# Risk factors pre-disposing to lobular carcinoma in-situ, and invasive lobular carcinoma: an analysis of the GLACIER study.

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## INTRODUCTION

Lobular carcinoma in-situ (LCIS) is thought of as a risk factor for breast cancer rather than a true pre-cursor lesion, because a diagnosis of LCIS increases the risk of developing breast cancer in both breasts. However, LCIS and invasive lobular cancer (ILC) are often found concurrently and there is evidence that co-existing LCIS and ILC are clonally similar, supporting the theory that it can also be a true precursor lesion. This study aims to investigate the risk factors predisposing to both ILC and LCIS, and compare the associations with both breast lesions, as similar risk factor associations would be expected if LCIS was truly a precursor of ILC.

## METHODS

The GLACIER case-control study recruited ILC, LCIS, and LCIS concurrent with invasive cases in the UK between 2007-2012. These studies collected data on risk factors such as reproductive history and hormone use (contraceptive and post-menopausal hormone replacement therapy). ILC and LCIS cases were firstly compared to healthy controls, and then to each other, to investigate associations with risk factors, using logistic regression, adjusted for age at diagnosis for cases and age at study entry for controls. Variables with data missing over 10% were multiple imputed using chained equations.

## RESULTS

3450 participants were included in this study; 338 LCIS cases, 1,528 ILC cases, and 1,584 controls.

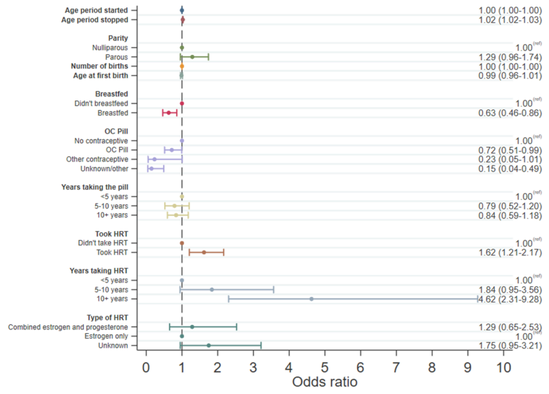
Table 1: characteristics of participants

| | **LCIS** N=338 | **ILC** N=1528 | **Controls** N=1584 |
|---|---|---|---|
| **Age at diagnosis (median, range)** | 51 (35-60) | 51 (35-60) | 48 (35-60) |
| **Menopausal status** | | | |
| Pre-menopausal | 120 (43.6%) | 444 (34.7%) | 680 (56.7%) |
| Post-menopausal | 155 (56.4%) | 835 (65.3%) | 520 (43.3%) |
| **HRT use** | | | |
| No | 241 (71.3%) | 1115 (73.0%) | 1319 (83.2%) |
| Yes | 97 (28.7%) | 413 (27.0%) | 265 (16.7%) |
| **Parity** | | | |
| Nulliparous | 63 (18.6%) | 249 (16.3%) | 384 (24.2%) |
| Parous | 275 (81.4%) | 1279 (83.7%) | 1200 (75.8%) |
| **Breastfed** | | | |
| No | 72 (26.2%) | 317 (24.8%) | 222 (18.5%) |
| Yes | 202 (73.5%) | 952 (74.4%) | 971 (80.9%) |

## RESULTS

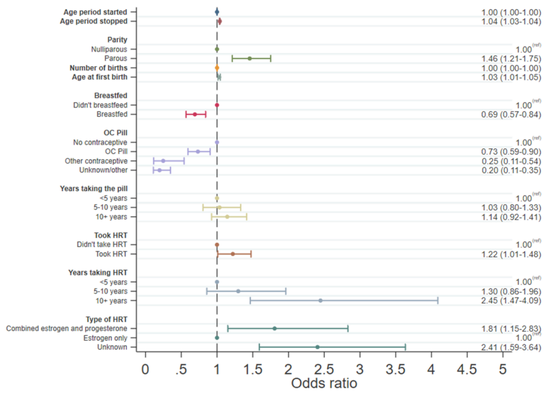
There was strong evidence of a protective effect of breastfeeding on both LCIS (OR: 0.63, 95%CI: 0.46-0.86) (Figure 1) and ILC (OR: 0.69, 0.57-0.84) (Figure 2), and evidence that HRT increased the risk of both LCIS (OR: 1.62, 95%CI: 1.21-2.17) and ILC (OR: 1.22, 95%CI: 1.01-1.48).

Figure 1: risk factor associations with LCIS compared to controls




Taking HRT for 10 years or more also increased the risk of both LCIS and ILC. However, combined estrogen and progestogen HRT was associated with increased risk of developing ILC (OR: 1.91, 95%CI: 1.15-2.83), but not LCIS. ILC was also associated with increasing age at first birth, while LCIS was not.

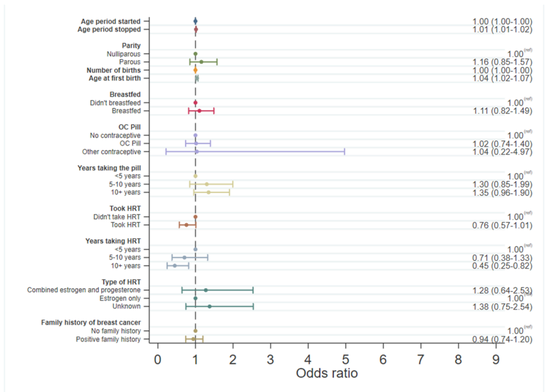
Figure 2: risk factor associations with ILC compared to controls




## RESULTS

When comparing LCIS to ILC (Figure 3), there were not many statistically significant differences in associations with risk factors, apart from increasing age at first birth being more strongly associated with ILC than LCIS, and HRT use being more strongly associated with LCIS than ILC.

Figure 3: risk factor associations with ILC compared to LCIS




## CONCLUSION

We conclude from this study that although there are some small differences, in general, the risk factors pre-disposing to ILC and LCIS are similar. Therefore, women should be made aware that taking long-term HRT can increase the risks of both LCIS and ILC.

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