

Socioeconomic inequalities in second primary cancer incidence: a competing risk analysis of women with breast cancer in England between 2000 – 2018

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Background

Breast cancer survival has substantially improved due to early detection and advances in treatment, leading to a greater risk of second primary cancer (SPC). In England, data on SPC incidence among women firstly diagnosed with breast cancer are scarce.

Aim

We aimed to investigate socioeconomic inequalities in SPC incidence among breast cancer survivors.

Methods

We used Data from National Cancer Registration and Analysis Service in England to construct a cohort of all women diagnosed with a first primary breast cancer (PBC) between 2000 and 2018 and aged between 18 – 99 years. Our main exposure was income deprivation, derived from Index of Multiple Deprivation 2015 and based on the Lower Super Output Area of patient's residence at the date of their PBC diagnosis. We followed up these women from 6 months after the PBC diagnosis until a SPC event, death, or 31 December, 2019, whichever came first. PBC survivors may die without a SPC event, and this corresponds to a competing risks situation. We used flexible parametric models and adjusted for age and year of PBC diagnosis, ethnicity, PBC tumour stage, comorbidity and PBC treatments to model the cause-specific hazards for SPC incidence and for death. Directly adjusted cumulative incidences were derived to contrast the risk of SPC incidence by deprivation. Multiple imputation was performed to account for missing data on ethnicity and stage.

Results

Among 668,398 included women, 47,399 SPCs and 186,326 deaths occurred during 4,706,701 person-years of follow-up. The crude SPC incidence rate was 11.6 (95% confidence interval (CI): 11.3, 11.8) per 1000 person-years in the most deprived vs. 9.2 (9.1, 9.4) in the least deprived quintile. In multivariable models, income deprivation was consistently associated with an increased risk of SPC incidence (Cause-Specific Hazard Ratio (CSHR) the most vs. least deprived quintile: 1.29; 95% CI: 1.24, 1.31) and death (CSHR: 1.36; 1.34, 1.49), and there was a clear trend along with increasing deprivation (Figure 1). These estimates translated into an absolute risk difference (the most vs. least deprived quintile) of 1.1% (95% CI: 0.9, 1.3) for SPC incidence and 4.9% (95% CI: 4.7, 5.2) for death at 10 years (Figure 2).

Conclusion

Women diagnosed with PBC from deprived areas in England faced a substantially higher risk of SPC than those from less deprived areas, making strategies specifically designed for monitoring, preventing, and identifying SPC at an early stage essential to minimise disparities in SPC among women suffering from breast cancer.

Image(s):

Figure 1: Cause-Specific Hazard ratios (CSHRs) of income deprivation on second primary cancer incidence and death

	Age-adjusted	Fully-adjusted MI	Fully-adjusted CC-1	Fully-adjusted CC-2
Second primary cancer incidence	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
2 nd quintile	1.03 (1.00, 1.06)	1.03 (1.00, 1.06)	1.02 (1.00, 1.05)	1.01 (0.97, 1.05)
3 rd quintile	1.08 (1.05, 1.11)	1.08 (1.05, 1.11)	1.07 (1.04, 1.10)	1.06 (1.02, 1.10)
4 th quintile	1.15 (1.12, 1.18)	1.16 (1.12, 1.19)	1.14 (1.11, 1.17)	1.11 (1.07, 1.15)
The most deprived	1.28 (1.24, 1.31)	1.29 (1.25, 1.33)	1.27 (1.23, 1.31)	1.28 (1.23, 1.32)
Death				
2 nd quintile	1.09 (1.07, 1.10)	1.07 (1.06, 1.09)	1.08 (1.06, 1.09)	1.07 (1.05, 1.09)
3 rd quintile	1.16 (1.14, 1.17)	1.13 (1.11, 1.14)	1.13 (1.11, 1.15)	1.13 (1.11, 1.15)
4 th quintile	1.28 (1.26, 1.29)	1.22 (1.20, 1.23)	1.22 (1.20, 1.24)	1.23 (1.20, 1.25)
The most deprived	1.45 (1.43, 1.47)	1.36 (1.34, 1.39)	1.38 (1.36, 1.40)	1.37 (1.34, 1.40)

HR: hazard ratio. MI: multiple imputation. CC: complete case. The least deprived quintile was set as reference group.

Age-adjusted: Models only included deprivation and restricted cubic spline transformed age (N=669,398).

Fully-adjusted MI: Models included deprivation and restricted cubic spline transformed age, ethnicity, year of primary breast cancer diagnosis group, comorbidity, primary breast cancer stage, surgery, chemotherapy, radiotherapy, and hormone therapy, and we multiply imputed missing data on ethnicity and stage (N=669,398).

Fully adjusted CC-1: Models were same as fully-adjusted MI, but the analysis was restricted to women with complete data on all variables except stage, in which women missing on stage was grouped into a new category (N=636,632).

Fully adjusted CC-2: Models were same as fully-adjusted MI, but the analysis was restricted to women with complete data on all variables (N=426,668).

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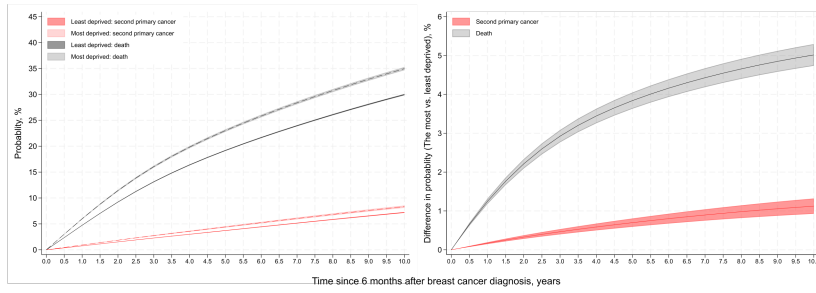
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Declaration of conflict of interest

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Figure 2: standardised cumulative incidence of second primary cancer and death in the least and most deprived women with breast cancer



- Cumulative incidence of second primary cancer and death were standardised after flexible parametric models adjusting for restricted cubic spline transformed age, ethnicity, year of primary breast cancer diagnosis group, comorbidity, primary breast cancer stage, surgery, chemotherapy, radiotherapy, and hormone therapy. Multiple imputation (10 times) was performed to account for missing data ethnicity and stage, and all estimates were combined with Rubin's rules.