Socioeconomic Status, Migration and the Risk of Breast Cancer in Italy

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Background. High socioeconomic status and migration to a higher risk area have been linked to increased breast cancer risk. To evaluate the occurrence of breast cancer in women of different social class and residential history, we conducted a multicentre case-control study in Italy.

Methods. A total of 2569 cases of incident breast cancer were ascertained in northern, central and southern Italy. The controls were 2588 women admitted for a wide spectrum of acute conditions to the same hospitals where cases had been hospitalized. The effect of socioeconomic variables was evaluated with multiple logistic regression after stratification and adjustment for age, origin, centre, and selected reproductive and dietary factors.

Results. Compared to housewives, managers and professionals had a 1.7-fold increased risk, whereas the relative risk was 0.7 and 0.6 respectively in helpers and manual workers. The risk of breast cancer also increased with increasing social level of the husband's occupation and subject's number of years of schooling. Women who originated in central and southern Italy, and migrated to northern Italy after age 24, but not those who migrated at a younger age, had a relative risk of 0.6 and 0.7 respectively, compared to lifelong residents in northern Italy.

Conclusions. Our findings show that correlates of social status and place of origin exert an influence on breast cancer risk which is not accounted for completely by known risk factors (i.e. reproductive and menstrual characteristics and recent dietary habits). Such influence may thus occur early in life.

Keywords: breast cancer, socioeconomic status, occupation, education, migration, case-control

Epidemiological investigations have suggested a positive relation between breast cancer and socioeconomic status1,2 including previous case-control studies from our group.3,4 High levels of education, occupational status and housing conditions have been linked to breast cancer risk, but the reasons for this relation are little understood. The role of these characteristics probably varies from one population to another, and most of the studies on this topic have been conducted in countries characterized by larger differences across social classes and different correlates of socioeconomic status than Italy.5–7

Moreover, studies on women migrating from areas of low to high incidence of breast cancer show a gradual increase in rates up to values that are above those of their country of origin, but still lower than the host country.8–15 These differences in the incidence as compared to the host population, however, depend upon age at migration and tend to disappear in subsequent generations. These patterns suggest that, apart from menstrual and reproductive factors, early life exposures and events could play a significant role in the aetiology of the disease.

A multicentre case-control study on breast cancer in different Italian areas has provided the opportunity to evaluate the occurrence of breast cancer in women of different social class and born in various Italian regions (i.e. high-risk regions such as the North or low-risk regions such as the Centre and South of Italy15), adjusting for known risk factors for breast cancer, such as reproductive history, recent diet, female hormone use, and other variables.

SUBJECTS AND METHODS
The case-control study involved six Italian areas in northern Italy (greater Milan, the province of Pordenone,
the urban area of Genoa, the province of Forli), central Italy (province of Latina, near Rome) and southern Italy (the urban area of Naples). Patients with histologically confirmed breast adenocarcinoma diagnosed within the year preceding the interview, aged ≤75, were eligible as cases. They were identified among residents who had been admitted in surgeries and oncology departments of major hospitals of the areas under surveillance and were interviewed in hospital between June 1991 and February 1994.

Controls were women residing in the same geographical areas as the cases admitted for a wide spectrum of acute conditions to the same hospitals where cases had been identified. Gynaecological, hormonal and neoplastic diseases were excluded, together with any conditions which might have resulted in long-term modification of diet. A total of 2569 cases and 2588 controls (median ages 55 and 56 years, respectively) were included in the analysis. Non-response was approximately 4% for both cases and controls.

Cases and controls were administered a structured questionnaire by trained interviewers, referring to the situation before the onset of the disease which led to hospital admission. The questionnaire included information on subject’s and spouse’s occupation, education, residence, birthplace, smoking habits, weight, physical activity, gynaecological and obstetric data, personal and family medical history, use of oral contraceptives and of female hormone preparations for other indications, including hormonal replacement therapy in menopause. Dietary habits in the 2 years prior hospital admission were evaluated by means of a validated food frequency questionnaire. Subject’s and spouse’s longest lifetime occupation and years of completed schooling have been used as indicators of socioeconomic status.

The measure of association between breast cancer risk and the study variables was the odds ratio (OR) as an estimate of the relative risk. OR and the corresponding 95% confidence intervals (CI) were derived from unconditional multiple regression equations, including terms for age (continuous), centre, and categories of origin, parity, age at first birth, age at menarche, age at menopause, use of oral contraceptives and oestrogen replacement therapy, total fat and beta-carotene intake.

Allowance for recent intake of several food groups, macro- and micronutrients was attempted. However, for the final model, only total fat and beta-carotene were retained since they were, respectively, the macro- and micronutrient most strongly associated with breast cancer risk in the present investigation, and the only ones to have either a small confounding effect or some interactive effect with socioeconomic variables.

RESULTS
The distribution of breast cancer cases and controls according to centre, selected covariates, and age is displayed in Table 1. Cases reported significantly fewer full-term births and older age at first birth and were more often premenopausal. A greater proportion of working women, especially in ‘white collar’ occupations, as well as higher educational attainment, emerged among women aged ≤55 rather than above.

Table 2 shows OR of breast cancer by subject’s occupation overall and in two age strata (<55 and ≥55). The estimates of the OR adjusted for age and centre, compared to estimates of the OR adjusted also for a number of other potential confounders, were slightly different for the upper class category only, i.e. managers and professionals. In this group, for all ages combined, adjustment for reproductive and nutritional variables reduced the strength of the associations between occupation and breast cancer, although managers and professionals retained a significant 70% excess risk when compared to housewives. For women aged ≥55 the fully adjusted OR was 2.0 (95% CI: 1.4–2.9) for manager and professional women. For women <55 years of age the corresponding OR was 1.5 (1.1–2.1). Significantly decreased risks were found for manual workers (OR = 0.6; 95% CI: 0.5–0.8) and helpers (OR = 0.7; 95% CI: 0.6–0.9), regardless of age. A decreased, albeit not significant, OR was also found for the older farmers (OR = 0.8; 95% CI: 0.6–1.1). In a model which included, for women of all ages, both terms for education and for subject’s occupation the increased risk associated with work as a manager or professional was almost fully explained by education, whereas the decreased risk associated with employment as a helper or a manual worker remained unchanged.

The association of the spouse’s occupation with breast cancer among ever married women is displayed in Table 3. The risk of cancer increased with increasing social level of the husband’s occupation, especially in women with no personal income (i.e. housewives) or low personal social level of occupation (i.e. farmer, helper or manual worker). For women who were craftsmen or clerical workers, the risk was somewhat higher if their husband was a manager or professional as compared to a farmer, helper or manual worker (OR = 1.4, 0.9–2.2). The occupation of the husband was not associated with breast cancer among women who were managers or professionals. Among women who never got married, their own occupation was examined with an OR of 1.9 (1.01–3.6) for managers/professionals and 1.6 (0.99–2.6) for craftsmen/clerical workers, as compared to farmers, helpers or manual workers.
### Table 1: Distribution of cases of breast cancer and controls according to selected covariates. 2569 cases and 2588 controls. Italy, 1991–1994

<table>
<thead>
<tr>
<th>Covariate</th>
<th>Age &lt;55 years</th>
<th>controls*</th>
<th>Age &gt;55 years</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cases* No. (%)</td>
<td>controls* No. (%)</td>
<td>Cases* No. (%)</td>
<td>Controls No. (%)</td>
</tr>
<tr>
<td>Centre</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pordenone</td>
<td>527 (42)</td>
<td>483 (42)</td>
<td>519 (39)</td>
<td>532 (37)</td>
</tr>
<tr>
<td>Milan</td>
<td>243 (20)</td>
<td>257 (22)</td>
<td>342 (26)</td>
<td>366 (26)</td>
</tr>
<tr>
<td>Genoa</td>
<td>113 (9)</td>
<td>98 (8)</td>
<td>177 (13)</td>
<td>212 (15)</td>
</tr>
<tr>
<td>Forlì</td>
<td>108 (9)</td>
<td>108 (9)</td>
<td>104 (8)</td>
<td>105 (7)</td>
</tr>
<tr>
<td>Naples</td>
<td>151 (12)</td>
<td>125 (11)</td>
<td>107 (8)</td>
<td>124 (9)</td>
</tr>
<tr>
<td>Latina</td>
<td>100 (8)</td>
<td>95 (8)</td>
<td>78 (6)</td>
<td>83 (6)</td>
</tr>
<tr>
<td>Patient's occupation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Housewife</td>
<td>445 (36)</td>
<td>412 (35)</td>
<td>582 (44)</td>
<td>630 (45)</td>
</tr>
<tr>
<td>Student/unemployed</td>
<td>18 (1)</td>
<td>18 (2)</td>
<td>13 (1)</td>
<td>15 (1)</td>
</tr>
<tr>
<td>Farmer</td>
<td>44 (4)</td>
<td>43 (4)</td>
<td>102 (8)</td>
<td>143 (10)</td>
</tr>
<tr>
<td>Helper</td>
<td>69 (6)</td>
<td>105 (9)</td>
<td>86 (7)</td>
<td>122 (9)</td>
</tr>
<tr>
<td>Manual worker</td>
<td>100 (8)</td>
<td>184 (16)</td>
<td>124 (9)</td>
<td>169 (12)</td>
</tr>
<tr>
<td>Craftsman</td>
<td>45 (4)</td>
<td>45 (4)</td>
<td>74 (6)</td>
<td>63 (4)</td>
</tr>
<tr>
<td>Clerical worker</td>
<td>365 (29)</td>
<td>277 (24)</td>
<td>244 (18)</td>
<td>222 (16)</td>
</tr>
<tr>
<td>Manager/professional</td>
<td>154 (12)</td>
<td>80 (7)</td>
<td>98 (7)</td>
<td>47 (3)</td>
</tr>
<tr>
<td>Years of schooling</td>
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<td></td>
<td></td>
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<tr>
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<td>44 (4)</td>
<td>85 (7)</td>
<td>272 (21)</td>
<td>407 (29)</td>
</tr>
<tr>
<td>5–7</td>
<td>398 (32)</td>
<td>485 (42)</td>
<td>601 (46)</td>
<td>658 (47)</td>
</tr>
<tr>
<td>8–12</td>
<td>478 (39)</td>
<td>415 (36)</td>
<td>333 (25)</td>
<td>265 (19)</td>
</tr>
<tr>
<td>13–15</td>
<td>199 (16)</td>
<td>125 (11)</td>
<td>63 (5)</td>
<td>58 (4)</td>
</tr>
<tr>
<td>&gt;16</td>
<td>115 (9)</td>
<td>46 (4)</td>
<td>52 (4)</td>
<td>21 (1)</td>
</tr>
<tr>
<td>Place of birth</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>North East</td>
<td>461 (37)</td>
<td>447 (38)</td>
<td>488 (37)</td>
<td>530 (37)</td>
</tr>
<tr>
<td>North West</td>
<td>217 (17)</td>
<td>200 (17)</td>
<td>332 (25)</td>
<td>325 (23)</td>
</tr>
<tr>
<td>Emilia-Romagna Region</td>
<td>102 (8)</td>
<td>108 (9)</td>
<td>120 (9)</td>
<td>118 (8)</td>
</tr>
<tr>
<td>Center</td>
<td>112 (9)</td>
<td>100 (9)</td>
<td>83 (6)</td>
<td>104 (7)</td>
</tr>
<tr>
<td>South and Islands</td>
<td>297 (24)</td>
<td>265 (23)</td>
<td>253 (19)</td>
<td>299 (21)</td>
</tr>
<tr>
<td>Abroad</td>
<td>53 (4)</td>
<td>46 (4)</td>
<td>51 (4)</td>
<td>45 (3)</td>
</tr>
<tr>
<td>Parity</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>175 (14)</td>
<td>178 (15)</td>
<td>226 (17)</td>
<td>202 (14)</td>
</tr>
<tr>
<td>1</td>
<td>282 (23)</td>
<td>253 (22)</td>
<td>302 (23)</td>
<td>241 (17)</td>
</tr>
<tr>
<td>2</td>
<td>527 (42)</td>
<td>440 (38)</td>
<td>441 (33)</td>
<td>469 (33)</td>
</tr>
<tr>
<td>≥3</td>
<td>258 (21)</td>
<td>295 (25)</td>
<td>358 (27)</td>
<td>510 (36)</td>
</tr>
<tr>
<td>Age at first birth</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;20</td>
<td>58 (5)</td>
<td>123 (12)</td>
<td>62 (6)</td>
<td>95 (8)</td>
</tr>
<tr>
<td>20–23</td>
<td>297 (28)</td>
<td>383 (39)</td>
<td>277 (25)</td>
<td>360 (30)</td>
</tr>
<tr>
<td>24–27</td>
<td>442 (41)</td>
<td>317 (32)</td>
<td>371 (34)</td>
<td>423 (35)</td>
</tr>
<tr>
<td>28–31</td>
<td>172 (16)</td>
<td>119 (12)</td>
<td>235 (21)</td>
<td>218 (18)</td>
</tr>
<tr>
<td>≥32</td>
<td>97 (9)</td>
<td>46 (5)</td>
<td>156 (14)</td>
<td>124 (10)</td>
</tr>
</tbody>
</table>

* Some figures do not add up to the total due to missing values.
TABLE 2 Odds ratios (OR) and 95% confidence interval (CI) for breast cancer by occupation and age. 2569 cases and 2588 controls. Italy, 1991–1994

<table>
<thead>
<tr>
<th>Subject's occupation</th>
<th>Age &lt;55 years</th>
<th>Age ≥55 years</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td>Housewife&lt;sup&gt;d&lt;/sup&gt;</td>
<td>1.1 (0.6–2.1)</td>
<td>0.9 (0.4–2.0)</td>
<td>0.9 (0.6–1.6)</td>
</tr>
<tr>
<td>Unemployed/student</td>
<td>1.0 (0.6–1.5)</td>
<td>0.8 (0.6–1.1)</td>
<td>0.8 (0.6–1.02)</td>
</tr>
<tr>
<td>Farner</td>
<td>0.6 (0.4–0.9)</td>
<td>0.8 (0.6–1.01)</td>
<td>0.7 (0.6–0.97)</td>
</tr>
<tr>
<td>Helper</td>
<td>0.6 (0.4–0.9)</td>
<td>0.8 (0.6–1.01)</td>
<td>0.7 (0.6–0.97)</td>
</tr>
<tr>
<td>Manual worker</td>
<td>0.6 (0.4–0.7)</td>
<td>0.8 (0.6–0.96)</td>
<td>0.6 (0.5–0.89)</td>
</tr>
<tr>
<td>Craftsman</td>
<td>0.6 (0.4–0.7)</td>
<td>0.8 (0.6–1.01)</td>
<td>0.6 (0.5–0.8)</td>
</tr>
<tr>
<td>Clerical worker</td>
<td>1.3 (1.0–1.6)</td>
<td>1.2 (0.95–1.5)</td>
<td>1.2 (1.1–1.4)</td>
</tr>
<tr>
<td>Manager/professional</td>
<td>1.8 (1.4–2.5)</td>
<td>2.3 (1.6–3.3)</td>
<td>2.0 (1.6–2.5)</td>
</tr>
<tr>
<td></td>
<td>1.5 (1.1–2.1)</td>
<td>2.0 (1.4–2.9)</td>
<td>1.7 (1.3–2.1)</td>
</tr>
<tr>
<td></td>
<td>2.0 (1.6–2.5)</td>
<td>1.2 (0.9–1.6)</td>
<td></td>
</tr>
</tbody>
</table>

* Adjusted for age and centre.

b Adjusted for age, centre, parity, age at first live birth, at menarche, and at menopause, use of oral contraceptives and oestrogen replacement therapy, total fat and beta-carotene intake.

c Adjusted for all the above-mentioned variables in addition to years of schooling.

d Reference category.

(i.e. consistent with previous results by head of the household's occupation) (Table 3).

The risk of breast cancer increased with increasing number of years of schooling (Table 4). Women with 0 to 4 years of education had the lowest risk of breast cancer and women with at least 16 years of schooling had an OR of 3.3 (2.4–4.7). For women <55 years of age, the association with schooling was somewhat stronger than for older ones.

Education was positively associated with breast cancer in all categories of parity. When women were stratified according to age at first birth, however, education was particularly strongly associated with breast cancer in women with age at first birth ≥28 (OR = 4.5,
TABLE 4  Years of schooling, odds ratios (OR) and 95% confidence interval (CI) for breast cancer according to selected covariates. 2569 cases and 2588 controls. Italy, 1991–1994

<table>
<thead>
<tr>
<th>Years of schooling</th>
<th>0–4*</th>
<th>5–7</th>
<th>8–12</th>
<th>13–15</th>
<th>≥16</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR^b (95% CI)</td>
<td>OR^b (95% CI)</td>
<td>OR^b (95% CI)</td>
<td>OR^b (95% CI)</td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>1.0 (0.6–1.8)</td>
<td>1.2 (0.9–1.6)</td>
<td>1.5 (1.0–2.2)</td>
<td>1.5 (1.0–2.2)</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>1.0 (0.6–1.8)</td>
<td>1.4 (0.8–2.5)</td>
<td>1.7 (1.0–3.4)</td>
<td>1.7 (1.0–3.4)</td>
<td></td>
</tr>
<tr>
<td>&lt;55</td>
<td>1.1 (0.9–1.3)</td>
<td>1.2 (1.0–1.5)</td>
<td>1.3 (0.9–2.0)</td>
<td>1.3 (0.9–2.0)</td>
<td></td>
</tr>
<tr>
<td>≥55</td>
<td>1.0 (0.8–1.4)</td>
<td>1.4 (1.0–1.9)</td>
<td>1.1 (0.7–2.0)</td>
<td>1.1 (0.7–2.0)</td>
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</tr>
<tr>
<td>Parity</td>
<td>1.0 (0.6–1.8)</td>
<td>1.4 (0.8–2.5)</td>
<td>1.7 (1.0–3.4)</td>
<td>1.7 (1.0–3.4)</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>1.1 (0.9–1.3)</td>
<td>1.2 (1.0–1.5)</td>
<td>1.3 (0.9–2.0)</td>
<td>1.3 (0.9–2.0)</td>
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</tr>
<tr>
<td>1</td>
<td>1.0 (0.8–1.4)</td>
<td>1.4 (1.0–1.9)</td>
<td>1.1 (0.7–2.0)</td>
<td>1.1 (0.7–2.0)</td>
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</tr>
<tr>
<td>≥3</td>
<td>1.0 (0.8–1.4)</td>
<td>1.4 (1.0–1.9)</td>
<td>1.1 (0.7–2.0)</td>
<td>1.1 (0.7–2.0)</td>
<td></td>
</tr>
<tr>
<td>Age at first birth (years)</td>
<td>1.0 (0.6–1.8)</td>
<td>1.4 (0.8–2.5)</td>
<td>1.7 (1.0–3.4)</td>
<td>1.7 (1.0–3.4)</td>
<td></td>
</tr>
<tr>
<td>&lt;23</td>
<td>1.1 (0.9–1.3)</td>
<td>1.2 (1.0–1.5)</td>
<td>1.3 (0.9–2.0)</td>
<td>1.3 (0.9–2.0)</td>
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</tr>
<tr>
<td>24–27</td>
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<td>1.4 (0.8–2.5)</td>
<td>1.7 (1.0–3.4)</td>
<td>1.7 (1.0–3.4)</td>
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</tr>
<tr>
<td>≥28</td>
<td>1.1 (0.9–1.3)</td>
<td>1.2 (1.0–1.5)</td>
<td>1.3 (0.9–2.0)</td>
<td>1.3 (0.9–2.0)</td>
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</tr>
<tr>
<td>Total fat intake (tertile)</td>
<td>1.0 (0.6–1.8)</td>
<td>1.4 (0.8–2.5)</td>
<td>1.7 (1.0–3.4)</td>
<td>1.7 (1.0–3.4)</td>
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<tr>
<td>Lower</td>
<td>1.1 (0.9–1.3)</td>
<td>1.2 (1.0–1.5)</td>
<td>1.3 (0.9–2.0)</td>
<td>1.3 (0.9–2.0)</td>
<td></td>
</tr>
<tr>
<td>Intermediate</td>
<td>1.0 (0.6–1.8)</td>
<td>1.4 (0.8–2.5)</td>
<td>1.7 (1.0–3.4)</td>
<td>1.7 (1.0–3.4)</td>
<td></td>
</tr>
<tr>
<td>Upper</td>
<td>1.1 (0.9–1.3)</td>
<td>1.2 (1.0–1.5)</td>
<td>1.3 (0.9–2.0)</td>
<td>1.3 (0.9–2.0)</td>
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<tr>
<td>Beta-carotene intake (tertile)</td>
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<td>1.4 (0.8–2.5)</td>
<td>1.7 (1.0–3.4)</td>
<td>1.7 (1.0–3.4)</td>
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<td>Lower</td>
<td>1.1 (0.9–1.3)</td>
<td>1.2 (1.0–1.5)</td>
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<tr>
<td>Intermediate</td>
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<td>1.4 (0.8–2.5)</td>
<td>1.7 (1.0–3.4)</td>
<td>1.7 (1.0–3.4)</td>
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<tr>
<td>Upper</td>
<td>1.1 (0.9–1.3)</td>
<td>1.2 (1.0–1.5)</td>
<td>1.3 (0.9–2.0)</td>
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<td></td>
</tr>
</tbody>
</table>

*Reference category.
^b Adjusted for age, centre, parity, age at first birth, at menarche and at menopause, use of oral contraceptives and oestrogen replacement therapy, total fat and beta-carotene intake, as appropriate.
^c Also adjusted for subject's occupation.

2.3–8.9), for at least 16 years of schooling, compared to 0–4 years. This positive association with education persisted in women with age at first birth 24–27 years, and weakened, but did not disappear entirely, in those who bore their first child at <24. Interaction between years of schooling and age at first birth was not statistically significant. Level of total fat and beta-carotene intake (Table 4) and use oral contraceptives and oestrogen replacement therapy (not shown) did not modify the effect of education.

Table 5 displays the effects of origin in central and southern Italy compared to lifelong residence in northern Italy among current residents in northern Italy. Current residents of central and southern Italy were excluded from this analysis because migration from the North was negligible. Women who originated in central and southern Italy and migrated to northern Italy after age 24 had an OR of 0.6 (0.4–0.9) and 0.7 (0.6–0.98) respectively. Women who migrated at a younger age did not show a significantly decreased risk as compared to those who were born in northern Italy. Persistence of a low risk associated with having been born in central and southern Italy in individuals who migrated after age 24 was seen in most categories of variables which may be effect modifiers, i.e. parity, and age at first birth (Table 5). No interactions were statistically significant. Use of oral contraceptives and oestrogen replacement therapy showed a similar lack of influence (not shown).

DISCUSSION
In this study, the risk of female breast cancer was higher among managers and professionals and lower
among farmers, helpers and manual workers as compared to housewives (i.e. the occupation of 40% of cases as well as controls in the present study population). The association with occupation was present among married and unmarried women, but breast cancer risk in the former was further enhanced by their husband’s occupation. Education, as measured by the number of years of schooling, was also directly associated with breast cancer, besides being correlated with occupation. The consistency between results pertaining to occupation and education suggests that social factors rather than occupational exposures are involved in breast cancer onset. This is supported further by the fact that women married to men whose occupation was at a higher social level than their own were at additional risk. However, since we were unable to obtain complete occupational history or exposure assessment, we cannot exclude completely the possibility of occupational risks associated with clerical work and managerial as well as professional responsibilities.

Some indicators of socioeconomic status have been positively associated with the occurrence of breast cancer in previous studies with relative risks for the highest versus the lowest category around or over two.\(^1,\)\(^5,\)\(^21,\)\(^23\) These included a case-control study investigation carried out by our group in Milan, northern Italy.\(^3\) Certain studies have also singled out occupations at higher risk, such as professional, managerial and clerical workers,\(^24,\)\(^25\) whereas breast cancer incidence was lower among service workers, craftsmen, and farmers in some studies.\(^4,\)\(^26\) Other studies on this topic, are, however, inconsistent, suggesting no association with any of these variables\(^27\) or with education.\(^28\) These discrepancies may be explained by overadjustment and high collinearity which may occur when broad occupational and educational variables are both kept in the
documented. In our study the direct association between occupation as a manager or professional and breast cancer disappeared after adjusting for education. Discrepancies can also derive from different correlates of socioeconomic status in different populations (e.g. dietary and alcohol drinking habits, physical activity, etc.).

Since the specific causal factor(s) correlated with higher occupation and education remain largely obscure, various possible explanations exist. First, earlier research found that the difference in the incidence of breast cancer between women with high and low social class was at least partly attributable to reproductive factors and hormonal status. High social status tends to be positively associated with age at first birth and negatively with parity. In addition, dietary factors may also be important in the occurrence of breast cancer. However, the distribution of reproductive and dietary factors did not explain or modify substantially the association with socioeconomic variables in our study. Indeed, in the present female population, recent dietary habits seemed largely uncorrelated with sociocultural indicators.

With respect to age, the present study was unable to disentangle the effect of age at diagnosis per se from a cohort effect. Occupation, however, showed a very similar risk pattern in women less than and over 55 years, especially when managers/professionals were compared with manual workers rather than with housewives. Education was most strongly associated with breast cancer risk in younger women, despite the fact that differences in the lifestyle of upper social class women were certainly more pronounced in the past than at present and high educational attainment was substantially rarer in older generations. Calibration methods should be developed to make different generations more comparable in terms of sociocultural status, since two thirds of women <55 had ≥5 years of schooling, compared to one third only among women ≥55 years. ‘White collar’ occupations have also proportionally increased among younger women.

If confounding by known variables was not sufficient in our study to explain the results, it is still possible that residual confounding was exerting its effect due to misclassification of certain confounding variables associated with insufficient validity of the data collection instrument. This explanation is, however, unlikely since the report of parity and age at first birth is reliable and good reproducibility and validity of information on recent dietary habits in the present study have also been documented.

An important factor which we considered in our study, but did not retain in the final analysis, was level of physical activity at different ages. It has been suggested that high physical activity may protect against breast cancer. In our study elevated levels of occupational physical activity were significantly protective against breast cancer, but this variable was highly correlated with employment (i.e. as a farmer, unskilled or skilled manual worker) and low education. When both occupational physical activity and occupation or years of schooling were included in the same model, socioeconomic variables seemed to exert a stronger effect than physical activity. Therefore, either the apparent benefit of high physical activity is largely due to social class, or socioeconomic status and physical activity are in the same causal pathway of disease. Hence, their mutual adjustment is inappropriate.

The possibility of unmeasured confounding factors cannot be excluded, but, in the light of the strength of the present association with socioeconomic status, these must be characteristics with an unusually strong relationship with breast cancer risk.

To elucidate, at least indirectly, factors which may act early in life, we collected information about migration of women from central and southern Italy to northern Italy. Central and southern Italy have lower incidence rates of breast cancer than northern Italy and migration has been almost exclusively northbound. We observed a protective effect of origin in central or southern Italy compared to lifelong residence in northern Italy, when northbound migration occurred after age 24, whereas migration at a younger age seemed to put women at the same risk as for lifelong residence in northern Italy.

This observation lends support to the hypothesis that some characteristics of Mediterranean areas, operating early in life and especially adolescence, may have given some protection against breast cancer risk in Italy, as confirmed by historical trends. Models of breast cancer also suggest that risk is set by events in early life. Exposures which have been implicated during adolescence and early adulthood, either directly or through decreased age at menarche, include nutrition, childhood infections, level of physical activity, irradiation, alcohol consumption, etc. However, our study did not find clear effects for a number of these exposures or events (e.g. age at menarche) which could explain the strong association with socioeconomic and geographical variables.

Bias must always be considered as a possible explanation of epidemiological findings, especially with respect to socioeconomic variables. Selection bias would have occurred if cases were drawn from hospitals serving selectively affluent and better educated subjects and controls came from hospitals that treated lower social classes. This is, however, unlikely in our
study. Socioeconomic differences among hospitals, which are clearly present in the US and in other coun-
tries which lack a developed national health service are
not marked in Italy. Furthermore, cases and controls
were enrolled from a network which included all major
local hospitals and all study centres showed the same
pattern. It is also unlikely that information such as years
of schooling, occupation and origin may be affected by
recall bias.

In conclusion, socioeconomic status as measured by
occupation and education was a major risk factor for
breast cancer in this study. Origin in low risk areas also
was a moderate protective factor if subsequent migra-
tion occurred in adulthood. The determinants of breast
cancer which underlie the association with socio-
economic and geographical variables remain largely
obscure. However, since education, professional achieve-
ments and geographical origin are closely related to
conditions of the subject and of her family early in life,
our findings support, albeit indirectly, the hypothesis
that factors which act at an early age, especially in
adolescence, play an important role in the aetiology of
breast cancer. 36

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