Milk and yogurt intake and breast cancer risk
A meta-analysis
Lu Chen, MMa, Min Li, MMb, Hao Li, MMa,∗

Abstract
Different patterns of milk and breast cancer rates across countries suggest that several components of milk could affect breast cancer risk. However, the components of diet are complex including milk that could potentially influence risk. Some milk products such as whole milk and cheese have a high fat content which may increase risk. Moreover, milk products may contain pesticides which have carcinogenic potential. In contrast, some contents of milk such as calcium and vitamin D have been hypothesized to reduce breast cancer risk. Therefore, we performed this meta-analysis to derive a more precise estimation of the association between dairy food intake and breast cancer risk. Using the data from 8 available publications, we examined low-fat/skim milk, whole milk, and yogurt in relation to risk of breast cancer by meta-analysis. Pooled odds ratio (OR) with 95% confidence interval (CI) was used to assess the association. However the results of all milk models and the available epidemiologic evidence do not support a strong association between the consumption of milk or milk products and breast cancer risk. Further studies with larger participants worldwide are needed to validate the relationship of dairy food intake and breast cancer.

Abbreviations: CI = confidence interval, EPIC = European Prospective Investigation into Cancer and Nutrition, OR = odds ratio, RR = relative risk.

Keywords: breast cancer, low-fat/skim milk, meta-analysis, whole milk, yogurt

1. Introduction
Breast cancer is the most common cancer type in women worldwide and is the main cause of cancer mortality in females in the world.[1,2] Both breast cancer incidence and mortality rates have been increasing over the past 30 years for our limited milk consumption.[4] However, inverse results were found in 1990 reported a modest increase in breast cancer risk with higher previous meta-analysis of 10 studies published from 1981 to breast risk has been analyzed in many epidemiological studies. A previous meta-analysis of 10 studies published from 1981 to 1990 reported a modest increase in breast cancer risk with higher milk consumption.[4] However, inverse results were found in some recent studies.[5–7] In addition, another review including 36 case-control and 10 cohort studies which analyzed the relationship of milk and milk products intake and breast cancer suggested that the epidemiologic evidence does not support a significant relevance of milk or milk products and breast cancer.[8] Therefore, an available data analysis is needed to provide consistent evidence for an association between milk and milk products and breast cancer risk.

The purpose of this study is to assess the connection of intakes of milk and milk products (yogurt) and risk of breast cancer by a meta-analysis of case-control studies. This analysis was based on separately ingredients of milk, including low-fat/skim milk, whole milk, and yogurt. We based on the previous meta-analysis and extend more case-control studies to identify the relationship of milk or milk products intakes with breast cancer incidence.

2. Material and methods

2.1. Publication search
We searched the available studies in PubMed and Chinese biomedicine databases for related articles published in any language to June 2, 2009. For the computer searches we used the key words as follows: “dairy products” or “milk” combined with “breast cancer”. Case-control studies containing available data which showed the relationship of milk (low-fat/skim milk and whole milk) or yogurt intakes and incidence or mortality from breast cancer were selected. All results of these studies must be shown as an odds ratio (OR) or a relative risk (RR) and 95% confidence interval (CI).

2.2. Data extraction and classification
Study characteristics data showed the first author, publication year, location of the study, year of data collection, measure of exposure and range of exposure, odds ratio, and risk estimates with corresponding 95% CI.

2.3. Statistical analysis
The measure of effect is the OR and the corresponding 95% CI. We listed all results as OR for simplicity and quantified
associations of milk and milk products intakes with breast cancer risk using random-effects models\cite{9} of OR comparing the highest with the lowest category. The summary OR estimates were obtained from random effects models\cite{10} which applied to the study-specific dose-response slopes.

The publication bias was assessed by an Egger linear regression asymmetry test and Begg-adjusted rank correlation test (funnel plot method) \( P < .05 \) considered representative of statistical significance\cite{10}. All meta-analyses were carried out using Stata software (version 9.0; Stata Corporation, College Station, TX).

2.4. Ethical approval
Ethical approval was waived or not necessary. Because we did not make any clinical research in this manuscript, we just collected the data from available publications.

3. Results
3.1. Characteristics of studies for meta-analysis
In this meta-analysis, we examined 8 potential publications on the association between milk intake and breast cancer. Among the 8 studies, 2 were conducted in the United States, 1 each in French, the Netherlands, Norwegian, Finland, and Japan and another was from EPIC (European Prospective Investigation into Cancer and Nutrition). We separate the results by different milk styles, including low-fat/skim milk, whole milk, and yogurt.

3.2. Low-fat/skim milk
The association between low-fat/skim milk intake and breast cancer risk was identified in 3 studies. The intake and range of low-fat/skim milk of each study were listed in Table 1. The overall OR for high and low yogurt consumption was 0.900 (95% CI = 0.800–1.132, \( P = .572 \)) (Table 2). This result indicated that high intakes of whole milk had no effect on breast cancer.

3.4. Yogurt
The meta-analysis of yogurt consumption included 4 studies. The intake and range in each study of yogurt were shown in Table 1. The overall OR for high and low yogurt consumption was 0.900 (95% CI = 0.684–1.183, \( P = .449 \)) (Table 2). The result suggested that yogurt intake had no effect on the risk of breast cancer.

3.5. Publication bias
We evaluated publication bias by Egger test and Begg test. The results of the Egger test \( (P > .05) \), and the Begg test \( (P > .05) \) provided statistical evidence for funnel plot symmetry in the overall results, suggesting the absence of publication bias (Table 2).

4. Discussion
The published epidemiologic data do not provide consistent evidence for an association between the consumption of milk or milk products and breast cancer risk. However, among these data many factors must be considered. Moreover, assessment of dietary factor in relation to cancer risk is very difficult and affected by many potential biases. Several methods used in epidemiologic studies, such as food frequency questionnaires and diet records or food diaries, have shown only moderate reliability, and some misclassification of intake is also unavoidable\cite{18,19}. Therefore, different dietary assessment methods may produce different results. It is generally believed that most dietary 

### Table 1

| Milk model       | Author       | Publication year (years of data collection) | Country      | Measure of exposure and range of exposure | OR (95% CI) | References |
|------------------|--------------|--------------------------------------------|--------------|------------------------------------------|-------------|------------|
| Low-fat/skim milk| Pala         | 2009 (1992–2003)                           | European     | > 210 g/d vs never/seldom                | 0.93 (0.87–1.01) | [11]       |
| Shin             | 2002 (1980–1996)            | United States    | > 1 glass/d vs never/seldom             | 0.72 (0.56–0.91) | [12]       |
| Whole milk       | Pala         | 2009 (1992–2003)                           | European     | > 150 g/d vs never/seldom                | 1.06 (0.97–1.15) | [11]       |
| Kesse-Guyot      | 2007 (1995–2003)            | French          | > 248 g/d vs < 25 g/d                   | 0.95 (0.52–1.73) | [13]       |
| Shin             | 2002 (1980–1996)            | United States    | > 1 glass/d vs never/seldom             | 0.80 (0.54–1016) | [8]        |
| HJARTÄKER        | 2001 (1991–1992)            | Norwegian       | High vs low                             | 0.51 (0.27–0.96) | [14]       |
| Männistö         | 1999 (1990–1995)            | Finland         | High vs low                             | 2.20 (1.00–4.30) | [12]       |
| Byrne            | 1996 (1982–1984)            | United States    | > 7 glasses/week vs < 7 glasses/week    | 0.50 (0.10–2.10) | [10]       |
| Hirose           | 1995 (1988–1992)            | Japan           | Daily vs lowest                         | 0.97 (0.79–1.20) | [16]       |
| van’t Veer       | 1989 (1985–1987)            | The Netherlands  | > 225 g/d vs never/seldom               | 0.82 (0.43–1.57) | [17]       |
| Yogurt           | Kesse-Guyot      | 2007 (1995–2003)                           | French       | > 125 g/d vs < 25 g/d                   | 0.79 (0.41–1.53) | [13]       |
| Shin             | 2002 (1980–1996)            | United States    | > 4 servings/week vs never/seldom       | 0.95 (0.66–1.37) | [8]        |
| Männistö         | 1999 (1990–1995)            | Finland         | High vs low                             | 1.20 (0.60–2.40) | [12]       |
| van’t Veer       | 1989 (1985–1987)            | The Netherlands  | > 225 g/d vs never/seldom               | 0.55 (0.24–1.27) | [17]       |

### Table 2

| Milk model         | Begg test | Egger test |
|--------------------|-----------|------------|
| OR (95% CI)        | P value   | P value    |
| Low-fat/skim milk  | .602      | .583       |
| Whole milk         | .621      | .272       |
| Yogurt             | .497      | .553       |

\( C.I = \) confidence interval, OR = odds ratio.
factors have relatively small effects on cancer risk and the inevitable misclassification of dietary variables increases the difficulty of detection in risk associated with consumption of milk products.

Consistently, in our meta-analysis no associations with breast cancer risk were identified for intake of low-fat skim milk, whole milk, and yogurt. Another challenge when evaluating milk and milk products in relation to breast cancer risk is the correlation among nutrients in diet. Persons with high consumption of milk products may likely to consume large amounts of meat or other high fat foods that could also contribute to an increased risk of breast cancer. [20] Although total energy intake is controlled for, it also difficult to completely separate the effects of milk intake from that of other dietary factors, including intake of various types of fat. Once again, it may be difficult to separate the effects of dairy products from those of other nutrients that alter breast cancer risk.

In addition, average intake varies should be considered between different populations such as a level of consumption that is defined as “low” in one population might be considered “high” in another population. For instance, in a Japanese study, daily intake of milk or milk products was identified as highest exposure category. [21] While, in a study conducted in the United States, the reference category of the lowest exposure level was reported consuming ≤ 1 serving/d and the highest level was reported > 3 servings/d. [20] In some cases, the investigators did not report the level of consumption within each quintile, which made it impossible to compare effects at similar levels of consumption across studies. Besides the challenges that are common to many studies of nutritional epidemiology, there are specific challenges related to evaluating milk products. A main hypothesis suggesting that dairy products may reduce breast cancer risk is based on vitamin D content of these products. In the United State, most manufacturers add vitamin D to many products, including milk and margarine. These differences suggest that studies from countries with different regulations and practices regarding vitamin D fortification are not strictly comparable. If vitamin D is the component of milk products that influences breast cancer risk, comparisons should take into account not only the milk products but also the level of vitamin D in milk products.

Generally, the epidemiology studies reviewed do not provide consistent evidence for an association between milk product consumption and breast cancer risk. In addition, some studies also suggest that certain types of fat, growth factors, or environmental contaminants found in milk could increase risk, comparisons should take into account not only the milk/milk products and breast cancer risk. In conclusion, although several interesting hypotheses link milk product and breast cancer, the available epidemiologic evidence does not support a strong association between the milk/milk products and breast cancer risk.

Author contributions

Conceptualization: Hao Li.
Data curation: Lu Chen, Min Li.
Project administration: Lu Chen.
Writing – original draft: Lu Chen, Min Li.
Writing – review & editing: Hao Li.

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