REVIEW

Occupational risk factors for female breast cancer: a review

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Abstract

Objectives—Although progress has been made in identifying personal risk factors and in improving treatment for female breast cancer, incidence rates continue to increase. With women now occupying a sizable fraction of the workforce, it is worth inquiring whether there are occupational risk factors for breast cancer. This is a review of occupational studies on female breast cancer.

Methods—Suitable reports and published articles with associations of female breast cancer and occupation were identified from technical reports, by searching the MEDLINE bibliographic data base, and by reviewing each paper on cancer that was published in 20 major journals during the period from about 1971–94.

Results—A total of 115 studies were identified; 19 studies relied exclusively on data collected for administrative purposes, and there were four incident case-control studies and 92 cohort studies. Although data for individual industries, occupations, and exposures were sparse, there was limited evidence of an association with employment in the pharmaceutical industry and among cosmetologists and beauticians. Associations were also found for chemists and occupations with possible exposure to extremely low frequency electromagnetic fields, but potential methodological weaknesses preclude drawing any definite conclusions. There was little support for increased risks among textiles workers, dry cleaning workers, and nuclear industry workers.

Conclusions—Few high quality occupational studies directed specifically toward women have been carried out to allow the unambiguous identification of occupational risk factors for breast cancer. It is suggested that investigations that account for non-occupational risk factors and that assess exposure in a more detailed way be carried out. One strategy already suggested is to conduct population based, case-control studies in which subjects are interviewed about their occupational histories and exposure to chemical and physical agents which are then attributed from the job descriptions by a team of experts. These studies can then be supplemented when necessary with cohort studies of specific populations.

Keywords: cancer female breast; occupational exposure; epidemiology; literature review

Breast cancer in western societies affects almost one in 10 women during their lifetime and is the leading cause of death from cancer in women. Over the past quarter century, the focus of research has been to improve treatments and to identify personal risk factors, such as family history of cancer and reproductive factors. Observations on reproductive factors have led to the hypothesis that breast cancer is caused by early and extended exposures to hormonal oestrogen and progesterone. Environmental risk factors have also been studied, but not as extensively. Exposure to ionising radiation has been shown to be clearly associated with a risk of breast cancer. Other environmental exposures have been investigated recently, including consumption of alcohol, exposure to persistent organochlorine compounds, and dietary fat, although results are controversial.

Against this large research effort is the unfortunate fact that incidence rates in most western societies have continued to increase over the past few decades. The reasons for these increases are largely unknown, but could be related to early detection in mass screening programmes, to temporal changes in accepted and suspected risk factors, to changes in the pathological definition of breast cancer, or to an artifact of detecting "histologically malignant but biologically benign" tumours (although this seems doubtful), or to other unidentified risk factors. It is likely that the accepted risk factors cannot account for a large fraction of cases or for all of the growth in incidences rates.

As women have taken a more active role in the workforce since the 1960s, it is possible that the secular increases in incidence rates may be related in part to exposure to carcinogens in the workplace. Although the occupational setting has not been studied with the intensity given to personal risk factors, interest in this field has increased. In considering new avenues of research, it is timely to provide a review of the current state of knowledge of the occupational environment. We therefore present a summary of results for breast cancer from occupational studies conducted within the past 25 years.

Materials

Reports and published articles with the potential for investigating associations of female
breast cancer and occupation were identified by searching the MEDLINE bibliographic data base, and by reviewing each paper on cancer that was published in 20 major journals during the period from about 1971 to about mid-1994 (table 1). We benefited from the earlier review carried out by Hoar Zahm and colleagues of papers in eight journals published between 1971 and 1990. Excluded from consideration were studies of the radium dial painters because they have limited relevance to women's occupations after the second world war.

A total of 147 reports from 115 independent studies, including non-peer reviewed technical reports, were reviewed (table 2). Studies were classified by type of design, although some investigations did not fit neatly into one simple category. Nineteen studies (of 40 reports) relied on routinely collected data or data collected for other administrative purposes—for example, special labour force surveys—whereby mortality or cancer incidence statistics were calculated with or without a census denominator—for example, proportional mortality (PMR) studies and standardised incidence ratio (SIR) studies, respectively. Twelve of these studies were based on mortality figures, six studies were based on incidence data, and one study combined incidence and mortality. There were also four incident case-control studies and 92 investigations of cohorts (from 106 reports; table 3).

**Results**

The studies with routinely collected data usually covered a wide variety of occupational circumstances and were from different parts of the world. Other administrative studies, not all independent from these, were directed toward specific types of industries or occupations: agriculture, beaurticians and cosmetologists, electrical workers, electronics industry, health care workers, jewellery, laundry and dry cleaning, pharmaceuticals, printing, shoe manufacturing, telephone workers, and textiles.

Two of the four case-control studies were population based, one was based on patients admitted to Roswell Park Memorial Institute, Buffalo, NY, and the fourth was a nested study among patients referred to a breast cancer screening clinic in New York City. In general, response rates in three of these studies were adequate and control populations were selected appropriately. The focus of the report by Franceschi et al. was on farming and agricultural occupations and that of Koenig and collaborators was on cosmetologists. We assumed that in all of these studies there was the opportunity to investigate a wide variety of occupational circumstances.

Thirty three different occupations or industries were investigated in the cohort studies, as well as 16 different exposures to chemical agents (table 3). Eight occupational circumstances were studied more than twice: asbestos workers (eight independent studies); chemical and related workers (five studies); cosmetologists (four studies); pharmaceuticals (three studies); rubber industry (six studies); shoe manufacturing (four studies); textiles and garment workers (five studies); and x-ray technicians and radiation workers (six studies).

Excluding cohort studies that relied on PMR or mortality odds ratio (MOR) analyses, the median number of women included in these studies was about 1500: 18 studies included more than 5000 subjects, and six studies included more than 10,000 subjects. The median number of breast cancer cases was 19 (mean of 64), and only five studies had more than 100 cases. Although table 3 shows that...
statistical power was above 80% in about 75% of studies, the small number of cases found indicates that the power to detect excess risks in subgroups and to test for trends in exposure was generally low.

A variety of indices of exposure or surrogates of exposure were used in these studies, but in only 10 studies were risks of breast cancer actually presented by level or duration of exposure.

Table 3 continued overleaf

<table>
<thead>
<tr>
<th>Reports</th>
<th>Study design</th>
<th>Exposure-response*</th>
<th>Women n</th>
<th>Cases</th>
<th>Relative risk</th>
<th>95% CI</th>
<th>Statistical power(%)</th>
<th>Reference</th>
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<td>Occupations or industries:</td>
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<td>Abattoirs</td>
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<td>N</td>
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<td>0.7 (0.5-0.9)</td>
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<td>65,66</td>
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<td>Actors</td>
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<td>NR (NC)</td>
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<td>Cable manufacturing (chlorinated naphthalenes)</td>
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<td></td>
<td>1</td>
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<td>Cosmetologists</td>
<td>4</td>
<td>SMR</td>
<td>N</td>
<td>7736</td>
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<td>0.6 (0.2-1.4)</td>
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<td>Dry cleaning</td>
<td>4</td>
<td>SMR</td>
<td>N</td>
<td>677</td>
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<td>0.7 (0.3-1.3)</td>
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<td>1.2 (0.8-1.6)</td>
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<td>Y, L</td>
<td>2243</td>
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<td>SMR</td>
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<td>0.7 (0.5-0.9)</td>
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<td>Gardeners</td>
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<td>N</td>
<td>151</td>
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<td>NR (NC)</td>
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<td>Jewellery workers</td>
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<td>PMR</td>
<td>N</td>
<td>1083</td>
<td>NR</td>
<td>NR (NC)</td>
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<td>N</td>
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<td>8</td>
<td>2.9 (2.5-4.7)</td>
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<td>Leather tanning</td>
<td>1</td>
<td>SMR</td>
<td>Y, L</td>
<td>482</td>
<td>NR</td>
<td>NR (NC)</td>
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<td>Motor vehicle manufacturing</td>
<td>2</td>
<td>SMR</td>
<td>N</td>
<td>NA</td>
<td>5</td>
<td>1.1 (0.4-2.5)</td>
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<td>Municipal workers</td>
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<td>SMR</td>
<td>N</td>
<td>1127</td>
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<td>0.7 (0.3-1.0)</td>
<td>96</td>
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<td>Pathologists</td>
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<td>SMR</td>
<td>N</td>
<td>803</td>
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<td>1.6 (0.4-4.1)</td>
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<td>Petroleum manufacturing workers</td>
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<td>SMR</td>
<td>L</td>
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<td>1.0 (0.5-1.9)</td>
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<td>Pharmaceutical, pharmacy technicians</td>
<td>3</td>
<td>SMR</td>
<td>N</td>
<td>NA</td>
<td>22</td>
<td>1.1 (0.9-1.3)</td>
<td>100</td>
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<tr>
<td>Polyurethane foam manufacture</td>
<td>1</td>
<td>SMR</td>
<td>N</td>
<td>2465</td>
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<td>PMR</td>
<td>N</td>
<td>946</td>
<td>NR</td>
<td>NR (NC)</td>
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<tr>
<td>Pulp and paper, sawmills</td>
<td>2</td>
<td>SMR</td>
<td>L</td>
<td>849</td>
<td>8</td>
<td>0.6 (0.3-1.3)</td>
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<td>Reindeer breeders</td>
<td>1</td>
<td>SMR</td>
<td>L</td>
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<td>0.4 (0.2-0.8)</td>
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<td>Rubber and affiliated industry</td>
<td>7</td>
<td>SMR</td>
<td>N</td>
<td>4200</td>
<td>56</td>
<td>0.8 (0.6-1.1)</td>
<td>100</td>
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<td>Semiconductor workers</td>
<td>2</td>
<td>SMR</td>
<td>N</td>
<td>3377</td>
<td>22</td>
<td>0.9 (0.6-1.4)</td>
<td>100</td>
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<tr>
<td>Shoe manufacturing</td>
<td>4</td>
<td>SMR</td>
<td>N</td>
<td>1649</td>
<td>5</td>
<td>0.4 (0.1-1.0)</td>
<td>90</td>
<td></td>
</tr>
<tr>
<td>Synthetic vitreous mineral fibre industry**</td>
<td>3</td>
<td>SMR</td>
<td>Y, L</td>
<td>4280</td>
<td>NR</td>
<td>NR (NC)</td>
<td>111</td>
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<tr>
<td>Telecommunications workers</td>
<td>2</td>
<td>SMR</td>
<td>N</td>
<td>267</td>
<td>7</td>
<td>0.6 (0.2-1.2)</td>
<td>83</td>
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<tr>
<td>Textiles and garments</td>
<td>6</td>
<td>SMR</td>
<td>N</td>
<td>923</td>
<td>6</td>
<td>0.5 (0.3-0.9)</td>
<td>114</td>
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<td>Waitresses and bartenders</td>
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<td>SMR</td>
<td>N</td>
<td>5314</td>
<td>83</td>
<td>0.8 (0.6-1.0)</td>
<td>100</td>
<td></td>
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<tr>
<td>x Ray technicians, radiation workers</td>
<td>8</td>
<td>SMR</td>
<td>C</td>
<td>594</td>
<td>NR</td>
<td>NR (NC)</td>
<td>133</td>
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</table>
| Table 3 shows the number of studies with at least one significant positive association for female breast cancer as well as the number of studies with the potential for investigating each occupational circumstance. This denominator was calculated from a baseline of 16 studies (four case-control studies and 12 other independent studies based on administrative data) and, for specific occupational cir-
cumstances, it was augmented from among other studies in which there was the possibility that these circumstances could have been investigated. These denominators should be considered to be approximate because information on the composition of the workforce, and consequently the types of occupational circumstances that could be investigated, were not usually described. In what follows, we will clarify some of the main points in table 4 and describe the more interesting results.

Clerical and professional

Associations with cancer incidence or mortality with clerical and professional jobs were reported primarily in studies based on administrative data. These studies were from widely different areas of the world, including Canada,17 24 33 35 China,17 Denmark,46 53 Finland,55 Holland,15 Italy,47 Japan,48 Russia,23 the United Kingdom,40 44 45 and the United States.22 27 29 46 The number of studies showing excess risks was rather striking for several occupational categories: white collar, professional and managerial occupations;17 27 28 29 33 34 43 49-51 clerical, secretarial, and related jobs;17 22 23 27 29 33 35 43 44 46 48 53-55 physicians and other health professionals;22 23 27 29 33 35 40 44 46 48 53 55 and clergy.22 25 27 29 46 49

In one case-control study,64 excess risks were found for clerical workers, for people employed in the insurance industry, but significant negative associations were also reported for people working in professional and related services, and managers and administrators. In seven cohort studies involving industrial populations,75 140 142 144 146 148 154 risks for a variety of administrative and secretarial or clerical occupations were not greater than expected. Also, a study of municipal workers57 did not show any associations for any job category, including clerks, professional, and technical.

In view of the fact that exposures to specific occupational agents cannot be identified easily in most of these occupational groups, one must inquire whether methodological weaknesses, such as uncontrolled confounding, in the administrative studies produced spurious results. In particular, the effect of confounding was examined in only one PMR study.32 35 Here it was found that PMRs for teachers and nurses were reduced when homemakers were removed from the control group (teachers: PMR 1.68 (P < 0.05) and 1.37 (P < 0.05); nurses: PMR 1.20 (P < 0.05) and 0.99,

Table 3 continued

<table>
<thead>
<tr>
<th>Chemical and other exposures:</th>
<th>Reports n</th>
<th>Study design</th>
<th>Exposure-response*</th>
<th>Women n</th>
<th>Cases n</th>
<th>Relative risk±95% CI</th>
<th>Statistical power(%)‡</th>
<th>Reference</th>
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<td>Asbestos</td>
<td>9 SMR</td>
<td>Y, D</td>
<td>922 NR NR NC NC</td>
<td>141,142</td>
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<td>Benzene</td>
<td>1 SMR</td>
<td>L</td>
<td>1005 4 0 9 (0-2-3)</td>
<td>55 119</td>
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<td>Nickel-cadmium</td>
<td>1 SMR</td>
<td>L</td>
<td>1401 NR NR NC</td>
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<td>Perfluorooctanoic acid</td>
<td>1 SMR</td>
<td>Y</td>
<td>749 3 0-5 (0-1-5)</td>
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<td>Polyvinylchloride</td>
<td>3 CRN</td>
<td>C-M</td>
<td>141 1-8 (P&lt;0-05)</td>
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<td>Silica</td>
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<td>N</td>
<td>1309 7 1-0 (0-6-4)</td>
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<td>Styrene</td>
<td>3 SMR</td>
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<td>Trichloroethylene</td>
<td>3 SMR</td>
<td>E</td>
<td>6128 9 0-5 (0-3-9)</td>
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<td>Vinyl chloride monomer</td>
<td>1 SMR</td>
<td>L</td>
<td>1037 0 0-0 (NC)</td>
<td>163</td>
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</table>
respectively), thus suggesting that some or all of the excess risk may be due to confounding by reproductive factors. Nevertheless, health professionals appear of considerable interest because they may be exposed to a wide variety of agents, including anaesthetic gases and organic solvents. In the one major longitudinal study of nurses, risks of breast cancer relative to the general population have not been reported. Lastly, a cohort study of scientists, laboratory technicians, and maintenance workers showed a significant increase in the risk of breast cancer (table 3). Exposures were diverse, including radiation, solvents, chemical mutagens, and viruses.

### Cosmetologists, hairdressers, and beauticians

Of the four cohort studies investigating cosmetologists, two studies showed increased risks of about 20% (table 3). The negative results may be due to low statistical power. In the case-control study of Koenig et al., a relative risk of 3.0 (95% CI 1.1-7.8) was found among beauticians employed for five or more years. Significantly increased relative risks were detected in three administrative studies: RR 1.6 (P < 0.05), RR 1.3 (P < 0.05), and RR 1.2 (95% CI 0.9-1.6). It is likely that cosmetologists have been exposed to several potentially toxic agents, such as organic dusts (hair), hair dyes, organic solvents (in nail products, settings, lotions, and hair sprays), and detergents. There is little information on the carcinogenicity of most of these substances, although some organic solvents are accepted animal and human carcinogens (benzene); hair dyes do not seem to be associated with a risk of breast cancer.

### Pharmaceutical industry

Positive associations were found in two cohort studies of pharmaceutical workers (table 3). There was a suggestion that incidence rates increased by duration of service among workers involved in the manufacture of insulin, sex hormones, and other pharmaceutical products. Confounding by reproductive factors may not be an important issue in this study, as current plant personnel and the general population were shown to have similar distributions of number of children, age of mother at first birth, age at menarche, and body mass index. However, a significantly higher frequency of oral contraceptive use, a weak risk factor for breast cancer, and a slightly higher use of non-contraceptive sex hormones were found among workers. No associations were found in the investigation of pharmacy technicians and in the case-control studies, and one study based on administrative data showed an excess risk among black women working in the pharmaceutical industry (RR 1.6, P < 0.05). The discrepant findings in the studies of pharmacy technicians and pharmaceutical manufactur-
ing workers are most simply explained by the fact that technicians are not likely to be exposed to the same extent as manufacturing workers.

Textiles and clothing
No associations were found in the two small cotton textile manufacturing cohort studies,126,127 among textile workers, dyers and bleachers,128 and among workers manufacturing synthetic fibres and textiles (mostly cellulose acetate)176 (table 3). There were no associations with formaldehyde exposure in the study of garment workers.129,130 In one case-control study, significant deficits were found among workers in the textile mill industry,69 and no associations were reported in the other case-control studies.61,62,64 Two studies based on regularly collected data showed excess risks,74,75 and significant deficits were found in four other studies.28,47-49

Radiation workers and x ray film technicians
Six cohort studies have been conducted among radiation workers, including diagnostic x ray film personnel,130 workers at a uranium fuel fabrication plant,131 a thorium processing plant,132 United Kingdom Atomic Energy Authority plants,134,135 the Sevillefield reprocessing plant,136 and the Hanford site in Washington state.137-140 (table 3). Exposures across the studies were quite varied, including whole body ionising radiation as well as exposure to radionuclides. Despite the fact that ionising radiation is a recognised risk factor for breast cancer,9 none of these studies showed any excess risks.

Potential exposure to extremely low frequency electromagnetic fields
In 1987, Stevens141 suggested that breast cancer may be caused by exposure to extremely low frequency electromagnetic fields. It was suggested that these fields would reduce pineal melatonin production, thereby allowing levels of oestrogen and prolactin to increase. Thus, extremely low frequency electromagnetic fields indirectly may affect hormonal secretions thereby increasing the risk of breast cancer. This hypothesis has stimulated much debate, but few epidemiological studies have been carried out among women. Four studies of male breast cancer175-178 have shown associations with employment in “electrical occupations”. The only reports on female breast cancer derive from six administrative studies42,70,71,73,74,99,124 of which four have shown associations with a variety of electrical occupations.42,70,71,73,74,99,124 (table 5)

Chemists and chemical workers
Higher than expected risks among chemists were found in MOR analyses of two cohorts,72,74 with considerably higher risks noted in single women (MOR 2·3, 95% CI 1·5-3·5).72 For chemical manufacturing workers, higher than expected incidence rates of breast cancer were found among Du Pont company workers77,78; there were higher risks among salaried workers (SMR 1·3) than among those paid on an hourly basis (SMR 0·9). No associations were found among Dow Chemical131 or Union Carbide workers.132 A difficulty in interpreting these studies is that workers were most likely exposed at various levels to a wide array of chemical agents. It is therefore unclear how to interpret the findings between salaried staff and hourly wage earners. One PIR study60 showed increased risks among black women working in the chemical industry (RR 1·4; P < 0·05), and no positive associations with general chemical occupations were reported in the case-control studies.

Other specific chemical exposures have been investigated (table 3), with negative results reported for women exposed to chlori-
nated naphthalenes in the cable manufacturing industry, "workers exposed to ethylene oxide, and rubber manufacturing workers. A positive association was found among women potentially exposed to diesel engine exhaust.

Potential exposure to organic solvents

We have hypothesised (Labrèche and Goldberg, submitted for publication) that exposure to organic solvents may be associated with an increased risk of breast cancer. The suggested mechanism is through migration of these lipophilic substances, and their metabolites, to adipose tissue in the breast where they can be stored, absorbed into the apocrine glands, possibly biotransformed, and then excreted into the ductal systems where they may remain in contact with the parenchyma for considerable amounts of time, thereby initiating or promoting carcinogenesis. There are experimental data that suggest that some organic solvents are carcinogenic in rats and mice (benzene, 1,2-dibromoethane, 1,1-dichloroethane, 1,2-dichloroethane, methylene chloride (benign tumours), styrene, 1,2,3-trichloropropane, and vinyl chloride).

Table 6 shows that the epidemiological data are rather sparse. Of interest are workers in laundry and dry cleaning establishments who have been exposed to several organic solvents. Stoddard solvent was used until the 1930s, after which carbon tetrachloride became the mainstay. Perchloroethylene slowly replaced the earlier solvents between the 1940s and the 1960s. Trichloroethylene and, more recently, fluorocarbons have been used. According to Brown and Kaplan, by 1977, 74% of the industry used perchloroethylene, 24% used petroleum based solvents, and about 2% used fluorocarbons. No increased risks of breast cancer were noted among workers exposed to perchloroethylene, or to a mixture of solvents, including Stoddard solvent, perchloroethylene, trichloroethylene, and fluorocarbons.

None of the case-control studies nor those studies based on administrative data showed any increased risks. The mortality study by Spirtas et al of aircraft maintenance workers exposed to trichloroethylene was consistent with the null results from the studies of dry cleaners. Excess risks were found, however, for exposure to freons, solder flux, and isopropyl alcohol. These substances were highly correlated and it was not possible to disentangle individual effects. Axelson and coworkers also investigated cancer incidence and mortality in workers
exposed to trichloroethylene. No risk estimates were provided for cancer of the breast, and one must assume that very few cases were found. Incidence of breast cancer was in excess among women employed in coiling and wire drawing\(^{46}\) in the manufacturing of lamps, in which methylene chloride and trichloroethylene were probably used.

Two cohort studies of female shoe manufacturers have been carried out.\(^{119,120}\) Exposures included organic solvents and solvent based adhesives; in the study by Paci et al\(^{119}\) benzene was originally an important component of glues used before the mid-1960s (up to 70% by weight) and may have been an impurity in the investigation by Walker and colleagues.\(^{120}\) Other solvents used typically were toluene, hexane, methyl ethyl ketone, and acetone in concentrations ranging from 10 ppm to 330 ppm.\(^{120}\) The small study by Paci et al\(^{119}\) showed no increased risks, and in the larger American study\(^{120}\) risk estimates were not reported for cancer of the breast.

Mikoczy and coworkers conducted a cohort study of leather tannery workers exposed to several compounds,\(^{14}\) including benzene and other chlorinated solvents, and found incidence rates to be between 30% and 50% above those expected. A case-control study in a small cohort of polyvinyl chloride workers showed a non-significantly increased risk of death from breast cancer (OR 1-8).\(^{161,162}\) No associations were found among workers exposed to styrene.\(^{166-168}\) Lastly, among the studies based on administrative records, there have been suggestions of increased risks for certain occupations that may involve exposures to solvents (printing, publishing, mechanics).\(^{24,49,46,50,55}\)

**Discussion and conclusions**

This review has summarised results from occupational investigations of female breast cancer carried out within the past 25 years. Our perspective on investigations based on routinely collected data is that they may convey spurious conclusions if used by themselves, although they can be used for generating hypotheses or providing additional information to that obtained from cohort and case-control studies. The reason for treating the administrative studies in this way is their inherent limitations,\(^{15,162,163}\) including: (1) misclassification of disease status leading to reductions in statistical power and attenuation of risk ratios. Mortality data are more susceptible to these types of problems than incidence data.\(^{184,187}\) Moreover, because of the relatively long survival rates for breast cancer, statistical power would be further reduced in mortality studies because of an underascertainment of cases. (2) Misclassification of exposure through the use of coarse occupational categories will also lead to a loss of statistical power and an attenuation of risk ratios.\(^{168}\) In the studies we reviewed, exposure was usually classified in terms of the last occupation (or industry) that the subject had had, or the occupation of the longest duration. This can also lead to bias, possibly away from the null, if workers changed occupations because of illness. Notable exceptions were the Chinese study by Zheng and coworkers,\(^{87}\) in which occupational histories were obtained directly from subjects (although denominators were based on census data), and the longitudinal studies from Canada,\(^{24}\) Italy,\(^{27}\) Denmark,\(^{46,55,56}\) Sweden,\(^{51,55,56}\) and Finland\(^{50}\) in which occupations from censuses or labour surveys\(^{51}\) were linked with subsequent cancer incidence or mortality data. (These were not considered as cohort studies in this report because person-years of observation by occupation at the time of enumeration were not calculable.) (3) Inability to account for key confounding factors may lead to incorrect inferences. Important risk factors for breast cancer were not accounted for in any of the investigations based on administrative data. That incorrect conclusions may be drawn from administrative studies is exemplified by the observation that although increased risks of developing breast cancer for clerical and white collar jobs were found in studies using administrative data, no associations were found in the cohort or case-control studies. It is possible that the studies of exposure to extremely low frequency electromagnetic fields, also based on routinely collected data, were biased.\(^{183}\) (4) No estimates of risk by duration of employment, latency, or other indices of exposure-response were presented, thus making it difficult to assess the veracity of the associations.

Thus, we relied whenever possible on information from cohort and case-control studies, that we considered to be more robust. Nevertheless, because few studies were designed specifically to investigate risks of breast cancer, the limitations inherent in these studies must be recognised when interpreting the data. In particular, statistical power and risk estimates would have been reduced in mortality studies in which broad occupational groups were used as surrogates for exposure. As well, statistical power was generally quite low for assessing trends or for assessing risks in subgroups.

Also, confounding by reproductive factors may have affected some of the cohort studies. For example, in the studies of chemists and chemical workers higher risks were found among clerical workers\(^{79}\) and among salaried workers\(^{75-77}\) than among hourly paid workers. On the other hand, no great differences for a variety of risk factors were found between workers and the general population in the one cohort study in which confounding was assessed indirectly.\(^{102}\)

It has been suggested that removing homemakers from reference populations will partly control for the confounding influence of reproductive and related factors.\(^{32,55}\) ‘This has been applied to studies based on administrative data, but could also be implemented in case-control studies in which confounding variables are not measured. In the analyses of cohort studies that used mortality rates derived from the general population as the reference, homemakers can also be eliminated if occupational
information has been captured on death certificates.

One would expect in cohort studies that misclassification of exposure would be less pronounced than in studies with routinely collected data because job titles from plants should be more homogeneous for exposure. Nevertheless, exposures were ascertained in but a handful of studies. In the case-control studies, although detailed information on occupational lifetime histories was obtained directly from subjects, broad occupational groupings were reported in the analyses, with main lifetime occupation used in two studies,61 62 ever employed or employed for more than five years used in another study,43 and duration of employment reported in one study.44 In this last study,44 important confounding variables for risk of breast cancer were accounted for.

Selection into and out of work among subjects enrolled in cohort studies (the healthy worker effect165) may also have led to underestimation of risks. It is difficult to control for these effects, although partial control of selection into and out of occupational exposures can be achieved through the use of internal control groups. However, no studies reported such analyses for breast cancer, although they were carried out for other endpoints in several studies.131-133-136-139-153-156-157-158

Bearing in mind these limitations, we conclude that there is little support for an association between female breast cancer and employment in the textile and garment industries. The studies of cosmetologists and beauticians and of pharmaceutical manufacturing workers can be regarded as providing limited evidence in favour of an association, but further studies are required before conclusions can be drawn. Although nuclear workers are exposed to ionising radiation, a recognised risk factor for breast cancer, no associations were found. In the absence of bias, it is likely that either the length of follow up or the doses incurred were not sufficiently high to induce any observable excess risks.

There are insufficient data to make any inferences about women employed as chemists or exposed occupationally to extremely low frequency electromagnetic fields. Because of the apparent heterogeneity of exposures among workers included in the cohort studies at the large chemical companies,73-75-77 it is difficult to draw any conclusions from these studies. However, the few studies carried out on specific occupational agents have not provided any evidence of associations. In particular, although we have postulated that exposure to organic solvents may increase the risk of developing breast cancer, with some evidence provided from animal carcinogenicity studies, increased risks have not been found among dry cleaning workers, those exposed to trichloroethylene, or shoe manufacturers. Studies of organic solvents may, however, be beset with health related differential selection into and out of work arising from pervasive early onset toxic effects (dermatitis, hepatic and renal toxicity, central nervous system depression, peripheral neuropathy).190 Thus, there will be a selection bias if susceptible or sensitive workers are at higher risk of developing breast cancer and are more likely to leave exposed jobs early so they are less highly exposed than insensitive people. In any event, as few organic solvents have been studied adequately, including the agents already mentioned, no conclusions on the relation between occupational exposure and risk of female breast cancer can be made.

It is clear from this review that few high quality studies directed specifically toward assessing occupational risks of breast cancer have been carried out to allow one to identify unambiguously occupational risk factors for breast cancer. The fact that the cohorts of women were generally small is understandable, as few women would have been in the workforce during the period covered by many of these retrospective studies. It is now feasible to carry out more detailed investigations. Juxtaposing job exposure matrices to already completed cohort or case-control studies190 will provide a cost effective method to study population based, case-control studies, with approaches similar to those developed by Siemiatycki et al, Gérin et al, and Stewart et al,182 192-194 although more expensive, should provide high quality data to investigate occupational risk factors. In fact, we are now carrying out such an investigation in Montreal. Cohort studies of specific industrial populations can then be carried out to follow up promising leads from the case-control studies.


Occupational risk factors for female breast cancer


Occupational risk factors for female breast cancer: a review.

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