies that assessed the relationship of monounsaturated fat [27, 28], only one reported a statistically significant correlation with the risk of BBD (OR: 1.32, 95% CI: 1.01-1.72, $p=0.04$) [27]. Three studies evaluated the association between vegetable fats and the risk of BBD [27, 28, 29]. Only one study that reported the significant association (OR: 0.69, 95% CI: 0.52-0.92, $p=0.02$) [27]. One study found that a significant decreased risk of higher vegetable protein intake for BBD (OR: 0.64, 95% CI: 0.43-0.95, $p=0.02$) [29]. Detailed results were presented in Appendix Figure S7.

Fiber

Three studies evaluated the association between total fiber intake and the risk of BBD [21, 27, 30]. They all showed negative correlations (OR ranged from 0.57 to 0.75, $p<0.05$). One study reported the fiber from different sources had no significant association the risk of BBD regardless of subtype ($p>0.16$) [30]. Detailed results were presented in Appendix Figure S8.

Nuts

Three studies evaluated the association between peanut butter and nut intake and the risk of BBD [18, 21, 31]. They all reported a negative association between peanut butter and nuts and the risk (OR ranged from 0.60-0.64, $p<0.03$). Detailed results were presented in Appendix Figure S8.

Vegetable and fruits

Two studies explored the relationship between fruit and vegetable intake and the risk of BBD, but no significant association was found ($p>0.25$) [27, 32]. Detailed results were presented in Appendix Figure S8.

Vitamin

Two studies evaluated the relationship between vitamin D and the risk of BBD, and both observed no correlation between them ($p>0.42$) [22, 33].

Two studies assessed the association of vitamin E with the risk [27, 28]. Only one study reported that an increase in vitamin E intake was associated with a reduced risk of BBD (OR: 0.76, 95% CI: 0.58-1.00, $p=0.02$) [27]. Detailed results were presented in Appendix Figure S9.

Micronutrients

Three studies evaluated the association between β-carotene and the risk of BBD [27, 28, 32]. One study shows a negative association between β-carotene intake and the risk of BBD (OR:0.58, 95% CI: 0.34-1.00, p=0.03) [32]. There were no associations were reported in the other two studies (p>0.18) [27, 28]. Detailed results were presented in Appendix Figure S9.

(8) Maternal factors

Three studies assessed the relationship between gestational weight gain and the risk of BBD regardless of subtypes [18, 24, 26]. One study reported that gestational weight gain was significantly associated with reduced risk (OR:0.53, 95% CI: 0.30-0.94, p=0.03) [24]. The other two studies reported no significant association (p>0.05) [18, 26]. One study assessed the relationship of maternal pre-pregnancy BMI and found no significant association (p>0.05) [26]. Detailed results were presented in Appendix Figure S10.

3.3.2. Non-proliferative diseases

(1) Lifestyle factor

One study assessed the association between alcohol consumption and the risk of non-proliferative BBD [19]. It shows that more alcohol consumption at ages from 15 to 17 or 18 to 22 was significantly associated with increased risk of non-proliferative BBD (OR:1.89, 95% CI: 1.18-3.03p<0.05). Detailed results were presented in Appendix Figure S11.

(2) Dietary factor

One study evaluated the association between dietary factors (including energy, fat, fiber, vitamin, retinol, carotene, folate and caffeine) and the risk of non-proliferative BBD; no significant association was found (p>0.05) [34]. Detailed results were presented in Appendix Figure S12.

3.3.3. Proliferative diseases with or without atypia

(1) Overall

Physical activity

One study observed that there was no association between physical activity and the risk of proliferative BBD (p>0.05) [23]. Detailed results were presented in Appendix Figure S13.

Lifestyle factors

Two studies assessed the association of alcohol consumption [19, 20]. One of the studies reported that the alcohol consumption of women aged 18 to 22 increased the risk of proliferative BBD (OR: 1.33, 95% CI: 1.05-1.69, p=0.007) [19]. However, another study did not observe a statistically significant association (p>0.05). Detailed results were presented in Appendix Figure S14.

Dietary factor

Two studies evaluated the association between fiber intake and the risk of proliferative BBD [27, 30]. They both reported a negative association (OR ranged from 0.71-0.75, p<0.03). Two studies assessed the relationship between fat intake and proliferative BBD [27, 28]. One study showed that women whose intake of animal fat was in the highest quartile during adolescence had a 55% higher risk of developing proliferative BBD than those in the lowest quartile group (p=0.03) [27]. Conversely, women with the highest quartile intake of vegetable fat had a 31% lower risk compared to the lowest group (p=0.02) [27]. In addition, higher intake of monounsaturated fats is associated with a 32% increased risk of proliferative diseases (p=0.04) [27]. Another study did not observe a significant association (p=0.55) [28]. Two studies evaluated the relationship between vitamin E and risk of proliferative BBD. One study observed that women in the highest intake quartile group of Vitamin E (including supplement) intake significantly decreased the risk of proliferative BBD (OR:0.76, 95% CI: 0.58-1.00, p=0.02) [27]. Detailed results were presented in Appendix Figure S15.

(2) Proliferative diseases without atypia

One study presented that high vegetable fat intake was associated with a reduced risk of proliferative diseases without atypia (OR:0.79, 95% CI: 0.65-0.95, p=0.02) [34]. Detailed results were presented in Appendix Figure S16 and S17.

(3) Atypical hyperplasia

This study also observed that higher caffeine intake was associated with an increased risk of atypical hyperplasia (p=0.05) [34].

4. DISCUSSION

I systematically reviewed the evidence for associations between BBD and various potential risk factors, including reproductive, hormonal, family history, lifestyle, physical activity, anthropometric measures, dietary and maternal risk factors. The findings indicated substantial variability in the strength and direction of associations across different risk factors and BBD subtypes. This variation highlights the complexity of BBD etiology and the need to consider subtype-specific mechanisms [8].

4.1. Overall BBDs

Overall BBDs represent a composite of multiple subtypes, and the proportion of each subtype may vary across studies. Consequently, the identified risk factors for overall BBDs could differ depending on the relative distribution of subtypes within each study population. In addition, any inconsistencies in findings may be also attributed to differences in studies themselves, such as variations in study design, population characteristics, confounder control, etc. This review primarily focused on these study-specific factors when interpreting the evidence.

Two studies reported inconsistent associations of the BBD or breast cancer history of mother [17, 18]. The reason for the different results might be due to the sample size of the cases, which may affect the accuracy of the results. A review shows that there is a significant association between a family history of breast cancer and risk of BBD [35]. One national study from Denmark also found that women with a family history of BBD or breast cancer had a significantly increased risk of developing BBD [36]. These findings collectively suggest that a first-degree family history may be a risk factor for BBD.

Three studies showed the inconsistent association of gestational weight gain [18, 24, 26]. The reasons for the heterogeneity of results may be: one of the studies adopted self-reported BBD outcomes instead of histologic confirmation, which may lead to bias [26]. Finally, there are differences among the studies in the adjustment for confounding factors. Another study also observed that a larger increase in gestational weight gain reduced the risk developing BBD [37]. Therefore, the gestational weight gain might have protective effect to BBD.

Both fiber and nuts could be associated with a decreased risk of BBD, according to the consistent results from the three studies on fiber [21, 27, 30], and four studies on peanuts butter and nuts [18, 21, 30, 31].These findings are also supported by a previous study [38].

Three studies presented that inconstant association between β-carotene and the risk of BBD [27, 28, 32]. The reasons for the heterogeneity may include differences in outcome definitions and exposure measurement methods. Studies reporting significant risk reduction took overall BBD as the outcome [32], while the other two studies focused on proliferative BBD [27, 28]. Furthermore, two studies that found no significant association used questionnaires to retrospectively collect exposure information, which might lead to recall bias and thus affect the accuracy of the results. The negative association was also consistent with a previous study [39]. Therefore, it is possible that the β-carotene negatively associated with the risk of BBD.

Two studies reported the inconsistent relationship between animal fat, monounsaturated fat and risk of BBD, one study reported a higher intake associated with an increased risk of BBD [27], while the other study found no significant association [28]. The inconsistency could be explained by differences in adjustment variables, with one study being only adjusted for age as a confounder [27]. Three studies reported the inconsistent relationship between vegetable and risk of BBD, the key reason for the differences in the results mainly lies in the inconsistent adjustment of variables, which affects the comparability and consistency of the results [27, 28, 29]. A systematic review study also concluded that the intake of animal fats and monounsaturated fats is associated with an increased risk of BBD and vegetable fat is associated with a decreased risk, which to some extent supports the observations in this study [40]. Therefore, the animal or monounsaturated fat may be risk factor of BBD, the vegetable fat may be the protective factor.

Five studies reported that inconsistent association between childhood BMI and the risk of BBD [16, 17, 18, 24, 25]. One study reported the result was not significant [18]. This difference might be due to that different numbers of sample subsets and adjustment variables. A review study also mentioned that BMI in childhood is significantly associated with the risk [41].

Two studies evaluated the inconsistent relationship between adult BMI and risk of BBD [16, 17]. The reason might be in the differences in adjustments: one study only adjusted for age [16], while the other study adjusted for family history on this basis [17]. Family history is an important confounding factor for breast diseases [8]. If not adjusted, it may lead to bias in risk estimation. A study in Brazil observed that higher BMI was associated with a reduced risk of BBD [42]. The BMI may be the protective factor of BBD. Three studies showed the inconsistent association of peak height velocity [16, 18, 24]. The reasons may be similar to those for the differences in the results of BMI in childhood, which are different numbers of sample subsets and adjustment variables. A previous study supported that greater peak height velocity was associated with a higher risk of BBD [38]. Therefore, the peak height velocity could be a risk factor for BBD.

4.2. Non-proliferative BBD

One study reported the consistent association between alcohol consumption during the ages of 15-17 and 18-22 and the risk of non-proliferative BBD [19]. However, a study showed that alcohol consumption was not significantly associated with the risk of BBD [43]. It remains uncertain whether alcohol consumption is a risk factor for BBD.

4.3. Proliferative BBD

Two studies reported the consistent association between fiber and the risk of proliferative BBD [27, 30]. The other study also shows that a high intake of fibers is significantly associated with a reduced risk of proliferative BBD [44], supporting the potential protective effect of fiber. The fiber could be a protective factor of proliferative BBD.

The two studies reported inconsistent associations between animal fat, vegetable fat and monounsaturated fat and the risk of proliferative BBD [27, 28]. The reasons for the inconsistency of such results may be as follows. Firstly, the number of cases in the two studies is different. One study had a larger number of cases and a larger sample size, which might have more statistical power to detect potential associations [28]. Secondly, the differences in adjusting variables may also affect the results. The study was only adjusted for age [27], while another study included dietary factors (such as vitamins and fiber, etc.) as confounding factors, thereby reducing potential confounding effects. Finally, the two studies also differed in their modeling approaches: one used quartile for grouping [27], while the other one used quintile for grouping [28]. One study also mentioned that animal fat would increase the risk of proliferative BBD [45]. The animal fat might be a risk factor of proliferative BBD, the other types of fat need future studies.

Two studies showed the inconsistent association of Vitamin E [27, 28]. One possible reason for the inconsistency in the results of the two studies is the different definitions of the exposures which may lead to differences in the results: one study included intake from dietary supplements as an exposure indicator, while the other did not. Another study also found potential protective effect of vitamin E [46]. The Vitamin E might be a protective factor for proliferative BBD.

Atypical hyperplasia

One study showed a positive association between caffeine intake and the risk of atypical hyperplasia [34]. However, this result was opposite to the findings from other studies [47, 48]. This may be because the review only included only one study examining the relationship between caffeine intake and atypical hyperplasia, and the limited number of available studies reduced the representativeness of the findings.

Proliferative disease without atypia

The review showed the negative association between vegetable fat and the risk of proliferative disease without atypia [34]. Another study reported a similar result [49]. The vegetable fat might the protective factor in proliferative disease without atypia.

Risk factor comparison across subtypes

This review also found that the associations between the same exposures and risk differ among different types of BBD. The high alcohol intake at age from 15 to 17 increased the risk of non-proliferative diseases, but it had no association with other types of BBD [19]. The higher fiber intake was negatively associated with the risk of BBD regardless of the subtypes and proliferative diseases [21, 27, 30]. However, it had no relationship with non-proliferative diseases. Moreover, the vegetable fat had a protect effect for the risk of proliferative diseases without atypia [34]. This negative association of vegetable fat cannot be found for other subtypes. Therefore, difference in the risk effects of the same factor across the BBD subtypes suggests that BBD should not be regarded as a single disease. Independent risk factors for different disease types should be identified through subtype-specific analysis.

5. STRENGTHS AND LIMITATIONS

This review provides a comprehensive and structured synthezed evidence on the factors that are associated with BBDs. The review also focused on the population-based studies which enhanced the representativeness and generalization of the findings. It made more comparison of risk factors across different BBD types. However, this study has certain limitations. Firstly, the number of available studies for certain subtypes were limited. For example, only one study specifically examined the risk factors for proliferative diseases without atypia and atypical hyperplasia, providing limited evidence for these subtypes. Secondly, the systematic review and meta-analysis cannot be conducted because of the high heterogeneity. The high heterogeneity arises from that the included studies were derived from overlapping datasets, had a wide range of exposures, and adjustment variables differently etc.

Implications

The research results indicate that the risk factors for different types of BBD are not consistent, implying that different mechanisms may underlie each subtype. Treating BBDs as a single disease entity could therefore lead to biased risk estimates, both when identifying risk factors for BBDs and when assessing their associations with subsequent breast cancer risk [8]. In the future studies, subtype-specific analyses should be adopted to better clarify the different effects of various BBD subtypes, thereby improving the accuracy of risk assessment. From a public health perspective, identifying and understanding the risk factors specific to each subtype can help formulate more targeted prevention and early screening strategies for women at risk.

6. CONCLUSION

This review systematically synthesizes the evidence regarding the risk factors associated with BBD. The results demonstrate that the associations between risk factors and disease occurrence vary across BBD subtypes, suggesting that BBD should not be regarded as a homogeneous disease type. Future research should conduct subtype-specific investigations to clarify these differences and enhance our understanding of the distinct etiologies and prevention opportunities for each subtype.

ACKNOWLEDGEMENTS

Thanks to the School of Population and Global Health for providing resources and a research environment for this study. I would also like to express my gratitude to other students and teachers who helped during the research process. Their support promoted the successful completion of this study.

REFERENCES

[1] Selvakumaran, S., & Sangma, M. B. (2016). Study of various benign breast diseases. International Surgery Journal, 4(1). https://doi.org/10.18203/2349-2902.isj2016040115

[2] Santen, R. J. (2000). Benign breast disease in women. In K. R. Feingold, R. A. Adler, S. F. Ahmed, B. Anawalt, M. R. Blackman, G. Chrousos, et al. (Eds.), Endotext. MDText.com, Inc.

[3] Courtillot, C., Plu-Bureau, G., Binart, N., Balleyguier, C., Sigal-Zafrani, B., & Goffin, V. (2005). Benign breast diseases. Journal of Mammary Gland Biology and Neoplasia, 10(4), 325–335. https://doi.org/10.1007/s10911-005-9009-7

[4] Srivastava, V., Meena, R. K., Ansari, M. A., Kumar, D., & Kumar, A. (2020). A Study of Anxiety and Depression in Benign Breast Disease. Journal of Midlife Health, 11(4), 200–209. https://doi.org/10.4103/jmh.jmh_70_20

[5] Hartmann, L. C., Sellers, T. A., Frost, M. H., Lingle, W. L., Degnim, A. C., Ghosh, K., et al. (2005). Benign Breast Disease and the Risk of Breast Cancer. The New England Journal of Medicine, 353(3), 229–237. https://doi.org/10.1056/NEJMoa042750

[6] Louro, J., Roman, M., Posso, M., Comerma, L., Vidal, C., & Saladie, F. (2020). Differences in breast cancer risk after benign breast disease by type of screening diagnosis. The Breast, 54, 343–348. https://doi.org/10.1016/j.breast.2020.07.007

[7] Dyrstad, S. W., Yan, Y., Fowler, A. M., & Colditz, G. A. (2015). Breast cancer risk associated with benign breast disease: systematic review and meta-analysis. Breast Cancer Research and Treatment, 149(3), 569–575. https://doi.org/10.1007/s10549-014-3242-5

[8] Burke, A., O'Driscoll, J., Abubakar, M., Bennett, K. E., Carmody, E., Flanagan, F., et al. (2025). A systematic review of determinants of breast cancer risk among women with benign breast disease. NPJ Breast Cancer, 11(1), 16. https://doi.org/10.1038/s41523-025-00682-9

[9] Rohan, T. E., & Miller, A. B. (1999). A cohort study of oral contraceptive use and risk of benign breast disease. International Journal of Cancer, 82(2), 191–196. https://doi.org/10.1002/(SICI)1097-0215(19990719)82:2<191::AID-IJC8>3.0.CO;2-#

[10] Franceschi, S., Vecchia, C. L., Parazzini, F., Fasoli, M., Regallo, M., Decarli, A., et al. (1984). Oral contraceptives and benign breast disease: a case-control study. American Journal of Obstetrics and Gynecology, 149(6), 602–606. https://doi.org/10.1016/0002-9378(84)90330-7

[11] Goehring, C., & Morabia, A. (1997). Epidemiology of Benign Breast Disease, with Special Attention to Histologic Types. Epidemiologic Reviews, 19(2), 310–327. https://doi.org/10.1093/oxfordjournals.epirev.a017948

[12] Johansson, A., Christakou, A. E., Iftimi, A., Eriksson, M., Tapia, J., Skoog, L., et al. (2021). Characterization of Benign Breast Diseases and Association With Age, Hormonal Factors, and Family History of Breast Cancer Among Women in Sweden. JAMA Network Open, 4(6), e2114716. https://doi.org/10.1001/jamanetworkopen.2021.14716

[13] Rohan, T. E., Cook, M. G., & Baron, J. A. (1989). Cigarette smoking and benign proliferative epithelial disorders of the breast in women: a case-control study. Journal of Epidemiology & Community Health, 43(4), 362–368. https://doi.org/10.1136/jech.43.4.362

[14] Parazzini, F., Ferraroni, M., Vecchia, C. L., Baron, J. A., Levuf, F., & Franceschi, S. (1991). Smoking Habits and Risk of Benign Breast Disease. International Journal of Epidemiology, 20(2), 430–434. https://doi.org/10.1093/ije/20.2.430

[15] Odenheimer, D. J., Zunzunegui, M. V., King, M. C., Shipler, C. P., & Friedman, G. D. (1984). Risk factors for benign breast disease: a case-control study of discordant twins. American Journal of Epidemiology, 120(4), 565–571. https://doi.org/10.1093/oxfordjournals.aje.a113868

[16] Berkey, C. S., Willett, W. C., Frazier, A. L., Rosner, B., Tamimi, R. M., & Colditz, G. A. (2011). Prospective study of growth and development in older girls and risk of benign breast disease in young women. Cancer, 117(8), 1612–1620. https://doi.org/10.1002/cncr.25721

[17] Berkey, C. S., Tamimi, R. M., Rosner, B., Frazier, A. L., & Colditz, G. A. (2012). Young women with family history of breast cancer and their risk factors for benign breast disease. Cancer, 118(11), 2796–2803. https://doi.org/10.1002/cncr.26623

[18] Berkey, C. S., Tamimi, R. M., Willett, W. C., Rosner, B., Hickey, M., Toriola, A. T., et al. (2019). Dietary intake from birth through adolescence in relation to risk of benign breast disease in young women. Breast Cancer Research and Treatment, 177(2), 513–525. https://doi.org/10.1007/s10549-019-05146-6

[19] Byrne, C., Webb, P. M., Jacobs, T. W., Peiro, G., Schnitt, S. J., Connolly, J. L., et al. (2002). Alcohol Consumption and Incidence of Benign Breast Disease. Cancer Epidemiology, Biomarkers & Prevention, 11(11), 1369–1374. https://doi.org/10.1158/1055-9965.EPI-02-0243

[20] Liu, Y., Tamimi, R. M., Berkey, C. S., Willett, W. C., Collins, L. C., Schnitt, S. J., et al. (2012). Intakes of alcohol and folate during adolescence and risk of proliferative benign breast disease. Pediatrics, 129(5), e1192–e1198. https://doi.org/10.1542/peds.2011-3060

[21] Berkey, C. S., Tamimi, R. M., Willett, W. C., Rosner, B., Hickey, M., Toriola, A. T., et al. (2020). Adolescent alcohol, nuts, and fiber: combined effects on benign breast disease risk in young women. NPJ Breast Cancer, 6(1), 61. https://doi.org/10.1038/s41523-020-00209-0

[22] Boeke, C. E., Tamimi, R. M., Berkey, C. S., Colditz, G. A., Giovannucci, E., Malspeis, S., et al. (2015). Adolescent dietary vitamin D and sun exposure in relation to benign breast disease. Cancer Causes & Control, 26(8), 1181–1187. https://doi.org/10.1007/s10552-015-0613-4

[23] Jung, M. M., Colditz, G. A., Collins, L. C., Schnitt, S. J., Connolly, J. L., & Tamimi, R. M. (2011). Lifetime physical activity and the incidence of proliferative benign breast disease. Cancer Causes & Control, 22(9), 1297–1305. https://doi.org/10.1007/s10552-011-9802-0

[24] Berkey, C. S., Rosner, B., Tamimi, R. M., Willett, W. C., Hickey, M., Toriola, A. T., et al. (2017). Body size from birth through adolescence in relation to risk of benign breast disease in young women. Breast Cancer Research and Treatment, 162(1), 139–149. https://doi.org/10.1007/s10549-016-3793-7

[25] Aarestrup, J., Jensen, B. W., Pedersen, D. C., Kroman, N., Mellemkjaer, L., Baker, J. L., et al. (2022). Early life body size, pubertal timing, and risks of benign breast disease in a large cohort of Danish female adolescents and women. European Journal of Pediatrics, 181(8), 3023–3030. https://doi.org/10.1007/s00431-022-04490-1

[26] Goldberg, M., Cohn, B. A., Houghton, L. C., Flom, J. D., Wei, Y., Cirillo, P., et al. (2019). Early-Life Growth and Benign Breast Disease. American Journal of Epidemiology, 188(9), 1646–1654. https://doi.org/10.1093/aje/kwz167

[27] Baer, H. J., Schnitt, S. J., Connolly, J. L., Byrne, C., Cho, E., Willett, W. C., et al. (2003). Adolescent Diet and Incidence of Proliferative Benign Breast Disease. Cancer Epidemiology, Biomarkers & Prevention, 12(11), 1159–1167. https://doi.org/10.1158/1055-9965.EPI-03-0224

[28] Su, X., Boeke, C. E., Collins, L. C., Baer, H. J., Willett, W. C., Schnitt, S. J., et al. (2015). Intakes of fat and micronutrients between ages 13 and 18 years and the incidence of proliferative benign breast disease. Cancer Causes & Control, 26(1), 79–90. https://doi.org/10.1007/s10552-014-0487-3

[29] Berkey, C. S., Willett, W. C., Tamimi, R. M., Rosner, B., Frazier, A. L., & Colditz, G. A. (2013). Vegetable protein and vegetable fat intakes in pre-adolescent and adolescent girls, and risk for benign breast disease in young women. Breast Cancer Research and Treatment, 141(2), 299–306. https://doi.org/10.1007/s10549-013-2647-4

[30] Su, X., Tamimi, R. M., Collins, L. C., Baer, H. J., Cho, E., Sampson, L., et al. (2010). Intake of fiber and nuts during adolescence and incidence of proliferative benign breast disease. Cancer Causes & Control, 21(7), 1033–1046. https://doi.org/10.1007/s10552-010-9544-1

[31] Berkey, C. S., Willett, W. C., Tamimi, R. M., Rosner, B., Frazier, A. L., & Colditz, G. A. (2013). Dairy intakes in older girls and risk of benign breast disease in young women. Cancer Epidemiology, Biomarkers & Prevention, 22(4), 670–674. https://doi.org/10.1158/1055-9965.EPI-12-1133

[32] Boeke, C. E., Tamimi, R. M., Berkey, C. S., Colditz, G. A., Eliassen, A. H., Malspeis, S., et al. (2014). Adolescent carotenoid intake and benign breast disease. Pediatrics, 133(5), e1292–e1298. https://doi.org/10.1542/peds.2013-3041

[33] Su, X., Colditz, G. A., Collins, L. C., Baer, H. J., Sampson, L. A., Willett, W. C., et al. (2012). Adolescent intakes of vitamin D and calcium and incidence of proliferative benign breast disease. Breast Cancer Research and Treatment, 134(2), 783–791. https://doi.org/10.1007/s10549-012-2099-3

[34] Webb, P. M., Byrne, C., Schnitt, S. J., Connolly, J. L., Jacobs, T. W., Baer, H. J., et al. (2004). A Prospective Study of Diet and Benign Breast Disease. Cancer Epidemiology, Biomarkers & Prevention, 13(7), 1106–1113. https://doi.org/10.1158/1055-9965.EPI-03-0417

[35] Schilling, M. P. R., & da Silva, I. F. (2020). Family history of breast cancer and risk of benign breast diseases: an integrative literature review. Mastology, 30, 332–342. https://doi.org/10.1590/2176-960X304003

[36] Bertelsen, L., Mellemkjaer, L., Balslev, E., & Olsen, J. H. (2008). Benign breast disease among first-degree relatives of young breast cancer patients. American Journal of Epidemiology, 168(3), 261–267. https://doi.org/10.1093/aje/kwn133

[37] Berkey, C. S., Rosner, B., Willett, W. C., Tamimi, R. M., Frazier, A. L., & Colditz, G. A. (2015). Prenatal factors and infant feeding in relation to risk of benign breast disease in young women. Breast Cancer Research and Treatment, 154(3), 573–582. https://doi.org/10.1007/s10549-015-3413-3

[38] Frazier, A. L., & Rosenberg, S. M. (2013). Preadolescent and adolescent risk factors for benign breast disease. Journal of Adolescent Health, 52(5, Suppl.), S36–S40. https://doi.org/10.1016/j.jadohealth.2013.01.013

[39] Tiznobeyk, Z., Sheikhi Mobarakeh, Z., Qorbani, M., Koohdani, F., Sotoudeh, G., Khajehnasiri, F., et al. (2016). Dietary patterns and benign breast diseases: a case-control study. British Journal of Nutrition, 116(2), 353–359. https://doi.org/10.1017/S000711451600174X

[40] Faghfouri, A. H., Azizi-Soleiman, F., Saleh-Ghadimi, S., & Jafari-Vayghan, H. (2025). The association between dietary fat intake and benign breast diseases: a systematic review. Clinical Nutrition Open Science, 62, 102–113. https://doi.org/10.1016/j.clinos.2025.100087

[41] Christopoulos, P., Matsas, A., Eleftheriades, M., Kotsira, G., Eleftheriades, A., & Vlahos, N. F. (2023). Investigating the Link between Early Life and Breast Anomalies. Children, 10(3), 462. https://doi.org/10.3390/children10030462

[42] Pena, G. G., Maia, Y. C., Mendes, M. C., Furtado, W. R., Machado-Coelho, G. L., & Freitas, R. N. (2014). Physical activity is associated with malignant and benign breast diseases in low-income Brazilian women. Nutrition and Cancer, 66(4), 707–715. https://doi.org/10.1080/01635581.2014.894336

[43] Tamimi, R. M., Byrne, C., Baer, H. J., Rosner, B., Schnitt, S. J., Connolly, J. L., et al. (2005). Benign breast disease, recent alcohol consumption, and risk of breast cancer: a nested case-control study. Breast Cancer Research, 7(4), R555. https://doi.org/10.1186/bcr1260

[44] Baghurst, P. A., & Rohan, T. E. (1995). Dietary fiber and risk of benign proliferative epithelial disorders of the breast. International Journal of Cancer, 63(4), 481–485. https://doi.org/10.1002/ijc.2910630481

[45] Hislop, T. G., Band, P. R., Deschamps, M., Ng, V., Coldman, A. J., Worth, A. J., et al. (1990). Diet and histologic types of benign breast disease defined by subsequent risk of breast cancer. American Journal of Epidemiology, 131(2), 263–270. https://doi.org/10.1093/oxfordjournals.aje.a115313

[46] London, S. J., Stein, E. A., Henderson, I. C., Stampfer, M. J., Wood, W. C., Remine, S., et al. (1992). Carotenoids, retinol, and vitamin E and risk of proliferative benign breast disease and breast cancer. Cancer Causes & Control, 3(6), 503–512. https://doi.org/10.1007/BF00051347

[47] Dupont, W. D., & Page, D. L. (1985). Risk Factors for Breast Cancer in Women with Proliferative Breast Disease. The New England Journal of Medicine, 312(3), 146–151. https://doi.org/10.1056/NEJM1985011731203

[48] Friedenreich, C. M., Bryant, H. E., Alexander, F., Hugh, J., Danyluk, J., & Page, D. L. (2000). Risk factors for benign proliferative breast disease. International Journal of Epidemiology, 29(4), 637–644. https://doi.org/10.1093/ije/29.4.637

[49] Sochacka-Tatara, E., Pac, A., Florek, M., Rolska, P., & Hodorowicz-Zaniewska, D. (2018). Preferring fried dishes increases risk of benign breast disease, but not breast cancer. Folia Medica Cracoviensia, 58(1), 43–52. https://doi.org/10.2478/fmc-2018-0005

APPENDICES

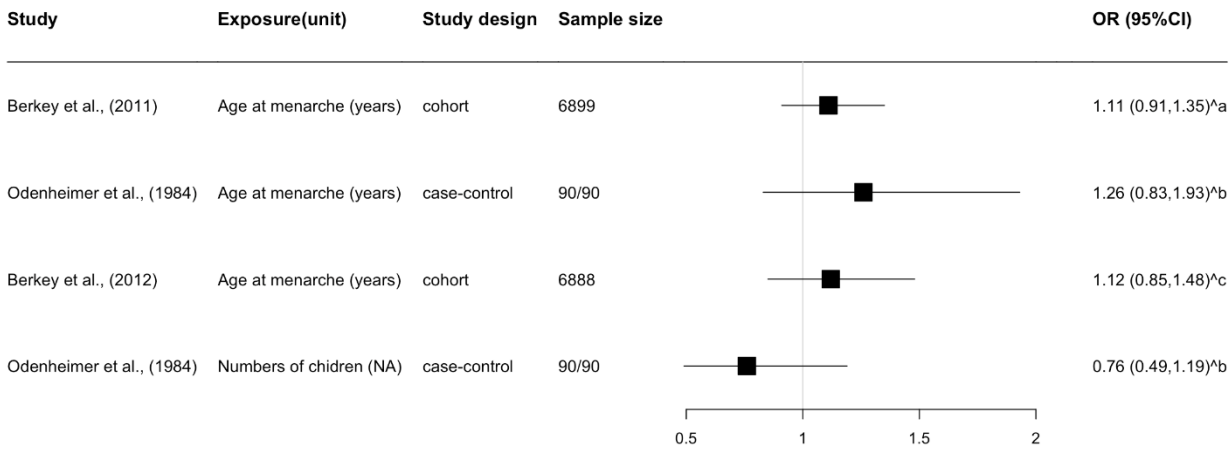

Figure S1. Association between reproductive factors and benign breast diseases regardless of the subtype

Footnote: ^a: adjusted for age; ^b: adjusted for coffee consumption, years of oral contraceptive use, body mass, no. of children, small breast, age at menarche, years of education; ^c: age, family history; OR: odds ratio; 95% CI: 95% confidence interval.

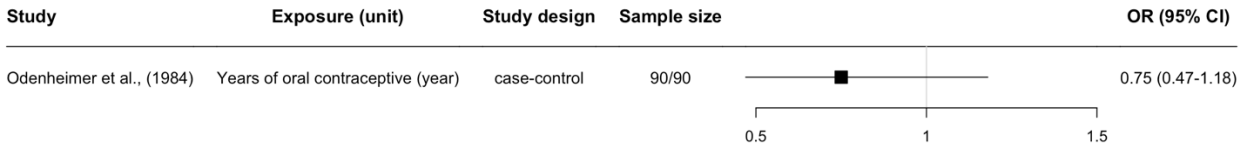

Figure S2. Association between hormonal factors and benign breast diseases regardless of the subtype

Footnote: OR is adjusted for coffee consumption, years of oral contraceptive use, body mass, no. of children, small breast, age at menarche, years of education; OR: odds ratio; 95%CI: 95% confidence interval.

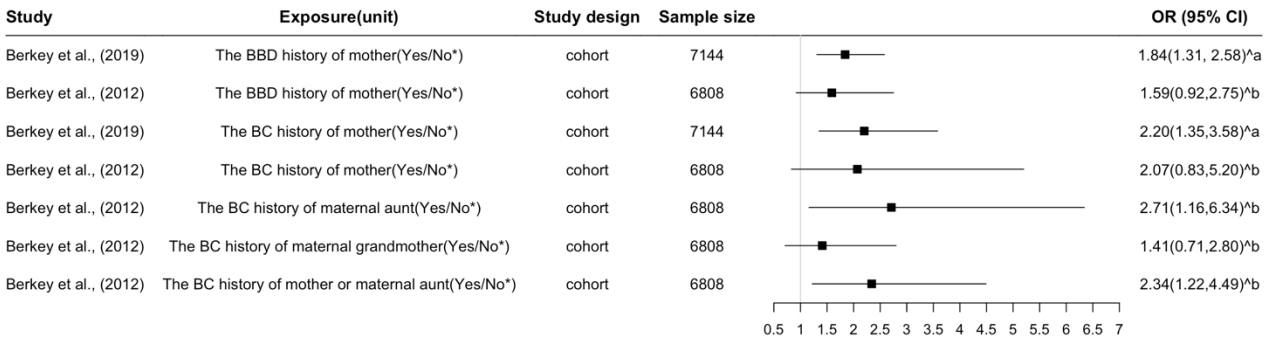

Figure S3. Association between family history of benign breast diseases or breast cancer and benign breast diseases regardless of the subtype

Footnote: ^a: adjusted for age in months at cohort initiation, maternal history of breast cancer, maternal history of benign breast disease, gestational weight gain, height at age 10, body mass index at age 10, and adolescent peak height growth velocity; ^b: adjusted for age, family history; OR: odds ratio; 95% CI: 95% confidence interval; BBD: benign breast diseases; BC: breast cancer; *: indicates the reference.

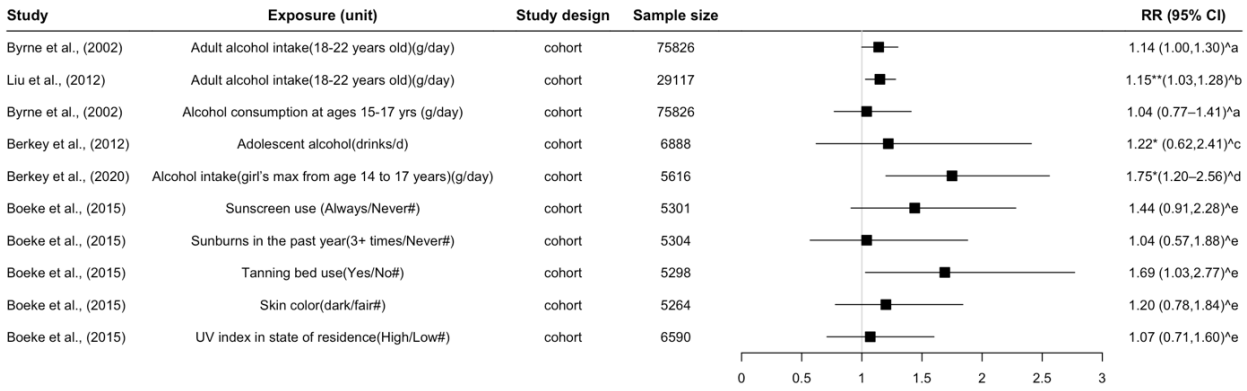

Figure S4. Association between Lifestyle factors and benign breast diseases regardless of the subtype

Footnote: ^a: adjusted for age and body mass index; ^b: adjusted for age; ^c: adjusted for age, family history; ^d: adjusted for maternal breast cancer, maternal BBD, participant's age, gestational weight gain, body mass index at 10 years, height at 10 years, and adolescent peak height growth velocity; ^e: adjusted for age, family history of breast cancer or BBD, mother's history of BBD, age at menarche, body mass index, nulliparity, average hours per week of moderate to vigorous physical activity and alcohol intake; *: odds ratio; **: hazard ratio; RR: relative risk; 95% CI: 95% confidence interval

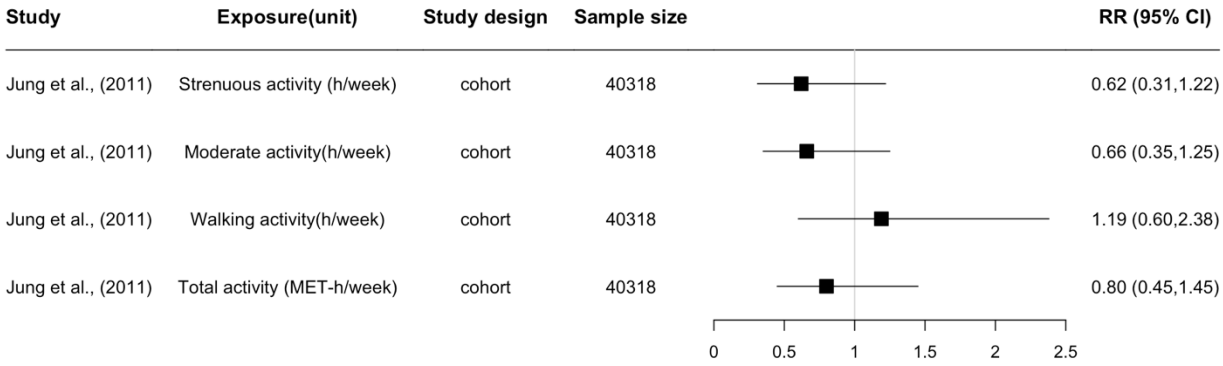

Figure S5. Association between Physical activity and benign breast diseases regardless of the subtype

Footnote: RR was adjusted for age, childhood body shape, use of oral contraceptives, family history of breast cancer of mother and/or sister, parity and age at first birth, current alcohol consumption and height, body mass index; RR: relative risk; 95% CI: 95% confidence interval.

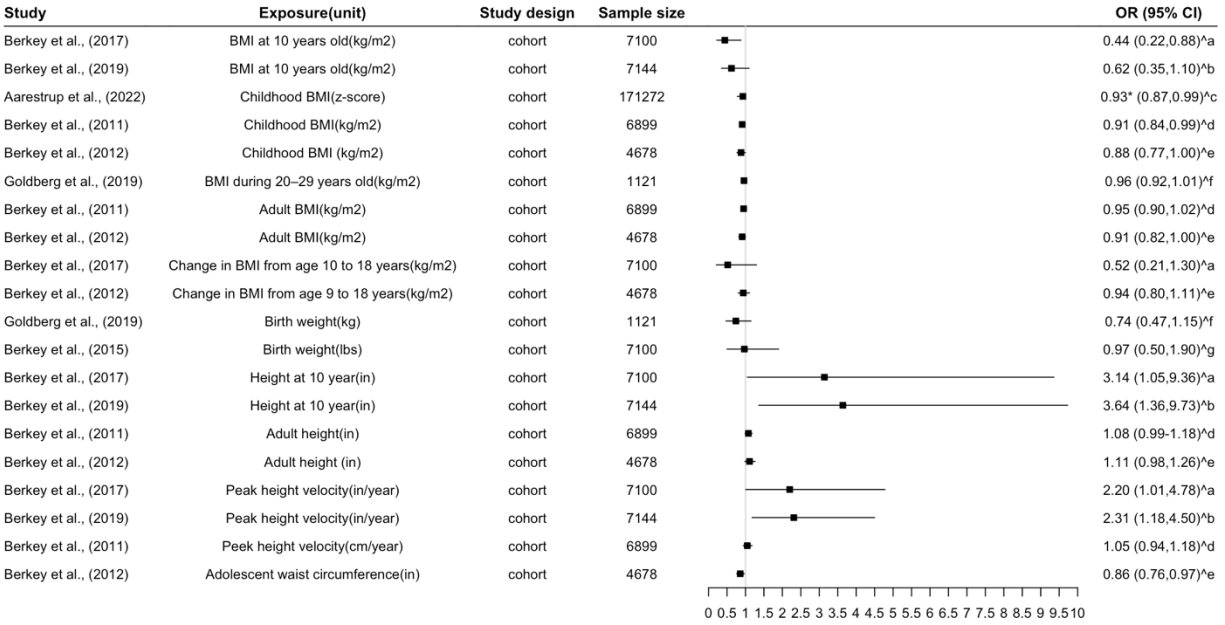

Figure S6. Association between Association between anthropometric measures and benign breast diseases regardless of the subtype

Footnote: ^a: adjusted for maternal breast cancer, maternal BBD, and girl's age at study initiation; ^b: adjusted for age in months at cohort initiation, maternal history of breast cancer, maternal history of benign breast disease, gestational weight gain, height at age 10, body mass index at age 10, and adolescent peak height growth velocity; ^d: adjusted for age; ^e: adjusted for age and BBD history of mother; ^f: site, age at interview, race/ethnicity, maternal age at registration, maternal education, maternal height, maternal cigarettes per day, and family history of breast cancer, maternal pre-pregnancy body mass index and prematurity;^g: age, maternal height, pre-pregnancy body mass index, weight gain during pregnancy, infant birth weight, birth body mass index; OR: odds ratio; 95% CI: 95% confidence interval; *: Hazard ratio.

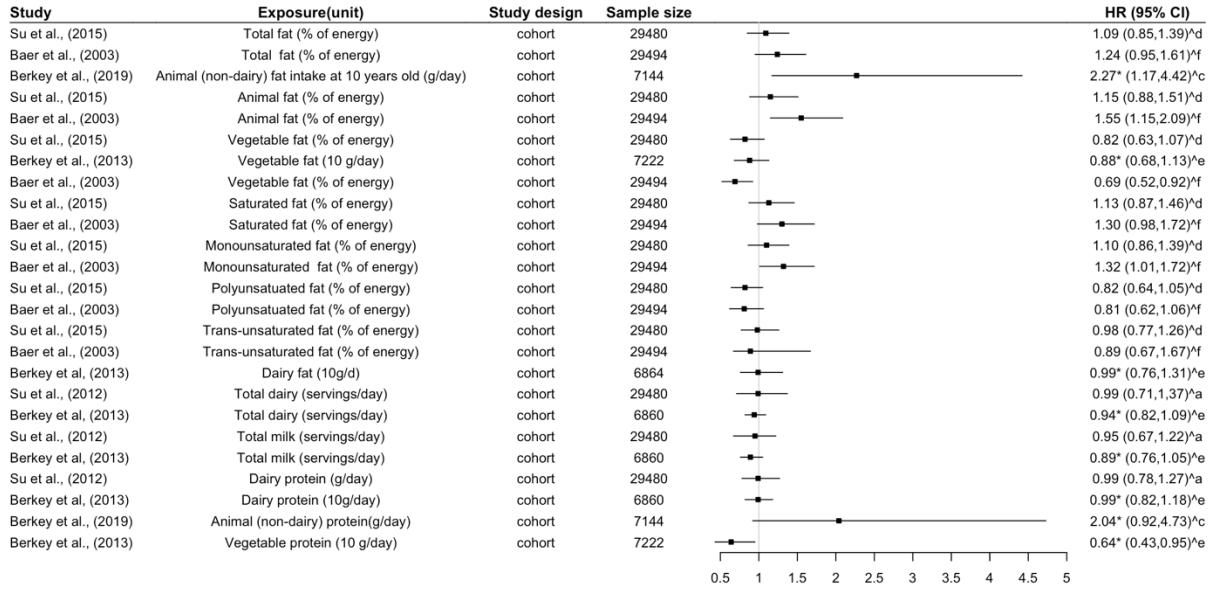

Figure S7. Association between Association between fat, dairy, milk, protein intake and benign breast diseases regardless of the subtype

Footnote:^a adjusted for age, total energy, age at menarche, menopausal status, childhood body size, family history of breast cancer, alcohol intake between ages 18 and 22, adolescent multivitamin use, recency and duration of oral contraceptive use, and parity and age at first birth; ^b adjusted for age-energy; ^c adjusted for age in months at cohort initiation, maternal history of breast cancer, maternal

history of benign breast disease, gestational weight gain, height at age 10, body mass index at age 10, and adolescent peak height growth velocity; ^d adjusted for age in months, time period, total energy intake, age at menarche, menopausal status, average body size between ages 5 and 10, family history of breast cancer in mother or sister, alcohol intake between ages 18 and 22 years, multivitamin use between ages 13 and 18 years, recency and duration of oral contraceptive use, parity and age at first birth; ^e adjusted for age-energy; ^f adjusted for age; HR: hazard ratio; 95% CI: 95% confidence interval; *: odds ratio

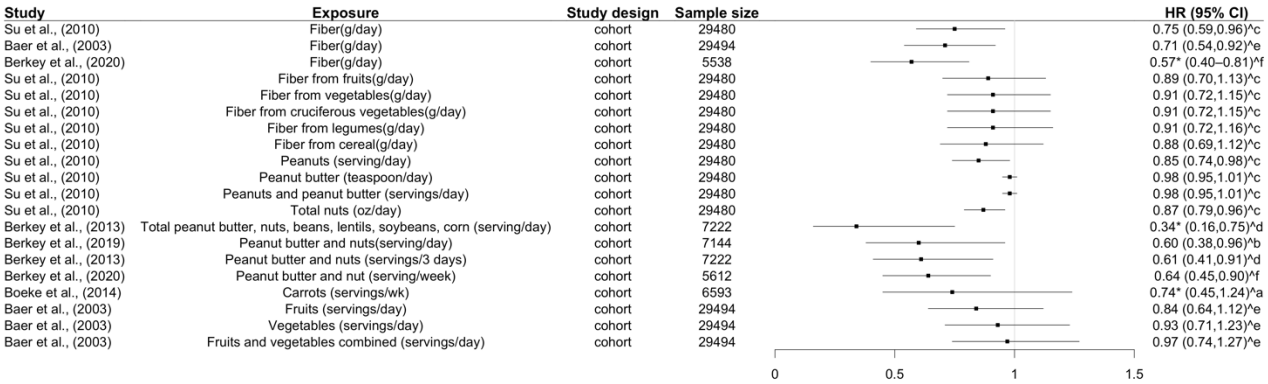

Figure S8. Association between Association between fiber, nuts, peanut butter, vegetable, fruits intake and benign breast diseases regardless of the subtype

Footnote:^a adjusted for age; ^b adjusted for age in months at cohort initiation, maternal history of breast cancer, maternal history of benign breast disease, gestational weight gain, height at age 10, body mass index at age 10, and adolescent peak height growth velocity; ^c adjusted for age in months, time period, total energy intake, age at menarche, menopausal status, history of breast cancer in mother or sisters, alcohol intake between apes 18 and 22, multivitamin use between ages 13 and 18, recency and duration of oral contraceptive, and panty and age at first birth, age at first birth; ^d adjusted for age-energy; ^e adjusted for age; ^f adjusted for maternal breast cancer, maternal BBD, participant's age, gestational weight gain, body mass index at 10 years, height at 10 years, and adolescent peak height growth velocity; HR: hazard ratio; 95% CI: 95% confidence interval; *: odds ratio

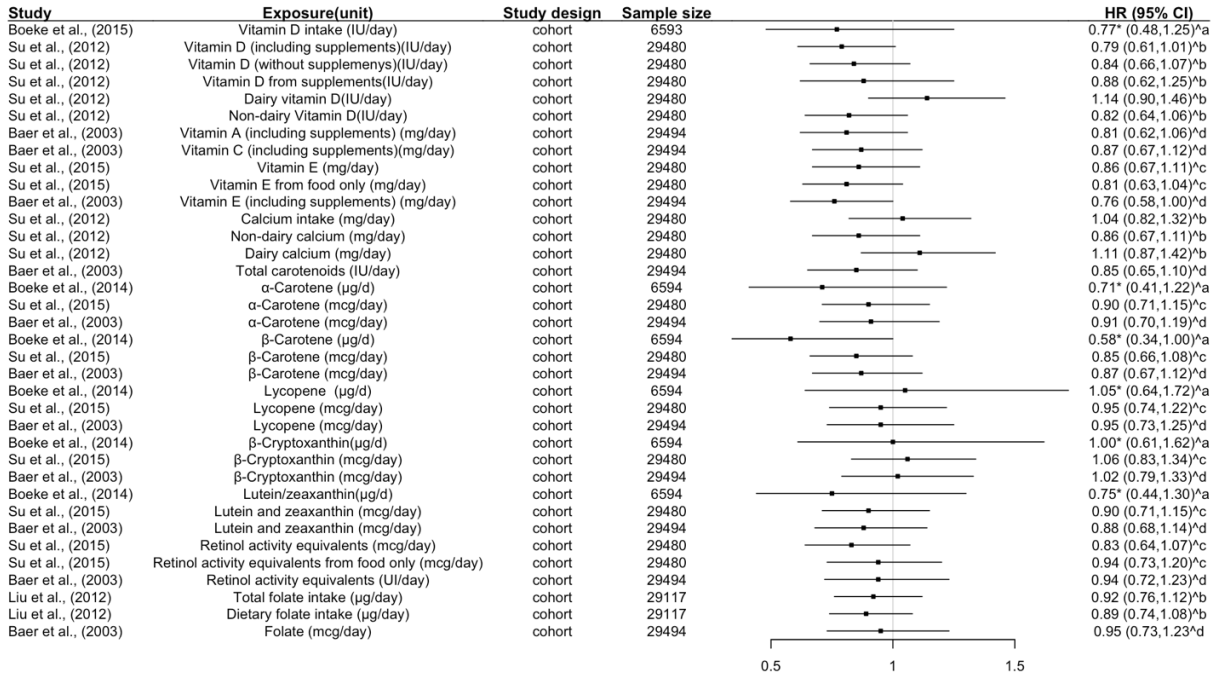

Figure S9. Association between Association between vitamin, calcium, micronutrients and benign breast diseases regardless of the subtype

Footnote: ^a: adjusted for age, family history of breast cancer or BBD, mother's history of BBD, age at menarche, body mass index, nulliparity, average hours per week of moderate to vigorous physical activity and alcohol intake; ^b: adjusted for age, total energy, age at menarche, menopausal status, childhood body size, family history of breast cancer, alcohol intake between ages 18 and 22, adolescent multivitamin use, recency and duration of oral contraceptive use, and parity and age at first birth; ^c: adjusted for age in months, time period, total energy intake, age at menarche, menopausal status, average body size between ages 5 and 10, family history of breast cancer in mother or sister, alcohol intake between ages 18 and 22 years, multivitamin use between ages 13 and 18 years, recency and duration of oral contraceptive use, parity and age at first birth; ^d: adjusted for age; HR: hazard ratio;95% CI: 95% confidence interval; *: odds ratio.

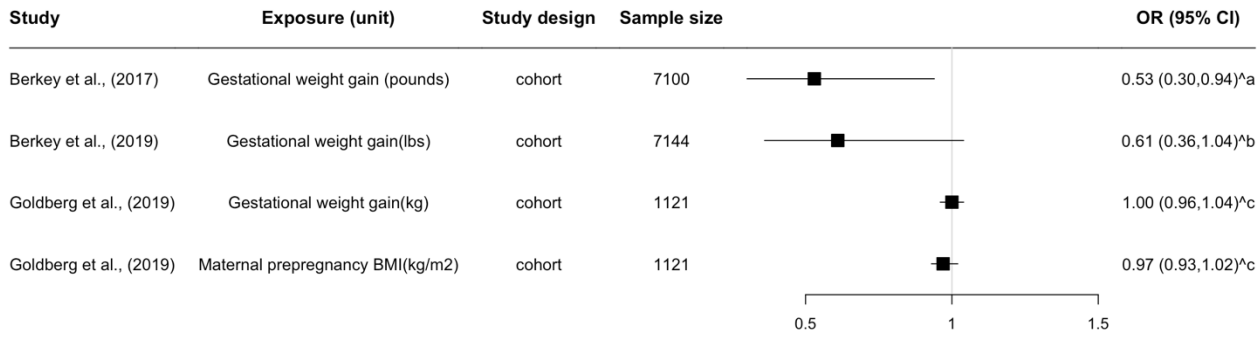

Figure S10. Association between Association between maternal factor and benign breast diseases regardless of the subtype

Footnote: ^a: adjusted for maternal breast cancer, maternal BBD, and girl's age at study initiation; ^b: adjusted for age in months at cohort initiation, maternal history of breast cancer, maternal history of benign breast disease, gestational weight gain, height at age 10, body mass index at age 10, and adolescent peak height growth velocity; ^c: adjusted for site, age at interview, race/ethnicity, maternal age at registration, maternal education, maternal height, maternal cigarettes per day, and family history of breast cancer, maternal pre-pregnancy body mass index and prematurity; OR: odds ratio; 95% CI: 95% confidence interval.

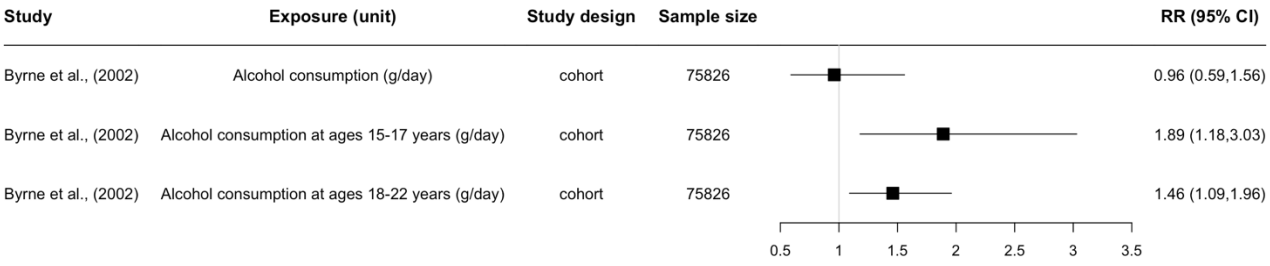

Figure S11. Association between Association between lifestyle factor and non-proliferative diseases

Footnote: RR: adjusted for age and BMI; RR: risk ratio; 95% CI: 95% confidence interval

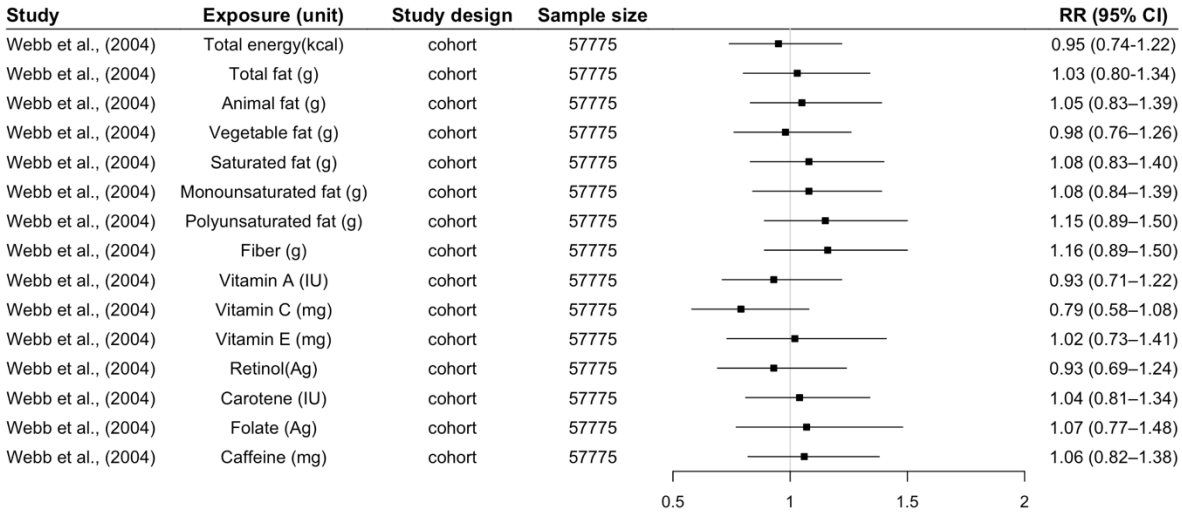

Figure S12. Association between dietary factors and non-proliferative diseases

Footnote: RR was adjusted for age, time period, total energy intake, supplement use, history of breast cancer in mother or sister, and body mass index; RR: risk ratio; 95% CI: 95% confidence interval.

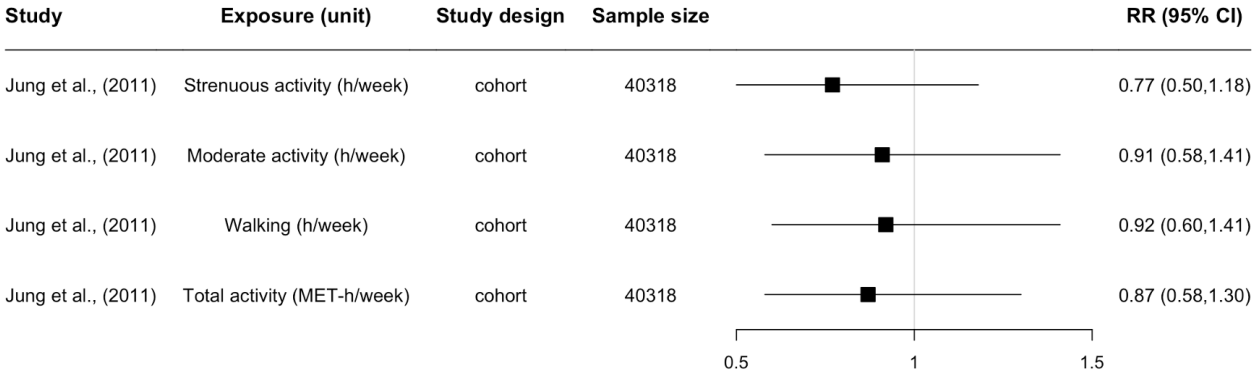

Figure S13. Association between physical activity and proliferative diseases

Footnote: RR was adjusted for age, average childhood body shape, use of oral contraceptives, family history of breast cancer of mother and/or sister, parity and age at first birth, current alcohol consumption, height and body mass index; RR: risk ratio; 95% CI: 95% confidence interval.

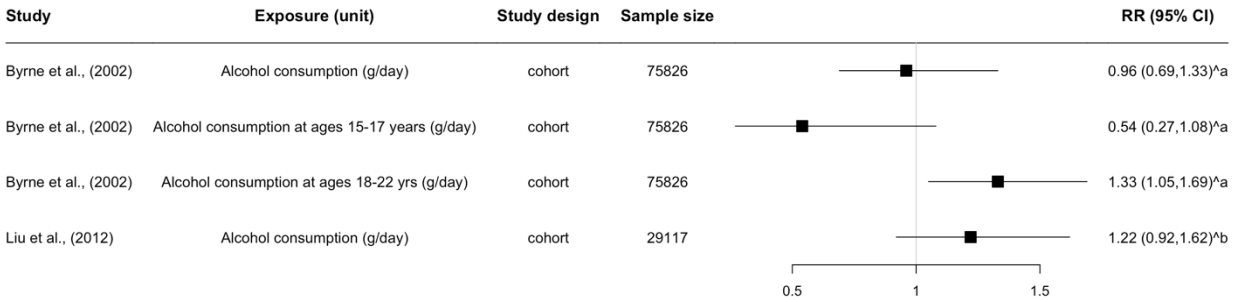

Figure S14. Association between lifestyle factors and proliferative diseases

Footnote: ^a: adjusted for age and body mass index; ^b: adjusted for age.; RR: risk ratio; 95% CI: 95% confidence interval.

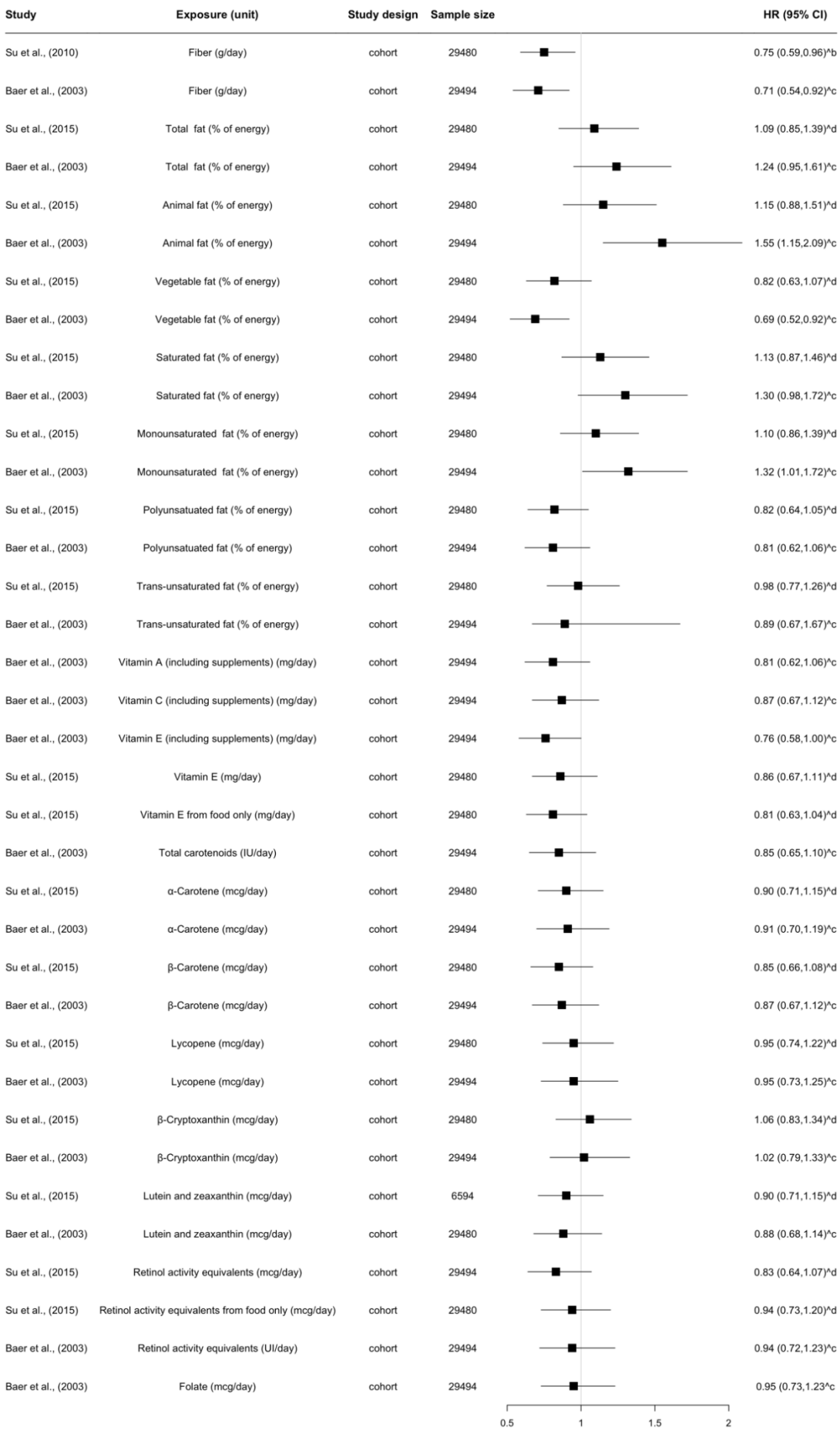

Figure S15. Association between dietary factor and proliferative diseases

Footnote: ^a: adjusted for adjusted for age (months), time period, total energy intake, supplement use, history of breast cancer in mother or sister, OC use, BMI; ^b: adjusted for age in months, time period, total energy intake, age at menarche, menopausal status, average body size between ages and 10, history of breast cancer in mother or sisters, alcohol intake between ages 18 and 22, multivitamin use between ages 13 and 18, recency and duration of OC use, and panty and age at first birth, age at first birth; ^c: adjusted for age; ^d: adjusted for age in months, time period (five periods), total energy intake, age at menarche, menopausal status, average body size between ages 5 and 10, family history of breast cancer in mother or sister, alcohol intake between ages 18 and 22 years, multivitamin use between ages 13 and 18 years, recency and duration of oral contraceptive use, parity and age at first birth; HR: hazard ratio; 95% CI: 95% confidence interval; *: risk ratio.

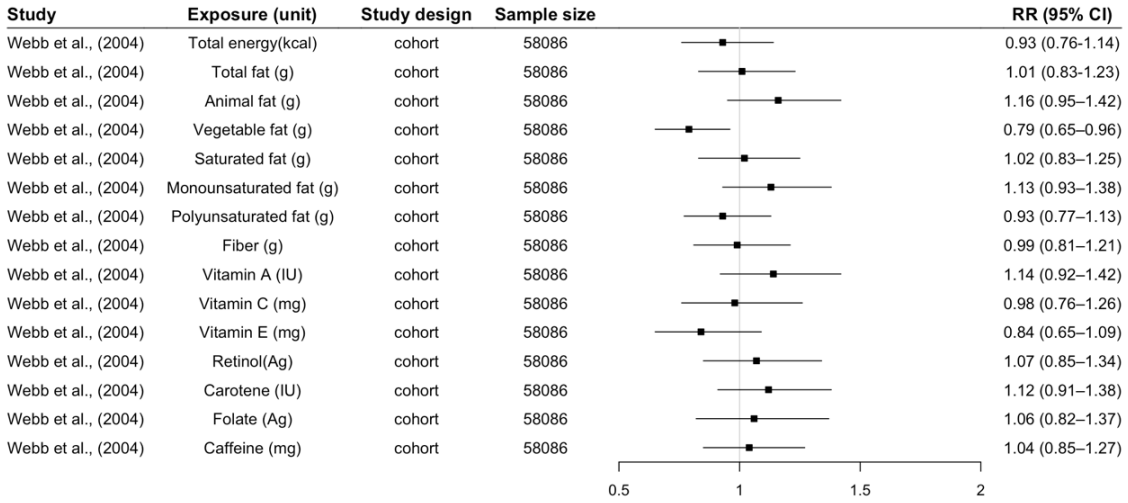

Figure S16. Association between risk factors for proliferative disease without atypia

Footnote: RR: adjusted for adjusted for age (months), time period, total energy intake, supplement use, history of breast cancer in mother or sister, BMI; RR: risk ratio; 95%CI: 95% confidence interval.

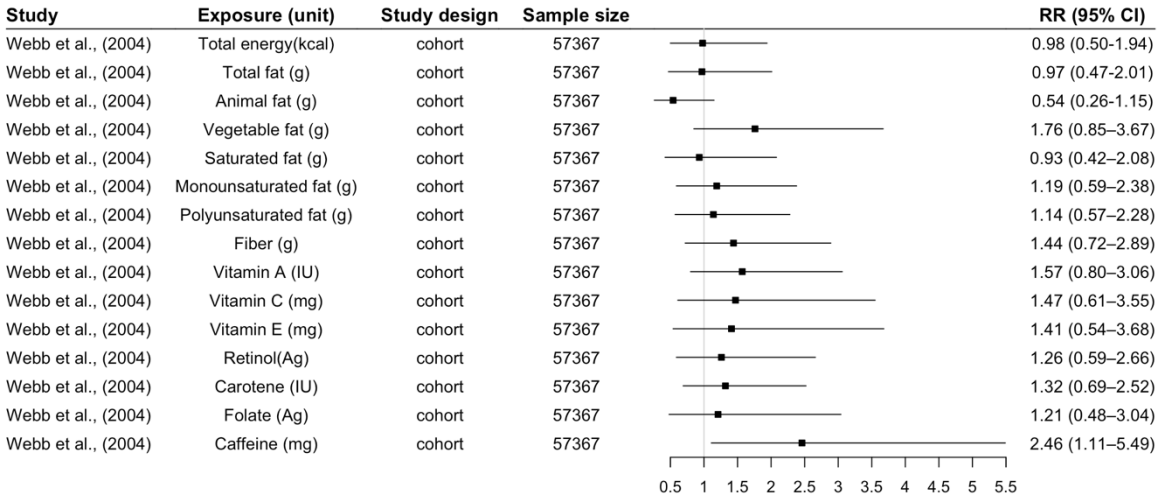

Figure S17. Association between risk factors and atypical hyperplasia

Footnote: RR: adjusted for adjusted for age, total energy intake, supplement use, history of breast cancer in mother or sister, BMI; RR: risk ratio; 95%CI: 95% confidence interval.