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Incidence and outcomes of pregnancy-associated cancer in Australia, 1994–2008: a population-based linkage study

Yuen Yi (Cathy) LEE BMathAdv Hons,[1] Christine L ROBERTS MBBS Dip Obs RACOG PhD,[1] Timothy DOBBINS BMath PhD,[2] Efty STAVROU MAppSc PhD,[3] Kirsten BLACK MBBS FRANZCOG PhD DDU,[4] Jonathan MORRIS MBChB FRANZCOG PhD ,[1] Jane YOUNG MBBS MPH PhD FAFPHM[2]

[1]Clinical and Population Perinatal Health Research, Kolling Institute of Medical Research, University of Sydney, New South Wales, Australia

[2]Cancer Epidemiology and Services Research Group, Sydney School of Public Health, University of Sydney, New South Wales, Australia

[3]Adult Cancer Program, Lowy Cancer Research Centre, University of New South Wales, New South Wales, Australia

[4]Department of Obstetrics and Gynaecology, University of Sydney, New South Wales, Australia

Corresponding author:

A/Prof Christine L Roberts

University Department of Obstetrics and Gynaecology

Building B52, Royal North Shore Hospital

St Leonards NSW 2065

Australia

Phone: + 61 2 9926 7013

Fax: +61 2 9906 6742

Email: clroberts@med.usyd.edu.au

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Abstract

Objectives To determine trends in pregnancy-associated cancer and associations between maternal cancer and pregnancy outcomes.

Design Population-based cohort study.

Setting New South Wales, Australia, 1994–2008.

Population 781,907 women and their 1,309,501 maternities.

Methods Cancer and maternal information were obtained from linked cancer registry, birth and hospital records for the entire population. Multivariable logistic regression was used to examine associations between cancer risk factors and pregnancy outcomes.

Main outcome measures Incidence of pregnancy-associated cancer (diagnosis during pregnancy or within 12 months of delivery), maternal morbidities, preterm birth, perinatal death, small- and large-for-gestational-age (LGA).

Results. 1,798 new cancer diagnoses were identified, including 499 during pregnancy and 1,299 during postpartum. From 1994 to 2007, the crude incidence rate of pregnancy-associated cancer increased from 112.3 to 191.5 per 100,000 pregnancies ($P < 0.001$) and only 14% of the increase was explained by increasing maternal age. Cancer diagnosis was more common than expected in women aged 15–44 years (observed-to-expected ratio 1.49, 95%CI 1.42–1.56). Cancers were predominantly melanoma (33.3%) and breast cancer (21.0%). Women with cancer diagnosed during pregnancy had high rates of labour induction (28.5%), caesarean section (40.0%) and planned preterm birth (19.7%). Novel findings included a cancer association with multiple pregnancies (adjusted odds ratio 1.52, 95%CI 1.13–2.05) and LGA (aOR 1.47, 95%CI 1.15–1.88).

Conclusions Pregnancy-associated cancers have increased and the increase was only partially explained by increasing maternal age. Pregnancy increases women's interaction with health services and the possibility for diagnosis, but may also increase the risk of cancer.

Keywords: Cancer, pregnancy, incidence, cohort study, record linkage

Introduction

Cancer is the second leading cause of death in women during their reproductive years. The incidence is generally reported to be one for every 1,000 pregnancies.[1-5] Despite its rarity, the trend of women postponing childbearing to older age has raised concern that the incidence of cancer in pregnancy is likely to increase.[2,3,5-8]

Pregnancy-associated cancer refers to instances in which the initial diagnosis of cancer is made during pregnancy or within 12 months of delivery.[1,6,9-11] The rationale for including cancers diagnosed after pregnancy are: women and physicians may incorrectly attribute cancer-related symptoms to physiologic changes of pregnancy; reluctance to perform radiographs or invasive procedures during pregnancy, leading to delayed diagnosis; and less aggressive tumours are more likely to be undetected until after delivery.[1]

To date, estimates of the incidence of pregnancy-associated cancer have been imprecise, for example malignant melanoma is reported to affect between 1 in 1,000 and 1 in 10,000 pregnancies, breast cancer between 1 in 3,000 and 1 in 10,000 pregnancies, and ovarian cancer between 1 in 10,000 and 1 in 100,000 pregnancies.[2,4,8] A population-based Californian study identified pregnancy-associated cancers with hospital data and was then repeated with linked hospital and cancer registry data. The study showed that cancer ascertainment from the population-based statutory cancer register produced more refined and reliable incidence estimates.[1,9] However, the majority of published incidence estimates of pregnancy-associated cancer have come from case reports or small case studies and have relied on data collected before 2000. Consequently, questions regarding the population incidence remain. In addition, few studies have examined the associated pregnancy outcomes and to date the majority have focused on one cancer type and their sample size was small.[7,10-13]

Accurate reporting of the incidence of pregnancy-associated cancer and the associated pregnancy outcomes is important for informing treatment and counselling for women. Our study had two aims: first to determine recent trends in incidence of pregnancy-associated cancer and the impact of

increasing maternal age; and second to compare risk factors and pregnancy outcomes for women with and without pregnancy-associated cancer.

Methods

The study population comprised 781,907 women who gave birth in New South Wales (NSW) in the period 1994 to 2008, which corresponded to 1,309,501 maternities and 1,329,306 infants. With a resident population of nearly 7 million people, NSW is the most populous State of Australia. Approximately one-third of all Australian births occur in NSW.

Data sources

Data were obtained from three linked NSW population databases: the Perinatal Data Collection (PDC), Central Cancer Registry (CCR) and Admitted Patient Data Collection (APDC). Record linkage was carried out by the NSW Centre for Health Record Linkage. As Australia does not have a unique registration number for citizens, the separate datasets were linked using probabilistic linkage methods.[14,15] This involves a process of blocking and matching combinations of selected variables such as name, date of birth, address and hospital and assigning a probability weight to the match. The validity of the probabilistic record linkage is extremely high with less than three in 1,000 false positive links and less than five in 1,000 missed links.[14] The researchers were provided anonymised data. Ethics approval for the study was obtained from the NSW Population and Health Services Research Ethics Committee.

The PDC is a legislated population-based surveillance system that includes births of at least 20 weeks gestation or at least 400 grams birth weight. Information is recorded by either the midwife or medical practitioner providing maternity care and includes demographic, medical and obstetric information on the mother, as well as details of labour, delivery and condition of the neonate.

The CCR is a statutory case-based registry that includes demographic, cancer diagnosis and mortality information for every new cancer diagnosed in NSW since 1972 with the exception of non-melanoma

skin cancers. Information is recorded by treating clinicians in public and private hospitals, departments of radiation oncology and pathology laboratories. Diagnosis, topography and morphology for each cancer notification are coded according to the 3rd edition of the International Classification of Diseases for Oncology.[16] Over 90% of cancers are verified by pathology and are confirmed as the primary diagnosis.[17] To preserve individuals' privacy and confidentiality, only month and year of diagnosis are available in the registry.

The APDC is a census of all hospitalisations that includes summary discharge information for every inpatient admission to NSW public and private hospitals. Diagnosis and procedures for each admission are coded according to the 10th revision of the International Classification of Disease, Australian Modification and the Australian Classification of Health Interventions.[18]

PDC birth records from 1994 to 2008 were linked to the maternal cancer notifications to identify a cohort of women with newly diagnosed cancer during pregnancy or within twelve months of delivery.[1,6,9-11] Linkage to the maternal birth-related hospital records was only available from 2000 to 2008 but allowed assessment of adverse pregnancy outcomes and antenatal hospitalisations for that period.

Study factors

Cancers were categorised into 13 clinical groupings based on treatment categories.[17] According to the International coding guidelines,[19] stage at diagnosis was defined as the highest degree of spread that occurs within four months from the date of cancer diagnosis. Pregnancy-associated cancers were stratified depending on the time of initial diagnosis as follows: "Pregnancy" if the diagnosis was made between conception and delivery or "Postpartum" if the diagnosis was made within 12 months following delivery.

Socio-demographic information included maternal age, country of birth, and based on postcode of residence, socio-economic status (Index of Relative Socio-economic Disadvantage)[20] and

rural/remoteness (Accessibility/Remoteness Index for Australia).[21] Pregnancy information included plurality and parity. Maternal factors included hypertensive disorders (chronic or gestational hypertension, preeclampsia or eclampsia) and diabetes (pre-existing or gestational), as well as the use of assisted reproductive technologies. All above information was obtained from the birth records except for the use of assisted reproductive technologies, which was obtained from the linked maternal birth-related hospital records and was only available for births occurring 2001 onwards.

Pregnancy outcomes from the PDC included induction of labour, mode of delivery (spontaneous vaginal birth, instrumental birth and caesarean section) and place of birth. Other pregnancy outcomes included antenatal hospitalisation, obstetric haemorrhage (antepartum or postpartum), thromboembolic events (antepartum pulmonary embolism, puerperal pulmonary embolism, cerebral ischemia or infarction and puerperal deep vein thrombosis), sepsis (septicaemia or Group B streptococcal or gram negative sepsis) and severe maternal morbidity, which were obtained from diagnosis and procedure codes in the linked pregnancy and postpartum hospital records. Severe maternal morbidity was measured using a validated composite indicator relating to serious adverse maternal health outcomes such as transfusion, pulmonary embolism, hysterectomy and mechanical ventilation.[22] Antenatal hospitalisation was defined as an admission prior to and without birth or an admission where a birth occurs with the admission date at least four days prior to the date of delivery.[23] Perinatal outcomes included spontaneous preterm birth (<37 weeks gestation), planned preterm birth (induction of labour or pre-labour caesarean < 37 weeks gestation), perinatal death and size at birth, obtained from the birth records. Small-for-gestational-age (SGA, <10th percentile)[24] was of interest as a potential consequence of cancer or cancer treatment. Large-for-gestational-age (LGA, >90th percentile)[24] is a recognised risk factor for infant and childhood cancers and was pre-specified as potentially associated with maternal cancer. Only variables that are well and accurately reported were included in the analyses.[25-28]

Statistical analyses

The crude incidence rates of pregnancy-associated cancer were calculated by dividing the number of newly diagnosed cancers during pregnancy and postpartum by the number of pregnancies, in which multi-fetal pregnancies were counted once. Each notification in the cancer registry is a primary diagnosis and more than one cancer in a pregnancy is possible. The crude rates were then standardised to the population in 1994 to obtain the direct age-standardised rates. All rates were expressed per 100,000 pregnancies.

To assess whether pregnancy increased the risk of cancer or cancer diagnosis, we compared the number of pregnancy-associated cancers with the number expected based on the population incidence for all women aged 15–44 years.[29] We used indirect standardisation by five-year age groups for the five most common pregnancy-associated cancers. The observed-to-expected ratios with 95% confidence intervals were estimated assuming a Poisson distribution for the observed frequency.

Cochran-Armitage trend tests were used to assess for a linear trend in incidence rates of pregnancy-associated cancer, both overall and by maternal age group, for births occurring in 1994–2007. Births occurring in 2008 were excluded because these women did not have 12 months of postpartum data thereby under-ascertaining the cancer incidence. Crude associations between maternal cancer and each outcome were examined via cross-tabulation and chi-square tests. Multivariable logistic regression was used to examine both risk factors for maternal cancer and maternal cancer as a risk factor for adverse pregnancy outcomes. The latter were adjusted for maternal age, socio-economic status, plurality, parity, diabetes and hypertensive disorders to estimate the adjusted odds ratios (aOR) with 95% confidence intervals (95%CI). Preterm birth was further adjusted for previous preterm birth. Sensitivity analysis was conducted excluding women with melanoma of skin diagnosed during pregnancy, with no material change to the magnitude of the adjusted odds ratios (data not shown). Analyses were carried out in SAS, Version 9.2 (SAS Institute, Cary NC, USA).[30]

Results

Incidence of pregnancy-associated cancer

Between 1994 and 2008, a total of 1,798 pregnancy-associated cancers were identified in 1,309,501 maternities among 781,907 women. This corresponds to an overall crude incidence of 137.3 per 100,000 pregnancies. Figure 1 shows that from 1994 to 2007 the crude incidence rate of pregnancy-associated cancer increased from 112.3 to 191.5 per 100,000 pregnancies ($P < 0.001$). During this period maternal age also increased; the percentage of women aged 35 years and over increased from 13.2% to 23.6% (including women aged 40 years and over from 1.9% to 4.0%). The impact of increasing maternal age is demonstrated in the direct age-standardised incidence rates which fall away from the crude incidence rates as the years advance (Figure 1). By 2007, the age-standardised rate (164.0 per 100,000 pregnancies) was 14.4% lower than the crude rate (191.5 per 100,000 pregnancies). Further, the rate per 100,000 pregnancies increased with increasing maternal age (<30 years: 70.7 in 1994 to 105.2 in 2007, $P = 0.05$; 30–34 years: 168.2 to 192.8, $P = 0.31$; and ≥35 years: 168.1 to 357.0, $P = 0.02$).

A total of 1,767 women had 1,785 cancer-affected maternities and 1,798 new cancer diagnoses, including 499 during pregnancy and 1,299 during postpartum. Twenty nine women had two diagnoses of cancer and one women had three cancer diagnoses (same or different type), including 12 women with multiple cancers in the same pregnancy and 18 in other pregnancies. Among the study population from 1994 to 2008, there were 18 maternal cancer deaths in the pregnancy group and 24 in the postpartum group. The proportion of cancer (of any type) increased steadily as the duration of pregnancy advanced (Figure 2). The highest proportion of cancer occurred in the two months postpartum and declined slowly thereafter. The most common cancers were melanoma of skin (n = 599, 45.7 per 100,000 pregnancies), breast cancer (n = 377, 28.8 per 100,000 pregnancies), thyroid and other endocrine cancers (n = 228, 17.4 per 100,000 pregnancies), gynaecological (n = 188, 14.3 per 100,000 pregnancies) and lymphohaematopoeitic cancers (n = 151, 11.5 per 100,000 pregnancies) (Table 1). These cancers accounted for 85.8% of the observed counts and most (47.8%) were localised (e.g., melanoma of skin 65.6%) with the exception of colorectal cancer (22.6%). Forty-five percent of cancers during pregnancy were diagnosed before 20 weeks of gestation.

Comparison to cancer incidence of general female population

There were approximately 49% more pregnancy-associated cancers than would have been expected based on the rates in the general female population for women aged 15–44 years from 1994–2007. The ratio of observed-to-expected with 95% confidence interval for all cancers was 1.49 (1.42–1.56), and for each of the five most common cancers: melanoma of skin 2.22 (2.05–2.41), followed by thyroid and other endocrine cancers 1.54 (1.35–1.75), lymphohaematopoeitic cancer 1.36 (1.15–1.59), breast 1.23 (1.11–1.36) and gynaecological cancers 1.20 (1.03–1.38).

Maternal characteristics and risk factors

Although increasing maternal age, Australian-born, high socio-economic status, multiparity, multiple pregnancy and prior diagnosis of cancer were all crude risk factors for pregnancy-associated cancer, only older maternal age, multiple pregnancy and prior diagnosis of cancer were retained as independent risk factors in the multivariable model (Table 2). Maternal age ≥40 years had the highest adjusted odds ratio but explained only 7.3% of cancers.

Pregnancy and perinatal outcomes

Women with cancer diagnosed during pregnancy were more likely to deliver at a tertiary hospital and have labour induced and pre-labour caesarean sections including preterm (Table 3 and Table S1). The mean gestational age at delivery was 37.7 (S.D. = 3.2) weeks for women with cancer diagnosed during pregnancy, 38.8 (S.D. = 2.3) weeks for women with cancer diagnosed postpartum and 39.0 (S.D. = 2.2) weeks for women without cancer. Rates of LGA infants were increased among women with cancer during or after pregnancy, but perinatal death rates were similar among women with or without cancer (Table 3). After adjusting for other risk factors, cancer during pregnancy was associated with a significantly increased risk of caesarean section (aOR 2.08, 95%CI 1.70–2.54), planned preterm birth (aOR 10.02, 95%CI 7.90–12.72) and LGA infants (aOR 1.47, 95%CI 1.15–1.88). A significant LGA association was observed for melanoma of skin (aOR 1.98, 95%CI 1.39–2.83) and thyroid and other endocrine cancers (aOR 2.31, 95%CI 1.10–4.86), but not breast (aOR 0.94, 95%CI 0.49–1.82), gynaecology (aOR 1.35, 95%CI 0.61–3.02) and lymphohaematopoeitic

cancers (aOR 1.13, 95%CI 0.48–2.66). The only pregnancy factor significantly associated with cancer after pregnancy was an increased risk of planned preterm birth (aOR 1.35, 95%CI 1.02–1.79) (Table S1).

From 2001 to 2008, 667,019 (99.2%) birth records had a linked hospital record and Table 4 shows the frequency of pregnancy complications. For women with cancer diagnosed during pregnancy, there were large increases in pregnancy risk of thromboembolic events (aOR 10.16, 95%CI 3.77–27.37), sepsis (aOR 4.31, 95%CI 2.60–7.15) and severe maternal morbidity (aOR 6.88, 95%CI 4.67–10.14) but no significant increase in pregnancy risk for obstetric haemorrhage (aOR 1.11, 95%CI 0.75–1.64). For women with cancer diagnosed after pregnancy, the only significant increase in postpartum risk observed was for sepsis (aOR 3.31, 95%CI 2.29–4.78).

Discussion

Consistent with expectation,[6,9,13] the incidence of pregnancy-associated cancer increased from 1994 to 2007. Although maternal age was a strong risk factor for cancer, increasing maternal age explained only 14% of the increase. Improved diagnostic techniques, detection and increased interaction with health services during pregnancy might also contribute to higher incidence rates. The cancer incidence was higher than expected among women of reproductive age and over two-thirds of pregnancy-associated cancers were diagnosed in the 12 months after delivery. Cancer diagnosed during or after pregnancy was more likely to result in planned preterm birth and maternal morbidity.

Between 1994 and 2008, the overall incidence of pregnancy-associated cancer in NSW was 137.3 per 100,000 pregnancies, which is higher than 100 per 100,000 pregnancies generally reported in literature.[1-5] Our reported estimates for the most common types of cancer are also higher than the published international estimates: melanoma of skin (45.7 vs. 8.7 per 100,000), breast cancer (28.8 vs. 19.3 per 100,000) and thyroid cancer (17.4 vs. 14.4 per 100,000), except for cervical (8.4 vs. 12.0 per 100,000) and ovarian cancers (3.6 vs. 5.2 per 100,000).[1] Our overall higher incidence is partly due to

the predominance of melanoma, in which Australia has the highest incidence over the world.[31] Slightly higher rates of the other cancers likely reflect our older and recent study population. The observation that the majority of cancers (72.2%) were diagnosed in the postpartum period has been noted elsewhere.[1,9] Some of these cancers may have been suspected given the high rate of planned preterm delivery, for women whose cancer was diagnosed postpartum. Another possible explanation is the physiologic changes of pregnancy may make cancer more challenging to diagnose, leading to a delay in diagnosis. The distribution of the timing of initial diagnosis is consistent with the contention that postpartum cancers are part of the cancer-in-pregnancy continuum and are appropriate to be included in the overall incidence.[1] The steady increase in the number of cancer diagnoses as the duration of pregnancy advanced to peak in the two months postpartum may be opportunistic due to pregnancy surveillance.[1]

The increased rate of cancer associated with pregnancy above that expected (based on the rates in the general female population) may be explained in twofold. First, antenatal and postnatal care, involving a standard protocol of history, physical examination, cervical cytology and blood pressure monitoring, is available for Australian women throughout and after pregnancy. On the basis of these routine care visits a screening effect might be expected thereby increasing the chance of detection of cancer in association with pregnancy. That the melanoma rate is over two times higher than expected in the general population is consistent with such an effect. Second, pregnancy is a proangiogenic state and it is plausible that the angiogenesis (driven by factors such as placental growth factor and vascular endothelial growth factor) required for successful placentation and pregnancy outcomes contributes to tumerogenesis or growth. In vitro placental growth factor increases proliferation of melanoma cells[32] and animal models demonstrate that metastasis is associated with increased expression of vascular endothelial growth factor receptor.[33] Furthermore, women with cancer diagnosed during pregnancy were more likely to have multiple pregnancies, and to have large-for-gestational-age infants even after adjustment for pre-existing or gestational diabetes. High birth weight is an established risk factor for childhood cancers: Wilms' tumour, infant and childhood leukaemia, osteosarcoma and astrocytoma[34], and twins have increased risks of endocrine, bone and breast cancers.[35,36] The postulated mechanism

is elevated levels of maternal hormone factors during pregnancy such as estrogens and insulin-like growth factor I levels or the abovementioned angiogenic factors.[37] This mechanism could also predispose maternal cancer and deserves further investigation. There are few studies that have examined these associations for mothers. We found only one study that examined infant size and breast cancer during pregnancy, which like us, found no increased risk in infant size for breast cancer.[37] Further, although studies of maternal cancer later in life have examined the risk for women who had multiple pregnancies, the findings have been contradictory and none have examined pregnancy-associated cancer.[38]

The timing of cancer diagnosis has an effect on adverse pregnancy outcomes. The risks of thromboembolic events, sepsis and severe maternal morbidity were higher among women with cancer diagnosed during pregnancy. Among postpartum cancers, we only demonstrated a significant risk of sepsis. This is consistent with the fact that these women are more prone to infections and malignancy-related immune-suppression, or may have had cancer treatments prior to delivery. The higher rate of caesarean delivery is likely to reflect the standard management plan of certain types of cancer (e.g., cervical cancer) in pregnant women.[9] Higher rates of planned preterm delivery, to allow postpartum initiation of cancer treatment, has been previously reported to be common for women with cancer in pregnancy.[9] The timing of obstetric delivery is a controversial issue surrounding the management of cancer associated with pregnancy. It has been reported that deliberate delay in treatment is not associated with poor survivorship for pregnant women with early stage cancer,[5] and therefore early elective delivery should be carefully considered to ensure the best outcomes for the mother and neonate. However, this general finding needs to be assessed by cancer type.

Our findings of higher risks of blood transfusion, caesarean delivery and premature birth are consistent with the findings of the population-based Californian studies of pregnancy-associated cancer.[9] Similar results have also been reported from cancer registry studies on breast, cervical and colorectal cancers independently.[7,10,11] These studies had methodological limitations, however. The Californian studies have assessed pregnancy outcomes solely based on hospitalisation records, in

which gestational age and perinatal death are poorly ascertained. Consequently, size at birth was defined by birth weight which does not differentiate size and maturity. Other limitations included restriction to a specific cancer type resulting in small sample sizes and no adjustment for socio-economic status and maternal clinical conditions (hypertensive disorders and diabetes) in assessing pregnancy outcomes.

The strength of our study is the population-based incidence and outcomes of cancer associated with pregnancy derived from large, validated and contemporary data sources. Importantly, there is a complete registration of cancers and births in statutory data collections in NSW. The linkage to cancer registry dating back to 1972 provided the opportunity to assess history of cancer as a risk factor for pregnancy-associated cancer. However, several limitations of our study warrant consideration. Since early pregnancy loss (spontaneous and therapeutic abortion) was not registered in the birth data, the number of pregnancy-associated cancers will be somewhat underestimated and the average gestational age at diagnosis will be over-estimated. We could not examine cancer treatment, as chemotherapy and radiotherapy are primarily provided in outpatient clinics and are under-ascertained in the hospitalisation records.[39] History of smoking and alcohol consumption, and maternal obesity were not available to provide adjustment for potential confounding of pregnancy outcomes. Finally, the exact date of cancer diagnosis was not available and therefore the timing of initial diagnosis may be misclassified to some extent.

Conclusion

In summary, we found a recent increase in pregnancy-associated cancers, such that by 2007 for every 10,000 pregnancies in Australia 19 women will have an associated cancer diagnosis. Our study provides contemporary cancer incidence rates by cancer type and informs women and clinicians about the pregnancy outcomes of cancer in pregnancy.

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Disclosure of interests

The authors declare no conflicts of interest.

Contribution to authorship

CLR and ES conceived the study. All authors participated in the study design, planning of analysis and interpretation of the results. YYL was involved in data preparation, statistical analyses and drafting the manuscript. TD provided statistical expertise and critical review of the manuscript. CLR provided clinical expertise, helped to draft the manuscript and coordinated the study. JM, JY, ES and KB provided clinical expertise and critical review of the manuscript. All authors read and approved the final manuscript.

Details of ethical approval

The study was approved by the NSW Population and Health Services Research Ethics Committee on 06 October 2009 (Ref: 2009/08/172).

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Table 1 The number and crude incidence rate of pregnancy-associated cancer, by the timing of initial diagnosis and clinical group of cancer, NSW, 1994–2008

	Pregnancy		Postpartum	All
Clinical group of cancer	*n (rate*[*]*)*	*<20 weeks*[†] *(%)*	*n (rate*[*]*)*	*n (rate*[*]*)*
Melanoma of skin	198 (15.1)	48.0	401 (30.6)	599 (45.7)
Breast	95 (7.3)	33.7	282 (21.5)	377 (28.8)
Thyroid and other endocrine	42 (3.2)	61.9	186 (14.2)	228 (17.4)
Gynecological	51 (3.9)	37.3	136 (10.4)	187 (14.3)
Cervix	24 (1.8)	50.0	86 (6.6)	110 (8.4)
Ovary	19 (1.5)	21.1	28 (2.1)	47 (3.6)
Other female genital organs	7 (0.5)	42.9	9 (0.7)	16 (1.2)
Uterus and body	1 (0.1)	0.0	7 (0.5)	8 (0.6)
Placenta	0 (0.0)	0.0	6 (0.5)	6 (0.4)
Lymphohaematopoeitic	53 (4.0)	47.2	98 (7.5)	151 (11.5)
Colorectal	10 (0.8)	20.0	52 (4.0)	62 (4.7)
Neurological	12 (0.9)	50.0	33 (2.5)	45 (3.4)
Bone and other connective tissue	8 (0.6)	50.0	26 (2.0)	34 (2.6)
Head and Neck	9 (0.7)	55.6	21 (1.6)	30 (2.3)
Upper gastrointestinal	6 (0.5)	16.7	24 (1.8)	30 (2.3)
Respiratory	3 (0.2)	0.0	19 (1.5)	22 (1.7)
Ill-defined and unknown primary sites	9 (0.7)	55.6	9 (0.7)	18 (1.4)
Urogenital	3 (0.2)	66.7	12 (0.9)	15 (1.1)
Total	499 (38.1)	44.7	1 299 (99.2)	1 798 (137.3)

[*]Crude incidence rate per 100 000 pregnancies

[†]Gestational age at diagnosis of less than 20 weeks among cancers diagnosed during pregnancy

Table 2 Maternal characteristics of 1 309 501 maternities among women with cancer diagnosed during pregnancy or postpartum compared to pregnant women without cancer

Maternal characteristic	Pregnancy *N* = 495 *n (%)*	Postpartum *N* = 1 290 *n (%)*	All *N* = 1 785 *n (%)*	No cancer *N* = 1 307 716 *n (%)*	Crude OR (95%CI)	Adjusted OR (95%CI)
Maternal age						
<30 years	147 (29.7)	362 (28.1)	509 (28.5)	654 593 (50.1)	Reference	Reference
30 – 34 years	172 (34.7)	505 (39.1)	677 (37.9)	413 643 (31.6)	2.10 [1.88,2.36]	2.09 [1.86,2.35]
35 – 39 years	137 (27.7)	332 (25.7)	469 (26.3)	200 242 (15.3)	3.01 [2.66,3.42]	3.03 [2.66,3.44]
≥40 years	39 (7.9)	91 (7.1)	130 (7.3)	38 615 (3.0)	4.33 [3.57,5.25]	4.38 [3.60,5.32]
Missing	0 (0.0)	0 (0.0)	0 (0.0)	623 (0.0)	-	-
Australian-born						
Yes	384 (77.6)	967 (75.0)	1 351 (75.7)	945 444 (72.3)	1.19 [1.07,1.33]	
No	110 (22.2)	321 (24.9)	431 (24.1)	359 634 (27.5)	Reference	Not retained
Missing	1 (0.2)	2 (0.2)	3 (0.2)	2 638 (0.2)	-	
Socio-economic status (IRSD)						
Lowest, 2nd–4th quintiles	362 (73.1)	1 001 (77.6)	1 368 (76.5)	1 064 664 (81.4)	Reference	
Highest 5th quintile	133 (26.9)	284 (22.0)	417 (23.4)	230 856 (17.7)	1.41 [1.26,1.57]	Not retained
Missing	0 (0.0)	5 (0.4)	5 (0.3)	12 196 (0.9)	-	
Remoteness (ARIA+)						
Urban	444 (89.7)	1 156 (89.6)	1 600 (89.7)	1 153 954 (88.3)	Reference	
Rural	51 (10.3)	130 (10.1)	181 (10.1)	150 882 (11.5)	0.87 [0.74,1.01]	Not retained
Missing	0 (0.0)	4 (0.3)	4 (0.2)	2 880 (0.2)	-	
Parity						
0	288 (58.2)	678 (52.6)	966 (54.1)	780 754 (59.7)	Reference	Not retained
≥1	207 (41.8)	612 (47.4)	819 (45.9)	526 962 (40.3)	1.26 [1.21,1.38]	
Plurality						
Singleton	484 (97.8)	1 256 (97.4)	1 740 (97.5)	1 288 370 (98.5)	Reference	Reference
Multiple pregnancy	11 (2.2)	34 (2.6)	45 (2.5)	19 346 (1.5)	1.72 [1.28,2.32]	1.52 [1.13,2.05]
Diabetes						
Yes	21 (4.2)	87 (6.7)	108 (6.1)	56 302 (4.3)	Not applicable	
No	474 (95.8)	1 203 (93.3)	1 677 (94.0)	1 251 414 (95.7)		
Hypertensive disorders						
Yes	38 (7.7)	96 (7.4)	134 (7.5)	88 130 (6.7)	Not applicable	
No	457 (92.3)	1 194 (92.6)	1 651 (92.5)	1 219 586 (93.3)		

Previous cancer (same or different type)						
Yes	7 (1.4)	23 (1.8)	30 (1.7)	4 454 (0.3)	5.00 [3.48,7.18]	3.79 [2.64,5.45]
No	488 (98.6)	1 267 (98.2)	1 755 (98.3)	1 303 262 (99.7)	Reference	Reference
Assisted reproductive technology						
Yes	10 (2.0)	27 (2.1)	37 (2.1)	13 301 (1.0)	1.95 [1.40,2.70]	Not retained
No	485 (98.0)	1 263 (97.9)	1 748 (97.9)	1 294 415(99.0)	Reference	
Stage of cancer						
In-situ	51 (10.3)	119 (9.2)	170 (9.5)			
Localised	230 (46.5)	622 (48.3)	852 (47.8)			
Regionalised	96 (19.4)	256 (19.8)	352 (19.7)		Not applicable	
Distant	21 (4.2)	83 (6.4)	104 (5.8)			
Unknown	97 (19.6)	210 (16.3)	307 (17.2)			

IRSD, Index of Relative Socio-economic Disadvantage; ARIA+, Accessibility Index for Australia; OR, odds ratio, CI, confidence interval, adjusted for age, plurality and previous cancer. Two women with two cancers diagnosed during pregnancy. Three women with two cancers and one with three cancers diagnosed during postpartum.

Table 3 Outcomes of 1 309 501 maternities among women with cancer diagnosed during pregnancy or postpartum compared to pregnant women without cancer

Pregnancy outcome	Pregnancy *N* = 495 *n (%)*	Postpartum *N* = 1 290 *n (%)*	All *N* = 1 785 *n (%)*	No cancer *N* = 1 307 716 *n (%)*
Place of birth				
Tertiary hospital	236 (47.7)	490 (38.0)	726 (40.7)	516 399 (39.5)
Private hospital	121 (24.4)	350 (27.1)	471 (26.4)	272 860 (20.9)
Public hospital	138 (27.9)	450 (34.9)	588 (32.9)	518 455 (39.6)
Missing	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.0)
Induction of labour				
Yes	141 (28.5)	342 (26.5)	483 (27.1)	310 017 (23.7)
No	354 (71.5)	948 (73.5)	1 302 (72.9)	997 319 (76.3)
Missing	0 (0.0)	0 (0.0)	0 (0.0)	383 (0.0)
Mode of delivery				
Spontaneous vaginal birth	253 (51.1)	794 (61.6)	1047 (58.7)	864 769 (66.1)
Instrumental birth	44 (8.9)	131 (10.2)	175 (9.8)	137 415 (10.5)
Caesarean section	198 (40.0)	365 (28.3)	563 (31.5)	304 741 (23.3)
Pre-labour	138 (27.9)	230 (17.8)	368 (20.6)	170 648 (13.0)
Intrapartum	60 (12.1)	135 (10.5)	195 (10.9)	134 093 (10.3)
Not stated	0 (0.0)	0 (0.0)	0 (0.0)	791 (0.1)
Preterm birth*				
Any <37 weeks	122 (24.0)	128 (9.6)	250 (13.6)	93 045 (7.0)
Spontaneous	22 (4.3)	68 (5.1)	90 (4.9)	57 309 (4.3)
Planned	100 (19.7)	60 (4.5)	160 (8.7)	35 700 (2.7)
No	373 (76.0)	1 162(90.4)	1 535 (86.4)	1 214 671 (93.0)
Perinatal death*				
Yes	5 (1.0)	8 (0.6)	13 (0.7)	12 019 (0.9)
No	502 (99.0)	1 315 (99.2)	1817 (99.2)	1 314 537 (99.0)
Missing	0 (0.0)	2 (0.2)	2 (0.1)	918 (0.1)
Birth weight percentiles*				
<10th	54 (10.7)	136 (10.3)	190 (10.4)	133 674 (10.1)
10th–90th	372 (73.6)	1016 (76.7)	1 389 (75.8)	1 043 541 (78.6)
>90th	75 (14.8)	165 (12.5)	240 (13.1)	136 415 (10.3)
Missing	5 (1.0)	8 (0.6)	13 (0.7)	13 844 (1.0)

*Based on number of neonates: 507 where cancer was diagnosed during pregnancy, 1 325 where cancer was diagnosed postpartum and 1 327 474 where no cancer was diagnosed.

Two women with two cancers diagnosed during pregnancy. Three women with two cancers and one with three cancers diagnosed during postpartum.

Table 4 Outcomes of 679 736 maternities among women with cancer diagnosed during pregnancy or postpartum compared to pregnant women without cancer

Pregnancy outcome	Pregnancy *N* = 287 *n (%)*	Postpartum *N* = 702 *n (%)*	All *N* = 989 *n (%)*	No cancer *N* = 678 747 *n (%)*
Number of antenatal admissions				
0	102 (35.5)	496 (70.7)	598 (60.5)	512 141 (74.5)
1	97 (33.8)	147 (20.9)	244 (24.7)	113 698 (16.8)
≥2	88 (30.7)	59 (8.4)	147 (14.9)	52 908 (8.7)
Obstetric haemorrhage				
Yes	28 (9.8)	76 (10.8)	104 (10.5)	60 022 (8.8)
No	259 (90.2)	626 (89.2)	885 (89.5)	618 725 (91.2)
Thromboembolic events				
Yes	4 (1.4)	2 (0.3)	6 (0.6)	878 (0.1)
No	283 (98.6)	700 (99.7)	983 (99.4)	677 869 (99.9)
Sepsis				
Yes	16 (5.6)	30 (4.3)	46 (4.7)	9 391 (1.4)
No	271 (94.4)	672 (95.7)	943 (95.3)	669 356 (98.6)
Severe maternal morbidity				
Yes	29 (10.1)	13 (1.9)	42 (4.2)	10 672 (1.6)
No	258 (89.9)	689 (98.1)	947 (95.8)	668 075 (98.4)

Data available from May 2001 onwards.
Two women with two cancers diagnosed during pregnancy. Three women with two cancers and one with three cancers diagnosed during postpartum.

Figure 1 Crude and direct age-standardised incidence rates of pregnancy-associated cancer, NSW, 1994–2007

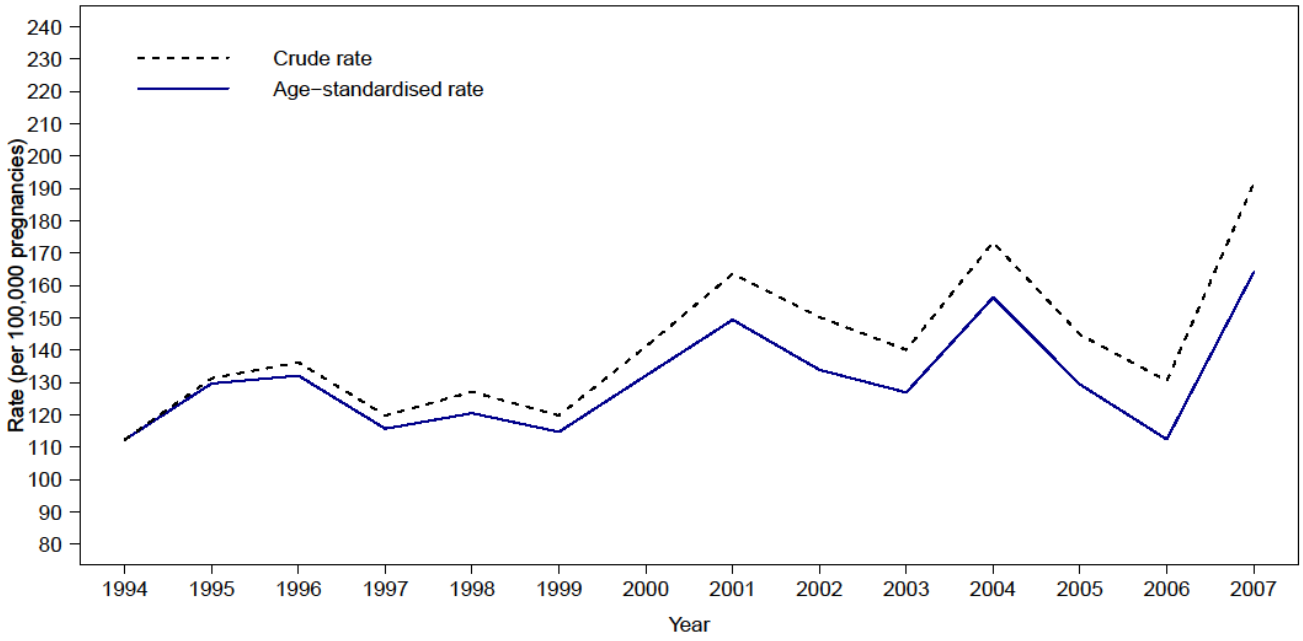

Figure 2 Timing of pregnancy-associated cancer diagnosis, NSW, 1994–2008