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# Multiple primary cancers of separate organ sites: implications for research and cancer control (Australia)

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## Abstract

*Objective*: To identify cancers which occur as second primaries following the diagnosis of cancers of other sites, as a basis for formulating causal hypotheses and planning medical surveillance.
*Methods*: Analyses of fifteen common cancer sites were undertaken to examine the occurrence of multiple primaries. These cancers were notified to the South Australian Cancer Registry during 1977–2001. Historic cohort models were used where standardised incidence ratios (95% confidence limits) were calculated to indicate the risk of second primary cancers.
*Results*: New associations detected included an increased risk of cancers of the bladder, colon, rectum, kidney and melanomas following a diagnosis of prostate cancer and an increased risk of leukaemia following both lung and rectal cancer. Many previously identified combinations of multiple primaries were confirmed.
*Conclusions*: From the wide range of associations identified, some such as leukaemias occurring as second primaries after the diagnosis of ovarian cancers and lymphomas may be a treatment effect. The diagnosis of multiple primary cancers in the same month (e.g. bladder–prostate cancers and ovarian–uterine cancers) may reflect patterns of medical testing and the long preclinical phases of some cancers.

## Introduction

Multiple primary cancers are defined by the International Association of Cancer Registries as the occurrence of two or more primary cancers, where each cancer originates in a separate primary site and is neither an extension, recurrence or metastasis [1]. Up to 10% of cancer patients have been reported to acquire multiple primary cancers of separate organ sites in the ten years following the diagnosis of their first cancer [2]. This susceptibility has long been recognised from North American and European studies [3–12], although limited data have been presented for Australia.

Sometimes host susceptibility is cited as the cause of these multiple primaries, with BRAC1 and BRAC2 genetic mutation related breast and ovarian cancers being one example [13]. Infection and immunodeficiency also have been implicated, as in the association between Kaposi sarcoma and non-Hodgkin lymphoma [14]. Environmental or lifestyle factors also can be instrumental, as in multiple cancers of the respiratory tract from tobacco smoking [7, 12, 15].

It is well known that cancer treatment can cause second primary cancers [11]. Examples include acute leukaemias from chemotherapy and these and other cancers from radiotherapy [11, 15]. There is also the potential for an increased detection of second primary cancers from medical investigations that follow an initial cancer diagnosis [11]. This would contribute, for example, to the common occurrence of multiple cancers of the bladder and prostate [3, 11].

There are a number of instances where identifying cancers that occur as multiple primaries can be useful. For example, females with histories of uterine or ovarian cancer have been found to be at increased risk of breast

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cancer [3, 11], which can lead to genetic testing or routine screening of the person at risk [11–13]. Also, by comparing treatment profiles according to whether second primaries were experienced, carcinogenic effects of treatment can be identified and safer treatment options adopted [11].

In this study, South Australian Cancer Registry data were used to investigate risks of second primary cancers of separate organ sites during 1977–2001. The 15 most common cancer sites notified to the Registry were included to optimise case numbers. Results are discussed in the context of earlier North American and European reports and implications for cancer control and further research are indicated [3].

## Materials and methods

The South Australian Cancer Registry has received over 160,000 statutory notifications of invasive cancer since 1977 [16]. The Registry is population-based and covers all regions of the State. Operational details have been reported previously [16]. Multiple primary cancers of separate organ sites, diagnosed in 1977 to 2001, have been recorded and coded using the Ninth Revision of the International Classification of Disease (ICD-9) [17].

The first three digits of the ICD-9 coding system were used in this study to signify separate organ sites, as in earlier North American and European research [3, 17], although lymphomas were combined, as were leukaemias, to increase case numbers. Other sites investigated were the lip; stomach; colon; rectum; pancreas; trachea, bronchus and lung; skin (melanoma); female breast; uterine body; ovary and other uterine adnexa; prostate; bladder; and kidney.

A de-identified registry file was extracted from the Registry and analysed in-house, with legal authority of the South Australian Public and Environmental Health Act, using STATA 8.0 software [18]. Fifteen sets of analyses were undertaken, one for each cancer as the index site. For people with more than two primary cancers, only the first two cancers were included. An historic cohort model was used where person-years following diagnosis of the index cancer were categorised by age (five-year categories, with an open-ended category from 85 years), sex and calendar year [12, 18]. The follow-up period was censored at time of death, date of diagnosis of a second primary cancer, or 31 December 2001, whichever came first.

Numbers of second primaries observed in the follow-up period were divided by expected numbers to produce standardised incidence ratios (SIRs) [18, 19]. Expected values were obtained by applying South Australian age-sex specific incidence rates by calendar year for the respective cancer site to the duration of the follow-up period, similarly classified. Ninety five per cent confidence limits were based on the Poisson distribution [18, 19].

These analyses were undertaken twice, examining two different scenarios. Initially all cancers diagnosed from the time of diagnosis of the index cancer were eligible for inclusion as second primary cancers. Then, the analyses were repeated excluding second primary cancers diagnosed in the same month. Results of the second analyses are discussed only where they differed substantially from the initial results. For cancers affecting both males and females, analyses were undertaken for both sexes combined and for each sex separately.

## Results

The multiple primary combinations with statistically significant SIRs for both sexes combined are listed in Table 1. There were 51 combinations with elevated SIRs and two with lower than expected SIRs. Primary sites where cancers tended to occur together included uterine body–ovary – female breast, lip – lymphoma – melanoma, and prostate – bladder – kidney. The SIRs and confidence intervals for all second primaries are listed in Tables 2–4 by initial (i.e. index) cancer site. The exclusion of same month diagnoses reduced SIRs listed in Table 1 to non-significant levels for all second primaries where stomach, pancreas, lung, uterine body and kidney were the index primaries. Other SIRs which became non-significant are identified in Table 1. In every instance of elevated and lowered SIRs, males and females had similar SIRs, although female SIRs were not always statistically significant due to lower numbers of cancers.

## Discussion

It has been demonstrated in this study that there are a wide range of index – second primary combinations where there is an elevated risk of the second primary. In only two instances melanoma – lung and prostate – lung was there a lowered risk of the second primary. Many multiple primary combinations identified in this study have been previously reported, but new combinations were also identified, about half of which involved either leukaemias or lymphomas as second primaries.

Previously identified multiple-primary combinations included lip cancer, cutaneous melanoma, and lymphoma [6, 10, 11, 20, 22]. Irrespective of which cancer arose first, the other two had elevated SIRs in this study. We

*Table 1.* Summary table of significant SIRs for second primary cancers – index primary cancers in bold

| Index primary | Lip | Stomach | Colon | Rectum | Pancreas | Lung | Skin (melano-ma) | Female Breast | Uterine body | Ovary | Prostate | Bladder | Kidney | Lympho-ma | Leukaemia |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Second Primary | Stomach | Co-lon*1.17 (0.68–1.87) | Rectum | Colon | Lympho-ma*2.04 (0.25–7.37) | Kidney* 1.17 (0.56–2.15) | Lip | Uterine body | Ovary* 1.07 (0.46–2.10) | Colon | Colon* 1.09 (0.94–1.26) | Lung | Stomach* 1.61 (0.77–2.95) | Lip | Lip |
| | Melanoma | | Female breast | Ovary*1.51 (0.65–2.97) | | Leukae-mia* 1.02 (0.51–1.82) | Lung (low) | Kidney | | Rectum* 1.73 (0.63–3.76) | Rectum* 1.13 (0.93–1.37) | Prostate | Colon* 1.11 (0.69–1.69) | Colon* 1.15 (0.81–1.60) | Stomach |
| | Lympho-ma | | Ovary* 1.39 (0.78–2.28) | Leukaemia* 1.44 (0.95–2.10) | | | Uterine body | Leukaemia* 1.21 (0.87–1.64) | | Pancreas | Lung (low) | | Prostate* 1.24 (0.91–1.63) | Lung* 1.30 (0.96–1.72) | Colon* 1.34 (0.92–1.90) |
| | | | Pros-tate*1.10 (0.95–1.27) | | | | Ovary | | | Uterine body* 0.00 (0.00–1.17) | Melanoma* 1.20 (0.98–1.45) | | | Melanoma | Lung |
| | | | Kidney | | | | Prostate | | | Leukaemia | Bladder | | | Female Breast* 1.30 (0.92–1.80) | Melanoma |
| | | | | | | | Lympho-ma | | | | Kidney* 1.20 (0.91–1.55) | | | Kidney* 1.62 (0.86–2.77) | |
| | | | | | | | | | | | | | | Leukaemia | |

All SIRs are elevated except where marked (low). Second primarys marked * do not have elevated SIRs after exclusion of same month diagnoses (SIRs and CIs shown).
NB: Where SIRs retained statistical significance after removing same month diagnoses, the associated changes in SIRs were not statistically significant ($p > 0.05$).

*Table 2.* SIRs (95% confidence limits) for second cancers following diagnosis of an index cancer of the lip, stomach, colon, rectum, pancreas; South Australia, 1977–2001[a]

| Second primary site | Index cancer site | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Lip | | Stomach | | Colon | | Rectum | | Pancreas | |
| | No. 2nd cancers | SIR (95% CL) | No. 2nd cancers | SIR (95% CL) | No. 2nd cancers | SIR (95% CL) | No. 2nd cancers | SIR (95% CL | No. 2nd cancers | SIR (95% CL) |
| Lip | – | – | 2 | 0.55 (0.07–2.00) | 23 | 1.10 (0.70–1.65) | 11 | 0.84 (0.42–1.50) | 1 | 1.61 (0.05–8.98) |
| Stomach | 22 | **1.63 (1.02–2.47)** | – | – | 41 | 1.36 (0.98–1.85) | 23 | 1.26 (0.80–1.89) | 2 | 2.27 (0.27–8.20) |
| Colon | 36 | 0.93 (0.65–1.29) | 30 | **2.06 (1.39–2.94)** | – | – | 183 | **3.27 (2.81–3.78)** | 4 | 1.48 (0.40–3.78) |
| Rectum | 19 | 0.86 (0.52–1.34) | 7 | 0.87 (0.35–1.79) | 161 | **3.25 (2.76–3.79)** | – | – | 4 | 2.74 (0.75–7.01) |
| Pancreas | 15 | 1.49 (0.83–2.46) | 4 | 1.04 (0.28–2.65) | 29 | 1.12 (0.75–1.61) | 8 | 0.54 (0.23–1.06) | – | – |
| Lung etc. | 61 | 1.14 (0.87–1.46) | 19 | 0.98 (0.59–1.53) | 89 | 0.83 (0.67–1.02) | 63 | 0.90 (0.69–1.16) | 2 | 0.61 (0.07–2.19) |
| Skin (melanoma) | 50 | **2.14 (1.59–2.83)** | 3 | 0.39 (0.08–1.15) | 53 | 1.08 (0.81–1.42) | 22 | 0.74 (0.46–1.11) | 1 | 0.73 (0.02–4.04) |
| Female breast | 13 | 0.89 (0.47–1.52) | 3 | 0.40 (0.08–1.17) | 99 | **1.29 (1.05–1.57)** | 46 | 1.21 (0.89–1.62) | 3 | 1.63 (0.34–4.77) |
| Uterine body | 0 | 0.00 (0.00–1.31) | 4 | 2.67 (0.73–6.83) | 19 | 1.22 (0.73–1.90) | 6 | 0.77 (0.28–1.68) | 0 | 0.00 (0.00–9.97) |
| Ovary etc | 1 | 0.51 (0.02–2.84) | 1 | 0.97 (0.03–5.41) | 22 | **2.03 (1.27–3.08)** | 16 | **3.01 (1.72–4.89)** | 0 | 0.00 (0.00–14.19) |
| Prostate | 95 | 1.02 (0.83–1.25) | 34 | 1.08 (0.75–1.51) | 190 | **1.18 (1.02–1.37)** | 131 | 1.19 (0.99–1.41) | 6 | 1.19 (0.44–2.57) |
| Bladder | 16 | 1.05 (0.60–1.71) | 3 | 0.53 (0.11–1.56) | 35 | 1.09 (0.76–1.51) | 20 | 1.00 (0.61–1.54) | 3 | 3.23 (0.67–9.43) |
| Kidney | 6 | 0.56 (0.21–1.23) | 5 | 1.34 (0.44–3.14) | 44 | **1.98 (1.44–2.66)** | 20 | 1.43 (0.88–2.21) | 1 | 1.52 (0.05–8.44) |
| Lymphomas | 27 | **1.81 (1.19–2.63)** | 10 | 1.88 (0.90–3.45) | 36 | 1.03 (0.72–1.43) | 18 | 0.87 (0.52–1.37) | 4 | **4.08 (1.11–10.45)** |
| Leukaemias | 13 | 0.95 (0.51–1.63) | 7 | 1.41 (0.56–2.90) | 35 | 1.11 (0.78–1.55) | 29 | **1.55 (1.04–2.23)** | 1 | 1.12 (0.03–6.26) |

[a] SIRs indirectly standardised by age, sex and calendar year (see text).

*Table 3.* SIRs (95% confidence limits) for second cancers following diagnosis of an index cancer of the lung, skin (melanoma), female breast, uterine body, ovary etc.; South Australia, 1977–2001[a]

| Second primary site | Index cancer site | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Lung | | Skin (melanoma) | | Female Breast | | Uterine body | | Ovary etc. | |
| | No. 2nd cancers | SIR (95% CL) | No. 2nd cancers | SIR (95% CL) | No. 2nd cancers | SIR (95% CL) | No. 2nd cancers | SIR (95% CL) | No. 2nd cancers | SIR (95% CL) |
| Lip | 5 | 0.61 (0.20–1.43) | 42 | **2.10 (1.52–2.84)** | 19 | 1.06 (0.64–1.65) | 3 | 0.73 (0.15–2.12) | 1 | 0.94 (0.03–5.21) |
| Stomach | 15 | 1.32 (0.74–2.18) | 15 | 0.63 (0.35–1.04) | 32 | 1.25 (0.85–1.76) | 6 | 0.99 (0.36–2.14) | 0 | 0.00 (0.00–2.40) |
| Colon | 26 | 0.83 (0.54–1.22) | 92 | 1.13 (0.91–1.38) | 129 | 1.03 (0.86–1.22) | 30 | 1.01 (0.68–1.45) | 21 | **2.79 (1.72–4.26)** |
| Rectum | 26 | 1.43 (0.93–2.09) | 46 | 1.05 (0.76–1.39) | 52 | 0.92 (0.69–1.21) | 16 | 1.23 (0.70–1.99) | 14 | **4.04 (2.20–6.77)** |
| Pancreas | 13 | 1.62 (0.86–2.76) | 13 | 0.64 (0.34–1.09) | 32 | 1.02 (0.70–1.44) | 8 | 1.06 (0.46–2.09) | 6 | **3.23 (1.18–7.02)** |
| Lung etc. | – | – | 55 | **0.60 (0.45–0.78)** | 83 | 1.05 (0.83–1.30) | 23 | 1.23 (0.78–1.84) | 2 | 0.40 (0.05–1.44) |
| Skin (melanoma) | 14 | 0.82 (0.45–1.38) | – | – | 79 | 1.13 (0.89–1.40) | 19 | 1.28 (0.77–2.00) | 6 | 1.32 (0.48–2.86) |
| Female breast | 17 | 1.26 (0.73–2.01) | 88 | 0.96 (0.79–1.14) | – | – | 66 | 1.21 (0.93–1.53) | 25 | 1.49 (0.96–2.19) |
| Uterine body | 1 | 0.37 (0.01–2.06) | 23 | 1.43 (0.90–2.14) | 90 | **1.80 (1.45–2.22)** | – | – | 23 | **7.28 (4.61–10.92)** |
| Ovary etc | 0 | 0.00 (0.00–2.05) | 19 | **1.71 (1.03–2.67)** | 41 | 1.22 (0.87–1.65) | 31 | **4.13 (2.80–5.86)** | – | – |
| Prostate | 88 | 1.15 (0.92–1.42) | 156 | **1.19 (1.01–1.39)** | – | – | – | – | – | – |
| Bladder | 18 | 1.42 (0.84–2.24) | 19 | 0.77 (0.47–1.21) | 16 | 0.81 (0.46–1.32) | 9 | 1.91 (0.87–3.62) | 1 | 0.86 (0.03–4.76) |
| Kidney | 23 | **2.68 (1.70–4.03)** | 22 | 1.05 (0.65–1.58) | 38 | **1.64 (1.16–2.26)** | 8 | 1.48 (0.64–2.92) | 2 | 1.36 (0.16–4.91) |
| Lymphomas | 17 | 1.45 (0.85–2.33) | 56 | **1.68 (1.27–2.18)** | 48 | 1.00 (0.74–1.32) | 10 | 0.92 (0.44–1.69) | 3 | 1.00 (0.21–2.93) |
| Leukaemias | 24 | **2.22 (1.42–3.30)** | 27 | 1.01 (0.67–1.47) | 47 | **1.39 (1.02–1.84)** | 7 | 0.89 (0.36–1.84) | 9 | **4.39 (2.01–8.33)** |

[a] SIRs indirectly standardised by age, sex and calendar year (see text).

*Table 4.* SIRs (95% confidence limits) for second cancers following diagnosis of an index cancer of the prostate, bladder, kidney, lymphomas, leukaemias; South Australia, 1977–2001[a]

| Second primary site | Index cancer site | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Prostate | | Bladder | | Kidney | | Lymphomas | | Leukaemias | | | |
| | No. 2nd cancers | SIR (95% CL) | No. 2nd cancers | SIR (95% CL) | No. 2nd cancers | SIR (95% CL) | No. 2nd cancers | SIR (95% CL) | No. 2nd cancers | SIR (95% CL) | | |
| Lip | 55 | 1.22 (0.92–1.59) | 7 | 0.75 (0.30–1.54) | 6 | 1.26 (0.46–2.74) | 16 | **2.39 (1.37–3.88)** | 14 | **2.50 (1.37–4.20)** | | |
| Stomach | 58 | 0.87 (0.66–1.12) | 16 | 1.13 (0.65–1.84) | 13 | **2.09 (1.11–3.57)** | 13 | 1.35 (0.72–2.32) | 15 | **1.95 (1.09–3.21)** | | |
| Colon | 198 | **1.17 (1.01–1.35)** | 34 | 0.91 (0.63–1.27) | 31 | **1.64 (1.11–2.32)** | 47 | **1.51 (1.11–2.00)** | 41 | **1.72 (1.24–2.34)** | | |
| Rectum | 122 | **1.26 (1.04–1.50)** | 17 | 0.81 (0.47–1.29) | 11 | 1.03 (0.51–1.84) | 13 | 0.77 (0.41–1.31) | 10 | 0.78 (0.37–1.43) | | |
| Pancreas | 49 | 1.12 (0.83–1.48) | 15 | 1.50 (0.84–2.48) | 6 | 1.24 (0.45–2.70) | 9 | 1.14 (0.52–2.16) | 7 | 1.12 (0.45–2.30) | | |
| Lung etc. | 225 | **0.84 (0.73–0.96)** | 101 | **1.90 (1.54–2.30)** | 33 | 1.30 (0.90–1.83) | 52 | **1.41 (1.05–1.84)** | 55 | **1.89 (1.42–2.46)** | | |
| Skin (melanoma) | 113 | **1.25 (1.03–1.51)** | 23 | 1.22 (0.77–1.83) | 10 | 0.91 (0.44–1.67) | 33 | **1.68 (1.16–2.36)** | 32 | **2.48 (1.70–3.50)** | | |
| Female breast | – | – | 9 | 0.74 (0.34–1.41) | 12 | 0.98 (0.51–1.71) | 45 | **1.59 (1.16–2.12)** | 20 | 1.25 (0.77–1.94) | | |
| Uterine body | – | – | 2 | 0.80 (0.10–2.88) | 6 | 2.51 (0.92–5.46) | 3 | 0.56 (0.12–1.65) | 3 | 0.95 (0.20–2.77) | | |
| Ovary etc | – | – | 1 | 0.57 (0.02–3.16) | 4 | 2.47 (0.67–6.32) | 7 | 1.91 (0.77–3.94) | 2 | 0.91 (0.11–3.28) | | |
| Prostate | – | – | 206 | **2.19 (1.90–2.51)** | 66 | **1.66 (1.29–2.12)** | 51 | 0.95 (0.71–1.25) | 50 | 1.08 (0.80–1.42) | | |
| Bladder | 191 | **2.27 (1.96–2.62)** | – | – | 9 | 1.32 (0.60–2.50) | 10 | 1.00 (0.48–1.84) | 13 | 1.56 (0.83–2.66) | | |
| Kidney | 74 | **1.55 (1.22–1.95)** | 11 | 1.14 (0.57–2.05) | – | – | 15 | **1.87 (1.05–3.08)** | 10 | 1.70 (0.82–3.13) | | |
| Lymphomas | 60 | 1.00 (0.76–1.28) | 11 | 0.82 (0.41–1.47) | 8 | 1.10 (0.48–2.17) | – | – | 7 | 0.78 (0.31–1.61) | | |
| Leukaemias | 67 | 1.08 (0.84–1.37) | 11 | 0.83 (0.41–1.48) | 6 | 0.94 (0.35–2.05) | 24 | **2.32 (1.49–3.46)** | – | – | | |

[a] SIRs indirectly standardised by age, sex and calendar year (see text).

consider, given the relative ease of screening for lip cancer and melanoma, and prospects for this to lead to early diagnosis, that screening for these cancers be undertaken among lymphoma survivors.

The occurrence of colonic and rectal cancers as multiple primaries, which is also consistent with earlier research results, probably reflects common lifestyle and genetic causes [3, 23]. It would support decisions to introduce ongoing bowel screening of patients with histories of these cancers.

An elevated incidence of ovarian cancer amongst colon cancer cases confirms British data where researchers cited genetic factors and nulliparity as possible explanations [5]. Patients with *hereditary non-polyposis colorectal cancer* may be genetically vulnerable to ovarian cancer, plus kidney cancer [24].

Meanwhile, the higher risks of prostate and female breast cancers among colonic cases is consistent with earlier results from the Connecticut Cancer Registry [3]. Nulliparity, obesity and sedentary behaviour are risk factors for both colonic and breast cancer and are possible contributors [23, 25].

The present data confirm links between cancers of the breast and uterine body, uterine body and ovary, and ovary and uterine body where researchers have cited endocrine interactions, genetic contributions, obesity and other common risk factors as probable reasons [3, 11, 12].

A link also was evident between lung cancer and second cancers of the kidney. Tobacco smoking is a common aetiological factor and likely contributed [12]. Previous Danish and Connecticut data have shown a similar link [3].

Lymphoma patients had elevated SIRs for leukaemias, lung and kidney cancers, as suggested by earlier research [3]. An elevated SIR for female breast cancer also was consistent with earlier Swedish results [6]. The Swedish data also showed an association between lymphoma and subsequent cancers of the colon in females, and between leukaemias and subsequent cancers of the colon and stomach in males [6]. The contribution of immunological impairment and other possible aetiological mechanisms to these findings warrants further investigation.

The occurrence of lip cancers as second primary cancers in leukaemia patients is consistent with Swedish and Danish data [3, 6]. The reasons are not known, but the potential for solar radiation to predispose to both lip cancer and leukaemia should be explored.

Women with breast cancer had a raised risk of kidney cancer, which is consistent with earlier Danish results [3]. Potentially excess body weight could have been a common risk factor that contributed to this association

[25]. Women with breast cancer also were at increased risk of leukaemia, which is consistent with Danish results and may be a treatment effect [3].

The occurrence of leukaemias as a second primary following lung cancer was not expected, and was not evident from earlier studies. It could not be attributed solely to lung cancer therapy, since there was an elevated SIR for lung cancer following a leukaemia diagnosis. Leukaemias occurred as second primaries following a range of other cancers including cancers of the rectum, female breast, ovary, and lymphoma. In the cases of ovarian cancer and lymphoma, the elevated SIR held after exclusion of same month diagnoses, indicating that leukaemia may be a treatment effect.

The elevated risk of lymphomas following pancreatic cancer, and leukaemias following rectal cancer, have not been reported previously. In both instances statistical significance did not hold when same month diagnoses were excluded.

There were five second primary cancers associated with prostate cancer in this study, including cancers of the bladder, colon, rectum, kidney and cutaneous melanoma. While none of these associations were demonstrated in the Connecticut and Denmark data, these data were collected when there were fewer diagnosed prostate cancer cases and the statistical power to detect such associations was much lower. [3, 16].

Other new cancer associations, which have not been previously reported, included colon cancer following stomach cancer, pancreatic cancer following ovarian cancer and stomach cancer following kidney cancer. We know of no obvious explanation for these findings and consider that they warrant verification with data from other cancer registries. With so many comparisons in this study, it is possible that some findings may have arisen by chance.

The diagnosis of multiple primary cancers in the same month was commonplace. It may reflect patterns of medical testing that follow an initial cancer diagnosis, plus the tendency for some cancer types to have long preclinical (*i.e.* occult) phases. This may explain the high percentage of the bladder cancers in prostate patients that were diagnosed in the same month (42%, 81 in 191) and the 39% (81 in 206) of prostate cancers in bladder cases that were diagnosed in the same month. Notably, all uterine body cancers detected in ovarian cases were diagnosed in the same month (23 in 23).

The potential existed in this study for incomplete follow-up of second primary cancers, due to case migration out of South Australia. If this were appreciable, it would have lowered SIRs. It is reassuring, therefore, that only two SIRs were lower than 1.00, namely, the 0.60 (0.45, 0.78) and 0.84 (0.73, 0.96) for cancers of the lung in melanoma and prostate cases, respectively. As a consequence, the ratio of elevated to low SIRs approximated 25 to 1.

The present study reveals combinations of multiple primary cancers in an Australian setting. The findings warrant verification with data from other Australian registries and further consideration of their aetiological significance. There is the potential for some findings to reflect adverse treatment effects, such as those where leukaemias have arisen as second primaries. On other occasions, as in the elevated risk of lip cancer and melanomas among lymphoma survivors, the value of ongoing screening should be considered.

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