

1 **Article**

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4 **The impact of mammographic screening on the subsequent breast cancer risk**  
5 **associated with biopsy-proven benign breast disease**  
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8 **Beca F et al.,**  
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31 **Supplementary Material:**  
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34 **Supplementary Tables 1-4**  
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## Supplementary Tables

**Supplementary Table 1. Odds ratios (OR) and 95% confidence intervals (CIs) for the associations of non-proliferative, proliferative, atypical ductal hyperplasia, and atypical lobular hyperplasia with breast cancer risk, stratified by pre- (before 1985) vs. post-mammography era (1985 and after)**

| Calendar year of benign breast disease detection | Benign breast disease subtype              | Cases/Controls | Model 1 <sup>a</sup>     | Model 2 <sup>b</sup>     |
|--|--|----------------|--------------------------|--------------------------|
|  |  |                | OR (95% CI)              | OR (95% CI)              |
| <b>Pre-mammography era (&lt;1985)</b><br>N=1469  | <b>Non-proliferative lesion</b>            | 72/474         | 1.0 (Ref)                | 1.0 (Ref)                |
|  | <b>Proliferative lesion without atypia</b> | 163/590        | <b>1.83 (1.35, 2.48)</b> | <b>1.74 (1.27, 2.37)</b> |
|  | <b>Atypical ductal hyperplasia</b>         | 36/71          | <b>3.66 (2.26, 5.92)</b> | <b>3.58 (2.18, 5.88)</b> |
|  | <b>Atypical lobular hyperplasia</b>        | 30/31          | <b>6.86 (3.88, 12.1)</b> | <b>6.16 (3.43, 11.1)</b> |
| <b>Post-mammography era (≥1985)</b><br>N=927     | <b>Non-proliferative lesion</b>            | 36/206         | 1.0 (Ref)                | 1.0 (Ref)                |
|  | <b>Proliferative lesion without atypia</b> | 93/446         | 1.13 (0.74, 1.73)        | 1.13 (0.73, 1.75)        |
|  | <b>Atypical ductal hyperplasia</b>         | 25/58          | <b>2.48 (1.36, 4.51)</b> | <b>2.55 (1.38, 4.71)</b> |
|  | <b>Atypical lobular hyperplasia</b>        | 30/32          | <b>5.90 (3.15, 11.1)</b> | <b>6.17 (3.23, 11.8)</b> |
| <b>p-interaction</b>                             |  |                | 0.42                     | 0.63                     |

<sup>a</sup> Model 1 includes matching factors (age at index date, time between benign biopsy to breast cancer diagnosis or index date, calendar year of benign breast biopsy)

<sup>b</sup> Model 2 includes matching factors, average body fatness at ages 5-10 years (level 1-2, 2.5-4, ≥4.5, missing), adult BMI at benign biopsy (kg/m<sup>2</sup>, continuous), parous/age at first birth (nulliparous, <25 years, 25-29 years, ≥30 years, missing), menopausal status at benign breast biopsy (premenopausal, postmenopausal, dubious/missing), current smoking (yes/no), alcohol intake (g/d, continuous), physical activity (MET-hr/wk, continuous), family history of breast cancer (yes/no)

**Supplementary Table 2. Odds ratios (OR) and 95% confidence intervals (CIs) for the associations between benign breast disease subtypes and breast cancer risk, stratified by menopausal status in the pre- (before 1985) and post-mammography (1985 and after) era of benign breast disease (BBD) diagnosis**

| Calendar year of benign breast disease detection | Benign breast disease subtype       | Cases/ Controls | Model 1 <sup>a</sup>     | Model 2 <sup>b</sup>     |
|--|-------------------------------------|-----------------|--------------------------|--------------------------|
|  |                                     |                 | OR (95% CI)              | OR (95% CI)              |
| <b>Pre-mammography era (&lt;1985)</b>            |                                     |                 |                          |                          |
| <b>N=1359</b>                                    |                                     |                 |                          |                          |
| Premenopausal women (N=1168)                     | Non-proliferative lesion            | 64/378          | 1.0 (Ref)                | 1.0 (Ref)                |
|  | Proliferative lesion without atypia | 131/470         | <b>1.66 (1.19, 2.31)</b> | <b>1.58 (1.13, 2.22)</b> |
|  | Atypical hyperplasia                | 51/74           | <b>4.42 (2.80, 6.99)</b> | <b>4.44 (2.77, 7.11)</b> |
| Postmenopausal women (N=191)                     | Non-proliferative lesion            | 5/57            | 1.0 (Ref)                | 1.0 (Ref)                |
|  | Proliferative lesion without atypia | 21/76           | <b>3.60 (1.22, 10.7)</b> | <b>5.32 (1.31, 21.7)</b> |
|  | Atypical hyperplasia                | 11/21           | <b>6.24 (1.86, 21.0)</b> | <b>8.68 (1.99, 37.9)</b> |
| <b>p-interaction by menopausal status</b>        |                                     |                 | 0.53                     | 0.66                     |
| <b>Post-mammography era (≥1985)</b>              |                                     |                 |                          |                          |
| <b>N=472</b>                                     |                                     |                 |                          |                          |
| Premenopausal women (N=472)                      | Non-proliferative lesion            | 20/100          | 1.0 (Ref)                | 1.0 (Ref)                |
|  | Proliferative lesion without atypia | 51/247          | 0.92 (0.51, 1.65)        | 0.88 (0.48, 1.65)        |
|  | Atypical hyperplasia                | 24/30           | <b>3.68 (1.71, 7.89)</b> | <b>3.22 (1.44, 7.22)</b> |
| Postmenopausal women (N=379)                     | Non-proliferative lesion            | 13/88           | 1.0 (Ref)                | 1.0 (Ref)                |
|  | Proliferative lesion without atypia | 33/168          | 1.30 (0.65, 2.62)        | 1.37 (0.66, 2.84)        |
|  | Atypical hyperplasia                | 25/52           | <b>3.29 (1.54, 7.03)</b> | <b>4.33 (1.93, 9.73)</b> |
| <b>p-interaction by menopausal status</b>        |                                     |                 | 0.57                     | 0.60                     |

<sup>a</sup> Model 1 includes matching factors (age at index date, time between benign biopsy to breast cancer diagnosis or index date, calendar year of benign breast biopsy)

<sup>b</sup> Model 2 includes matching factors, average body fatness at ages 5-10 years (level 1-2, 2.5-4, ≥4.5, missing), adult BMI at benign biopsy (kg/m<sup>2</sup>, continuous), parous/age at first birth (nulliparous, <25 years, 25-29 years, ≥30 years, missing), menopausal status at benign breast biopsy (premenopausal, postmenopausal, dubious/missing), current smoking (yes/no), alcohol intake (g/d, continuous), physical activity (MET-hr/wk, continuous), family history of breast cancer (yes/no). Additional adjustment for height (inches, continuous) and age at menarche (years, continuous) did not change the results, and thus were not included in the final model.

**Supplementary Table 3 Odds ratios (OR) and 95% confidence intervals (CIs) for the associations between benign breast disease subtypes and breast cancer risk, stratified by pre- (before 1980) vs. post-mammography era (1980 and after) of BBD diagnosis**

| Calendar year of benign breast disease detection | Benign breast disease subtype       | Cases/Controls | Model 1 <sup>a</sup>     | Model 2 <sup>b</sup>     |
|--|-------------------------------------|----------------|--------------------------|--------------------------|
|  |                                     |                | OR (95% CI)              | OR (95% CI)              |
| Pre-mammography era (<1980)<br>N=1063            | Non-proliferative lesion            | 56/349         | 1.0 (Ref)                | 1.0 (Ref)                |
|  | Proliferative lesion without atypia | 118/433        | <b>1.72 (1.22, 2.45)</b> | <b>1.64 (1.14, 2.34)</b> |
|  | Atypical hyperplasia                | 42/65          | <b>4.27 (2.61, 6.97)</b> | <b>3.92 (2.37, 6.48)</b> |
| Post-mammography era (≥1980)<br>N=1333           | Non-proliferative lesion            | 52/331         | 1.0 (Ref)                | 1.0 (Ref)                |
|  | Proliferative lesion without atypia | 138/603        | <b>1.42 (1.00, 2.02)</b> | 1.37 (0.96, 1.96)        |
|  | Atypical hyperplasia                | 82/127         | <b>4.32 (2.85, 6.55)</b> | <b>4.22 (2.77, 6.45)</b> |
| <b>p-interaction</b>                             |                                     |                | 0.73                     | 0.75                     |

<sup>a</sup> Model 1 includes matching factors (age at index date, time between benign biopsy to breast cancer diagnosis or index date, calendar year of benign breast biopsy)

<sup>b</sup> Model 2 includes matching factors, average body fatness at ages 5-10 years (level 1-2, 2.5-4, ≥4.5, missing), adult BMI at benign biopsy (kg/m<sup>2</sup>, continuous), parous/age at first birth (nulliparous, <25 years, 25-29 years, ≥30 years, missing), menopausal status at benign breast biopsy (premenopausal, postmenopausal, dubious/missing), current smoking (yes/no), alcohol intake (g/d, continuous), physical activity (MET-hr/wk, continuous), family history of breast cancer (yes/no)

**Supplementary Table 4 Odds ratios (OR) and 95% confidence intervals (CIs) for the associations between benign breast disease subtypes and breast cancer risk, stratified by pre- (before 1985) vs. post-mammography era (1985 and after), after excluding individuals with follow-up time >13 years**

| Calendar year of benign breast disease detection | Benign breast disease subtype       | Cases/Controls | Model 1 <sup>a</sup>     | Model 2 <sup>b</sup>     |
|--|-------------------------------------|----------------|--------------------------|--------------------------|
|  |                                     |                | OR (95% CI)              | OR (95% CI)              |
| Pre-mammography era (<1985)<br>N=823             | Non-proliferative lesion            | 36/252         | 1.0 (Ref)                | 1.0 (Ref)                |
|  | Proliferative lesion without atypia | 89/321         | <b>1.89 (1.24, 2.89)</b> | <b>1.70 (1.10, 2.63)</b> |
|  | Atypical hyperplasia                | 45/80          | <b>4.22 (2.52, 7.07)</b> | <b>4.03 (2.35, 6.91)</b> |
| Post-mammography era (≥1985)<br>N=926            | Non-proliferative lesion            | 36/205         | 1.0 (Ref)                | 1.0 (Ref)                |
|  | Proliferative lesion without atypia | 93/446         | 1.12 (0.73, 1.71)        | 1.11 (0.72, 1.72)        |
|  | Atypical hyperplasia                | 57/89          | <b>3.54 (2.15, 5.82)</b> | <b>3.66 (2.19, 6.11)</b> |
| <b>p-interaction</b>                             |                                     |                | 0.23                     | 0.34                     |

<sup>a</sup> Model 1 includes matching factors (age at index date, time between benign biopsy to breast cancer diagnosis or index date, calendar year of benign breast biopsy)

<sup>b</sup> Model 2 includes matching factors, average body fatness at ages 5-10 years (level 1-2, 2.5-4, ≥4.5, missing), adult BMI at benign biopsy (kg/m<sup>2</sup>, continuous), parous/age at first birth (nulliparous, <25 years, 25-29 years, ≥30 years, missing), menopausal status at benign breast biopsy (premenopausal, postmenopausal, dubious/missing), current smoking (yes/no), alcohol intake (g/d, continuous), physical activity (MET-hr/wk, continuous), family history of breast cancer (yes/no)