Population attributable risk of modifiable risk factors associated with invasive breast cancer in women aged 45–69 years in Queensland, Australia

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ABSTRACT

Objectives: To quantify the population attributable risk of key modifiable risk factors associated with breast cancer incidence in Queensland, Australia.

Study design: Population attributable fractions (PAFs) for high body mass index (BMI), use of hormone replacement therapy (HRT), alcohol consumption and inadequate physical activity were calculated, using prevalence data from a representative survey of women attending mammographic screening at BreastScreen Queensland in 2008 and relative risk estimates sourced from published literature. Attributable cancers were calculated using ‘underlying’ breast cancer incidence data for 2008 based on Poisson regression models, adjusting for the inflation of incidence due to the effects of mammographic screening.

Main outcome measures: Attributable burden of breast cancer due to high body mass index (BMI), use of hormone replacement therapy (HRT), alcohol consumption and inadequate physical activity.

Results: In Queensland women aged 45–69 years, an estimated 12.1% (95% CI: 11.6–12.5%) of invasive breast cancers were attributable to high BMI in post-menopausal women who have never used HRT; 2.8% (95% CI: 2.7–2.9%) to alcohol consumption; 7.6% (95% CI: 7.4–7.9%) to inadequate physical activity in post-menopausal women and 6.2% (95% CI: 5.5–7.0%) to current use of HRT after stratification by BMI and type of HRT used. Combined, just over one quarter (26.0%; 95% CI: 25.4–26.6%) of all invasive breast cancers in Queensland women aged 45–69 years in 2008 were attributable to these modifiable risk factors.

Conclusions: There is benefit in targeting prevention strategies to modify lifestyle behaviours around BMI, physical activity, HRT use and alcohol consumption, as a reduction in these risk factors could decrease invasive breast cancer incidence in the Queensland population.

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1. Introduction

Trends in breast cancer incidence may be affected by the introduction of population-based mammography screening [1–3], changing demographics (i.e. ageing) in a population [1,4], and changing trends in risk factors (e.g. increasing obesity prevalence [1,4]), and changing patterns of hormone therapy use [1,3,4]).

At the population level, the impact of a risk factor depends upon both the strength of association of that factor with the disease as well as the prevalence of the risk factor in the population of interest. The population attributable fraction (PAF) measures the amount of disease attributable to a risk factor in a particular population by calculating the proportion of cancer cases that may be prevented if the risk factor could be removed from the population; on the assumption that the risk factor is causal to the disease, measurement of the risk association and prevalence of the risk factor are unbiased and the elimination of the risk factor will have no effect on the distribution of other risk factors [5].

Some of the strongest risk factors for breast cancer include age, family history, reproductive factors, previous breast disease and breast density [6–8]. These risk factors, while strong in terms of the magnitude of the effect size, are not amenable to
modification through behaviour change. However, modifiable lifestyle and environmental factors also play a role in breast cancer risk [6]. These factors may be associated with smaller effect sizes, but they can be more prevalent in the population. The World Cancer Research Fund (WCRF) has concluded that there is causal evidence of a positive association between body mass index (BMI) and breast cancer in post-menopausal women, and between alcohol and breast cancer in both pre- and post-menopausal women [9]; as well as a protective effect for physical activity against breast cancer in post-menopausal women [9]. The International Agency for Research on Cancer (IARC) has concluded that there is evidence that combined oestrogen + progesterone and oestrogen-only hormone replacement therapy (HRT), prescribed to women who have had natural or surgical menopause, causes breast cancer [10]. These four risk factors have been selected for this study on the basis of this evidence; in addition, prevalence can be influenced through suitable prevention and education strategies that impact on the lifestyle and behaviour of individuals, even at a later stage in life.

The attributable risk of sets of modifiable risk factors and breast cancer have been calculated for Canada [11], Germany [12], Italy [13], the United States [14,15], the United Kingdom [16] and globally [17]. While it is useful to compare international results with those in an Australian context, there will likely be national differences in the prevalence of these risk factors, limiting generalisability, and the specificity of policy and prevention approaches in the local context. Two studies undertaken in Australia have investigated attributable risk of breast cancer, however, both have focussed on only a single risk factor (use of hormone replacement therapy [18] and family history [19]). To our knowledge, there have been no published analyses that have explored the attributable risk of a set of key modifiable risk factors known to be associated with breast cancer in the Australian context.

The aim of this study was to quantify the proportion of breast cancers in Queensland that could be attributed to key modifiable lifestyle risk factors of higher BMI, use of hormone replacement therapy, alcohol consumption and inadequate physical activity.

2. Methods

2.1. Estimates of relative risks

Relative risks used to calculate the PAF for each of the selected modifiable risk factors were sourced from published meta-analyses or large prospective cohort studies. All of the studies had to be consistent with the conclusions of the WCRF [9] or IARC [10] regarding the respective risk factor and breast cancer, have relative risks with multiple exposure categories (not just high vs low) that could be replicated in the prevalence data, and adjust for the known confounders for breast cancer (age, reproductive history, age at first birth and hormone use [9]). Table 1 details the sources [20–23] and relative risks used for each exposure.

2.2. Prevalence data

Risk factor prevalence was estimated using results from a cross-sectional prevalence survey of 9792 women attending BreastScreen Queensland Screening and Assessment Services between November 2008 and February 2009 (BreastScreen Queensland survey). Details of recruitment and study variables have been described elsewhere [24]. Briefly, the BreastScreen Queensland survey was conducted between November 2008 and February 2009 through inclusion of a self-report questionnaire with appointment confirmation letters for mammography screening. Of the 17,000 questionnaires distributed, 11,537 completed questionnaires were returned via the 74 BreastScreen service locations throughout Queensland (68% response rate). Women aged under 45 years (9.5%) and women who returned questionnaires that could not be linked to the BreastScreen Queensland Registry (5.6%) were excluded, leaving a total of 9792 responses for this analysis (58% of the number of questionnaires initially distributed) [24].

Information was collected on a wide range of variables including reproductive factors, modifiable behavioural factors, HRT use and alternatives, demographic factors, past and current co-morbidities and personal and familial family history of breast cancer [24]. This range ensured that the stratifications reported in the literature for selected risk factors could be replicated from this survey dataset. Only those with known exposure were included in the prevalence estimates.

Body mass index (BMI) was calculated as a continuous variable from self-reported responses to questions on height and weight (BMI = weight in kg/(height in metres)²). This continuous variable was then categorised into five levels, reflecting the relative risk categories used by Reeves [20]: <22.5 kg/m²; 22.5–24.9 kg/m² (reference category); 25–27.4 kg/m²; 27.5–29.9 kg/m²; ≥30 kg/m². The variable was then stratified by menopausal status and whether or not women were ‘never users’ or ‘ever users’ of HRT. Prevalence of BMI in post-menopausal women who never used HRT were used for the PAF.

Alcohol consumption was measured by self-report of the number of glasses of wine (250 ml), beer (250 ml) and spirits (30 ml) consumed on average each week. From this information the average alcohol consumption of grams per day (10 g alcohol per glass) was calculated as a continuous variable. The continuous variable was then categorised to reflect the relative risks associated with levels of alcohol reported by the Collaborative Group on Hormonal Factors in Breast Cancer [21]: 0 g/day (reference category), 5 g/day, 5–14 g/day, 15–24 g/day, 25–34 g/day, 35–44 g/day and ≥45 g/day.

Physical activity questions were based on items included in the Active Australia Survey [24]. Self-reported responses were given to questions that asked for an estimate of how many minutes and hours per week were spent walking, engaged in moderate activity (e.g. gentle swimming, social tennis, golf) and vigorous activity (jogging, cycling, aerobics, competitive tennis). Metabolic equivalent (MET) values for walking, moderate activity and vigorous activity of 3.3, 4.0 and 8.0 were assigned respectively in accordance with the levels recommended by the International Physical Activity Questionnaire, which asks similar questions to the Active Australia Survey [25]. A total physical activity variable (continuous) was calculated by multiplying the MET level for the activity by the hours exercised per week and totalling the values across the three activity levels. This continuous variable was then categorised to reflect the relative risk categories used by Eliassen [22]: <3 MET hours/week, 3 to <9 MET hours/week, 9 to <18 MET hours/week, 18 to <27 MET hours/week, and ≥27 MET hours/week (reference category; equivalent to 1 h of brisk walking per day). This variable was then stratified by whether women were premenopausal or post-menopausal. The prevalence data on post-menopausal women were used for the PAF calculation.

To assess hormone replacement therapy (HRT) use, women were asked “have you ever used HRT”; and if they had, how many years in total they had used HRT, if they were currently using HRT and the type of HRT they had most recently used. Type of HRT was categorised into “oestrogen only”, “oestrogen + progesterone”, “Tibolone”, “Other” and “Don’t Know”. For the PAF analysis, HRT use was categorised into current users and never/past users (reference category). Current users were stratified into the categories of type of HRT used (oestrogen only, oestrogen + progesterone, Tibolone) and BMI category (<25 kg/m² and ≥25 kg/m²) as reported by the Million Women Study [23].
Table 1
Relative risk, exposure prevalence, PAF and estimated cases of invasive breast cancer due to exposure in Queensland women aged 45–69 years in 2008.

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Relative risk (95% CI)</th>
<th>Exposure prevalence % (95% CI)</th>
<th>PAF (95% CI)</th>
<th>N cases due to exposure (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Body mass index</strong> (measured at recruitment)**</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reeves et al. [20]: Million Women Study. Prospective cohort study of 1.2 million UK women aged 50–64 years; 5629 breast cancer cases</td>
<td>In post-menopausal women who have never used HRT: &lt;22.5 kg/m²</td>
<td>0.85 (0.80–0.91)</td>
<td>1.00 (reference)</td>
<td>17.6 (16.4–18.9)</td>
</tr>
<tr>
<td></td>
<td>22.5–24.9 kg/m²</td>
<td>1.10 (1.04–1.16)</td>
<td></td>
<td>17.6 (16.4–18.9)</td>
</tr>
<tr>
<td></td>
<td>25–27.4 kg/m²</td>
<td>1.21 (1.13–1.29)</td>
<td></td>
<td>13.5 (12.3–14.7)</td>
</tr>
<tr>
<td></td>
<td>≥30 kg/m²</td>
<td>1.29 (1.22–1.36)</td>
<td></td>
<td>28.4 (26.9–29.9)</td>
</tr>
<tr>
<td><strong>Alcohol consumption</strong> (current drinking habits at recruitment in each study)**</td>
<td>Pre- and post-menopausal women combined: 0 g/day</td>
<td>1.00 (reference)</td>
<td>1.00 (reference)</td>
<td>1.00 (reference)</td>
</tr>
<tr>
<td>Collaborative Group [21]: Meta-analysis of 53 studies including 58,515 women with breast cancer and 95,067 women without, that examined associations between alcohol and tobacco with breast cancer</td>
<td>&lt;5 g/day</td>
<td>1.01 (0.98–1.04)</td>
<td>32.3 (31.3–33.3)</td>
<td>0.3 (0.3–0.3)</td>
</tr>
<tr>
<td></td>
<td>5–14 g/day</td>
<td>1.03 (1.00–1.06)</td>
<td>26.8 (25.8–27.7)</td>
<td>0.8 (0.7–0.8)</td>
</tr>
<tr>
<td></td>
<td>15–24 g/day</td>
<td>1.13 (1.08–1.18)</td>
<td>6.4 (5.9–6.8)</td>
<td>0.8 (0.7–0.9)</td>
</tr>
<tr>
<td></td>
<td>25–34 g/day</td>
<td>1.21 (1.14–1.28)</td>
<td>3.6 (3.2–4.0)</td>
<td>0.8 (0.7–0.8)</td>
</tr>
<tr>
<td></td>
<td>≥45 g/day</td>
<td>1.46 (1.34–1.58)</td>
<td>0.1 (0.03–0.2)</td>
<td>0.04 (0.01–0.07)</td>
</tr>
<tr>
<td><strong>Physical activity</strong> (current activity at most recent survey – 2004)**</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eliassen [22]: Nurses’ Health Study. Prospective cohort study with a study population of 95,396 post-menopausal women; 4782 breast cancer cases</td>
<td>In post-menopausal women only: &gt;27 MET hours/week</td>
<td>1.00 (reference)</td>
<td>13.4 (12.6–14.3)</td>
<td>0.3 (0.2–0.3)</td>
</tr>
<tr>
<td></td>
<td>18 to &lt;27 MET hours/week</td>
<td>1.02 (0.94–1.11)</td>
<td>19.8 (18.9–20.9)</td>
<td>1.8 (1.7–1.8)</td>
</tr>
<tr>
<td></td>
<td>9 to &lt;18 MET hours/week</td>
<td>1.09 (0.99–1.18)</td>
<td>21.3 (20.3–22.4)</td>
<td>2.9 (2.8–3.0)</td>
</tr>
<tr>
<td></td>
<td>3 to &lt;9 MET hours/week</td>
<td>1.14 (1.03–1.25)</td>
<td>15.6 (14.7–16.6)</td>
<td>2.7 (2.6–2.9)</td>
</tr>
<tr>
<td></td>
<td>&lt;3 MET hours/week</td>
<td>1.18 (1.08–1.28)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Hormone replacement therapy</strong> (current users)**</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beral [23]: Million Women Study. Prospective cohort study of 1.2 million women aged 50–64 years; 9364 breast cancer cases</td>
<td>All women Current HRT users with BMI &lt;25 kg/m²: Never users</td>
<td>1.00 (reference)</td>
<td>1.00 (reference)</td>
<td>3.8 (3.3–4.4)</td>
</tr>
<tr>
<td></td>
<td>Oestrogen only</td>
<td>1.52 (1.36–1.71)</td>
<td>1.3 (1.0–1.6)</td>
<td>1.7 (1.3–2.1)</td>
</tr>
<tr>
<td></td>
<td>Oestrogen + progesterone</td>
<td>2.31 (2.12–2.53)</td>
<td>1.1 (0.8–1.4)</td>
<td>0.5 (0.4–0.6)</td>
</tr>
<tr>
<td></td>
<td>Tibolone</td>
<td>1.45 (1.25–1.67)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Current HRT users with BMI ≥ 25 kg/m²: Never users</td>
<td>1.00 (reference)</td>
<td>1.00 (reference)</td>
<td>5.0 (4.4–5.6)</td>
</tr>
<tr>
<td></td>
<td>Oestrogen only</td>
<td>1.17 (1.05–1.29)</td>
<td>1.2 (0.9–1.5)</td>
<td>0.3 (0.7–1.2)</td>
</tr>
<tr>
<td></td>
<td>Oestrogen + progesterone</td>
<td>1.78 (1.64–1.94)</td>
<td>0.9 (0.6–1.2)</td>
<td>0.4 (0.3–0.5)</td>
</tr>
<tr>
<td></td>
<td>Tibolone</td>
<td>1.45 (1.25–1.67)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

a Exposure prevalence from BreastScreen BreastScreen survey (2008), 95% CIs: Binomial (Fisher’s exact).
b Calculated from expected incidence of invasive breast cancer in women aged 45–69 years (and 50–64 years for HRT use) in Queensland in 2008.
2.3. Breast cancer incidence data

Breast cancer incidence data were obtained from the Queensland Cancer Registry. Initial and subsequent screening data were obtained from BreastScreen Queensland. Population denominator data were sourced from the Australian Bureau of Statistics and Office of Economic and Statistical Research (OESR) [26–29]. Breast cancer incidence data were adjusted to allow for the effect of mammographic screening using an age-cohort Poisson regression model with adjustments for initial and subsequent screens. Population-based mammography screening was introduced into Queensland in 1991, and achieved full geographic coverage by 1997. The introduction of screening leads to an inflation in incidence as cancers that would normally have been diagnosed at a later time are brought forward through detection by screening [1–3]. This incidence inflation may persist [2,3], which is evident in Queensland, particularly for the target screening group of 50–69 years [1]. Adjustment of incidence for the screening effect provides more realistic (or ‘underlying’) estimates of breast cancer incidence and has been used elsewhere [16,18,19,30,31] (Table 2).

### Table 2
Observed and expected incidence rate (per 10,000) and counts (95% CI) for invasive breast cancer in Queensland women by 5-year age group (45–69 years) in 2008 – age-cohort models.

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Observeda rate/10,000</th>
<th>n.</th>
<th>Age-cohort model adjusted for initial and subsequent screens</th>
</tr>
</thead>
<tbody>
<tr>
<td>45–49</td>
<td>19.33</td>
<td>303</td>
<td>17.97</td>
</tr>
<tr>
<td>50–54</td>
<td>25.81</td>
<td>363</td>
<td>21.52</td>
</tr>
<tr>
<td>55–59</td>
<td>27.46</td>
<td>353</td>
<td>25.79</td>
</tr>
<tr>
<td>60–64</td>
<td>34.96</td>
<td>382</td>
<td>31.80</td>
</tr>
<tr>
<td>65–69</td>
<td>39.03</td>
<td>319</td>
<td>36.91</td>
</tr>
</tbody>
</table>

a Observed – actual number of breast cancers (rate per 10,000).
b Expected – estimated number of breast cancers (rate per 10,000 and number of cases – with 95% CI).

2.4. Statistical analysis

The population attributable fraction (PAF) describes the proportion of disease among the population that could theoretically be prevented if the exposure were removed from the population. Information on risk factor prevalence and relative risk (RR) were used to estimate the PAF using the following formula:

\[
PAF = \frac{\sum p(RR - 1)}{(1 + \sum p(RR - 1))}
\]

where \( p \) is the prevalence of the risk factor (from data in the BreastScreen Queensland survey) and RR is the relative risk taken from the published literature. For physical activity 1/RR is used. The referent exposure levels used in this study were a BMI of <25 kg/m², no alcohol consumption, no HRT use and to be physically active for the equivalence of at least 1 h of brisk walking per day.

A joint PAF across all risk factors was also calculated using the formula [32]:

\[
PAF(\text{combined}) = 1 - \prod_{r=1}^{R} (1 - PAF_r)
\]

where \( r \) is each individual risk factor. The underlying assumptions that risk factors are independent and uncorrelated has been mitigated through the use of relative risks that have been adjusted for potential confounders and/or stratified by mediating variables (e.g. BMI and HRT).

Monte-Carlo simulation models using Ersatz Software 1.31 [33] were used to estimate the 95% confidence intervals for PAF% estimates, to account for the uncertainty around the prevalence and relative risk estimates included in the present study. These simulation models allowed the multiple re-calculation of estimates taken from randomly drawn values from the distributions defined for each input parameter. A beta probability distribution was used for prevalence estimates (based on cases and non-cases) using the ErBeta function, and a normal distribution was used for relative risk estimates (based on a normal distribution for the natural logarithm of the RR) using the ErRelativeRisk function, to estimate 95% confidence intervals for PAF% estimates after 2000 iterations to ensure convergence of model outcomes.

To obtain the number of invasive breast cancer cases attributable to each risk factor, the PAF was multiplied by the estimated underlying incidence of invasive breast cancer cases (derived using an age-cohort Poisson regression model) in 2008 – the period corresponding to the BreastScreen Queensland survey.

3. Results

Of the 1574 estimated underlying invasive breast cancers for women aged 45–69 years in 2008, 12.1% (95% CI: 11.6–12.5%) were attributable to a BMI of over 25 kg/m² in post-menopausal women who had never used HRT (191 cases) (Table 1). For alcohol consumption, only 4.0% of the study population engaged in risky (2–4 standard drinks per day) or high risk (more than 4 standard drinks per day) alcohol consumption resulting in 2.8% (95% CI: 2.7–2.9%) of all estimated underlying breast cancers being attributable to alcohol consumption for women aged 45–69 years in 2008 (46 cases) (Table 1). Inadequate physical activity was attributable to 7.6% (95% CI: 7.4–7.9%) of all estimated underlying invasive breast cancers in post-menopausal women (45–69 years) in 2008 (121 cases) (Table 1). For HRT use in women aged 50–64 years, 6.2% (95% CI: 5.5–7.0%) of all estimated underlying invasive breast cancers were attributable to current use of HRT after stratification by BMI and HRT type (62 cases) (Table 1). Of the estimated 62 cancers, 66.1% (41 cases) were attributed to lean women with a BMI <25 kg/m² who currently used oestrogen only, oestrogen + progesterone or Tibolone.

Combined, just over one quarter (26.0%; 95% CI: 25.4–26.6%) of all invasive breast cancers in Queensland women aged 45–69 years in 2008 were attributable to the modifiable risk factors of high BMI, inadequate physical activity, HRT use and alcohol consumption. The largest PAF was for high BMI, followed by physical activity and current HRT use (Table 3).

4. Discussion

This study quantified the theoretical reduction in invasive breast cancer in women aged 45–69 years in Queensland (Australia) associated with the reduction of exposure to the key modifiable risk factors of body mass index, alcohol consumption, physical activity and hormone replacement therapy. Findings suggest that the
joint population attributable fraction for these risk factors is 26.0% (95% CI: 25.4–26.6) with high BMI associated with the largest attributable fraction, followed by inadequate physical activity, and HRT use.

A number of international studies have used similar PAF methodologies [11,14,16,17]. The results of this study fall in between those of two studies that have calculated PAFs for the same risk factors for the United Kingdom [16,17] (Table 4). The variability across results demonstrates the impact of differences in the prevalence of the risk factors between populations, the selection of relative risk estimates and exposure categories (Parkin [16] used dose–response relative risks while the WCRF used low vs high risk categories [17]), and the age groups used (i.e. all adult women in the UK studies vs women 45–69 years in this study).

This study has a number of strengths and weaknesses. A key strength is that the prevalence data used, from the unit-record cross-sectional survey of women attending BreastScreen Queensland [24], could be manipulated to directly correspond with the exposure categories for the reported relative risk estimates in the literature, restricted to post-menopausal women for BMI, physical activity and HRT, stratified by interacting variables where applicable, and could be related to a population of women at highest risk of breast cancer (45–69 years).

The impact of changing behaviours in mid-life on cancer outcomes is not clear. While there is evidence that an increase in physical activity in the menopause transition can decrease risk of breast cancer [22], and the risk of breast cancer is restricted to current and recent use of HRT [23], there is less certainty around the impact of reducing BMI and alcohol consumption in later life.

Selection and recall bias are potential limitations of the prevalence data. The 68% response rate (of the women sent the questionnaire) may introduce selection bias due to the characteristics of non-response and refusals; however, the response rate for this study is consistent with previous prevalence studies of women attending mammography screening in Australia (71%) [35] and Spain (74%) [36], and is higher than for the UK Million Women Study, which used a comparable recruitment method to ascertain breast cancer risk factors in women of a similar age (53% response from women sent the questionnaire) [37]. The BreastScreen Queensland survey was completed only by women who attended appointments for mammographic screening, and previous studies have shown that women who attend for mammography screening have different characteristics to women that do not attend [35,36]. Respondents in the BreastScreen Queensland survey were more likely to be of a higher socio-economic status (using tertiary education as a proxy indicator) than the general Queensland female population [24], and so risk factors associated with lower socio-economic status (e.g. higher BMI and inadequate physical activity) may be less in the survey (underestimating the PAF), and those associated with a higher socio-economic status (e.g. HRT use) larger (over-estimating the PAF). Attempts were made to reduce recall bias in the survey through the use of previously validated questions from the National Health Survey 2007–2008 (NHS 2007–08) (BMI), Active Australia Survey (physical activity) and the Australian Longitudinal Study on Women’s Health (ALSWH) (HRT use) [24].

Prevalence is similar to other population-based representative studies of Australian women such as the NHS 2007–08 [39] and ALSWH [40] for BMI distributions (60% vs 64% NHS), and HRT use (14% vs 17% ALSWH), and for other co-morbidities such as diabetes (7% vs 7% ALSWH), asthma (11% vs 10% ALSWH), osteoarthritis (13% vs 16% NHS), osteoporosis (8% vs 6% ALSWH), high blood pressure (30% vs 27% ALSWH), and heart disease (4% vs 4% ALSWH) [24,39,40], indicating that the higher socio-economic status of respondents has not biased the results for these risk factors.

Alcohol consumption prevalence in the BreastScreen Queensland survey was lower to that reported in the NHS 2007–08 where the combined prevalence of “risky” and “high risk” drinking (2–4 standard drinks/day and >4 standard drinks/day respectively), for women aged 45–64 years, was 13.6% [39]; compared to 4.0% in the BreastScreen Queensland survey. Differences in how the questions were framed in each survey may explain this. The NHS 2007–08 asked participants to report on their alcohol consumption in the past week; while the BreastScreen Queensland survey asked respondents how many standard drinks they consumed on average each week. If the true prevalence of alcohol consumption of Queensland women, aged 45–69 years, is closer to that reported in the NHS 2007–08 rather than the BreastScreen Queensland survey, the attributable burden of alcohol consumption is likely to have been under-estimated (by around 2%) in this study.

An additional methodological consideration relates to estimates of the ‘underlying’ incidence of invasive breast cancers in 2008 in Queensland. Breast cancer incidence was estimated using an age-cohort Poisson regression model, adjusted for the effects of initial and subsequent screening. The ‘identification problem’ that arises in age-period-cohort (APC) models due to the dependent nature of the relationship between these variables [41] was minimised with the use of the age-cohort model. Initial and subsequent screens, specified as continuous variables, served as proxies for the period effect, with the period variable being omitted from the model. A similar approach of using proxy measures for the period effect has been used in other studies including the examination of birth cohort effects in suicide in New South Wales [41], suicide mortality in England and Wales [42], and breast cancer incidence in Norway [3].

The estimated number of attributable cancers have been calculated using 2008 underlying incidence and 2008 prevalence data. This does not take into account the latency period between exposure and cancer incidence. However, as latency periods are known to vary between risk factors and, in this study, would have required the use of cancer incidence projections which bring with them a range of assumptions about trends in risk factor prevalence and cancer treatment and diagnosis, this is considered a reasonable

### Table 3

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>PAF% (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI</td>
<td>12.1 (11.6–12.5)</td>
</tr>
<tr>
<td>Physical activity</td>
<td>7.6 (7.4–7.9)</td>
</tr>
<tr>
<td>HRT</td>
<td>6.2 (5.5–7.0)</td>
</tr>
<tr>
<td>Alcohol</td>
<td>2.8 (2.7–2.9)</td>
</tr>
</tbody>
</table>

Joint PAF combinations (in descending order)

<table>
<thead>
<tr>
<th>PAF% (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI + Physical activity + HRT + Alcohol</td>
</tr>
<tr>
<td>BMI + Physical activity + HRT</td>
</tr>
<tr>
<td>BMI + Physical activity + Alcohol</td>
</tr>
<tr>
<td>BMI + HRT + Alcohol</td>
</tr>
<tr>
<td>Physical activity + HRT + Alcohol</td>
</tr>
</tbody>
</table>

### Table 4

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Population attributable fraction %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Queensland estimate</td>
</tr>
<tr>
<td>Body mass index</td>
<td>12.1</td>
</tr>
<tr>
<td>Physical activity</td>
<td>7.6</td>
</tr>
<tr>
<td>Hormone replacement therapy</td>
<td>6.2</td>
</tr>
<tr>
<td>Alcohol</td>
<td>2.8</td>
</tr>
</tbody>
</table>

* Not evaluated in study.
approach and is consistent with that of other studies including the WCRF [17] and Global Burden of Disease Study 2010 [34].

The PAF can be useful in the public health context as it can estimate the level of preventable disease. However, as outlined by Benichou [5], three conditions underpin the PAF. First, the PAF for an individual risk factor assumes that all other risk factors have been held constant, i.e., the elimination of the PAF risk factor has no effect on the distribution of other risk factors. For a range of chronic diseases and cancers, this condition is unlikely to hold true. In this present study the stratification of some of the risk factors by other risk factors (for example BMI by HRT) may have mitigated the contravention of this condition to some extent. Second, the estimate of the PAF has to be unbiased. Potential bias in the prevalence data used in the present study is discussed above. The relative risks used in the PAF calculations were sourced from published cohort studies and meta-analyses which adjusted for a range of confounders; however, a level of uncontrolled confounding and bias is likely to remain which may result in an over-estimate of the PAF. Third, the PAF exposure factor is causal rather than merely associated with the disease. In the present study, one reason for selecting the four risk factors was the strength of evidence (both epidemiologic and biological), and level of consensus, relating to the likely causal association between the given exposure and outcome.

This study has focussed on potentially modifiable lifestyle risk factors that have been positively associated with the risk of invasive breast cancer. While the estimated attributable burden of each of these risk factors was relatively modest (with the exception of overweight/obesity with a PAF of 12.1%), the joint PAF of these four risk factors, in theory, accounted for over a quarter of the attributable burden of invasive breast cancer in women aged 45–69 years in Queensland. There is benefit in targeting prevention strategies to modify lifestyle behaviours around BMI, physical activity, HRT use and alcohol consumption as a reduction in these risk factors could decrease invasive breast cancer incidence in the Queensland population.

Ethical approval

Approval for this study was sought and obtained from the BreastScreen Queensland Monitoring, Evaluation and Research Subcommittee (MERS).

Contributors

Louise Wilson and Andrew Page contributed to the acquisition of the study data, analysis and interpretation of the data, drafting of the manuscript and critical revision of the manuscript. Nathan Dunn contributed to the acquisition of the study data, analysis and interpretation of the data and critical revision of the manuscript. Melinda Protani, Nirmala Pandeya and Richard Taylor contributed to critical revision of the manuscript. The final version of the manuscript was approved by all authors.

Competing interest

The authors declare that they have no conflict of interest.

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