

Pregnancy-associated cancer: An exploration of women's experiences and perinatal and neonatal outcomes

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Elizabeth Sullivan, Associate Professor Antoinette Anazodo and Dr
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Certificate of original authorship

I, Sultana Farhana, declare that this thesis is submitted in fulfilment of the requirements for the award of Doctor of Philosophy, in the School of Public Health, Faculty of Health at the University of Technology Sydney.

This thesis is wholly my own work unless otherwise referenced or acknowledged. In addition, I certify that all information sources and literature used are indicated in the thesis.

This document has not been submitted for qualifications at any other academic institution. This research is supported by the Australian Government Research Training Program.

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Format of the thesis

This PhD thesis is in a compilation format. Each of the four studies is reported in a thesis chapter. Chapter 4 (Study 1) has been published in the *Journal of Obstetrics and Gynaecology Research*. Chapter 5 (Study 2) has been published in the *BMJ Open* journal. Chapter 6 (Study 3) has been published in the *Midwifery* journal, and Chapter 7 (Study 4) has been published in the *Women's Reproductive Health Journal*.

Statement of contributions to jointly authored works contained in the thesis

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Abbreviations

ACHI	Australian Classification of Health Interventions
AOR	Adjusted odds ratios
APDC	Admitted Patient Data Collection
CI	Confidence intervals
COD URF	Cause of Death Unit Record File
CS	Caesarean section
CT	Computed tomography
FCR	Fear of cancer recurrence
GEE	Generalised Estimating Equation
HCPs	Healthcare providers
IUFD	Intrauterine foetal death
IUGR	Intrauterine growth restriction
LBW	Low birth weight
MMOI	Maternal Morbidity Outcome Indicator
NAOI	Neonatal Adverse Outcome Indicator
NICU	Neonatal Intensive Care Unit
NSW	New South Wales
NSWCR	NSW Cancer Registry
PACRC	Pregnancy-associated colorectal cancer
PBS	Pharmaceutical Benefits Scheme
PDC	Perinatal Data Collection
PDR	Perinatal Death Review
PIS	Participant information sheet
pORs	Pooled odds ratios
PTSD	Post-traumatic stress disorder
RBDM	Register of Births, Deaths, and Marriages
RoCC	Register of Congenital Conditions
SD	Standard deviation
SGA	Small for gestational age
UTS	University of Technology Sydney

Glossary of Key Terms

Term	Definition
Maternal outcomes	Health outcomes for the woman during pregnancy and up to 12 months postpartum, such as mode of birth, maternal morbidity (e.g., thromboembolic events, haemorrhage), and maternal mortality.
Perinatal outcomes	Outcomes from 20 weeks' gestation to 7 days after birth, including stillbirth, perinatal mortality, and major complications affecting the foetus or newborn.
Neonatal outcomes	Outcomes from birth to 28 days postpartum, such as preterm birth, NICU admission, congenital anomalies, and neonatal mortality.
Cancer-related outcomes	Outcomes related to the cancer diagnosis, treatment, recurrence, and survival, including treatment timing and modality.
Gestational cancer	Any cancer diagnosed during pregnancy.
Postpartum cancer	Any cancer diagnosed within 12 months after childbirth.
PACRC	Pregnancy-associated colorectal cancer —diagnosis of colorectal cancer during pregnancy or postpartum (see List of Abbreviations).
Person-centred care	An approach to healthcare that respects and responds to patients' preferences, needs, and values, ensuring patient values guide all clinical decisions.

Abstract

Background

The incidence of pregnancy-associated cancer is increasing; however, research in this area remains limited due to the complexity of care and ethical constraints that restrict participation in clinical trials during pregnancy. Managing pregnancy-associated cancer presents unique clinical challenges, requiring a balance between optimising outcomes for the mother and their baby.

This thesis aimed to explore the impacts and maternal, perinatal and neonatal outcomes following a pregnancy-associated cancer diagnosis. This thesis highlights a) maternal and perinatal outcomes after a diagnosis of pregnancy-associated cancer, b) perinatal and neonatal outcomes following exposure to systemic therapies (chemotherapy, hormonal therapy, immunotherapy) during pregnancy, and c) healthcare experiences and impacts on the mental health and well-being of women diagnosed with pregnancy-associated cancer.

Methods

A multi-method research design was employed, incorporating both quantitative and qualitative approaches, which were conducted as separate but complementary studies. The quantitative phase consisted of a linked data study (Study 1) utilising New South Wales (NSW) data from 1994 to 2013, as well as a systematic review and meta-analysis (Study 2). The systematic review followed PRISMA-P guidelines, while the linked data study examined epidemiological trends, incidence, and outcomes of pregnancy-associated colorectal cancer (PACRC) in NSW. The qualitative phase (Studies 3 and 4) involved in-depth, semi-structured interviews to identify key themes. Study 3 focused on communication practices between healthcare providers (HCPs) and women diagnosed with pregnancy-associated cancer, and Study 4 explored the mental health and well-being of these women.

Results

A significant increase in PACRC incidence in NSW was observed over the study period, independent of maternal age. Increased birth interventions following the diagnosis of colorectal cancer during pregnancy or postpartum reflect management challenges with higher maternal and neonatal morbidities. The systematic review with meta-analysis found that systemic therapy is associated with higher rates of preterm birth; however, no significant differences were observed in other adverse outcomes, such as spontaneous abortion or congenital anomalies. Furthermore, communication gaps between healthcare professionals and women diagnosed with pregnancy-associated cancer were identified, and a critical gap in mental health support for women with pregnancy-associated cancer emphasised the need for early screening, specialised counselling, and peer support to address mental health challenges.

Conclusion

This research emphasises the complexity of managing pregnancy-associated cancer and the importance of coordinated multidisciplinary care to improve maternal and neonatal outcomes. It is necessary to tailor healthcare strategies that focus on effective communication and mental health support for women throughout their cancer journey.

Chapter 1: Background

1.1 Chapter introduction

Pregnancy-associated cancer is relatively rare; however, its incidence has increased over time (Eastwood-Wilshere et al. 2019). This increase is primarily attributed to delayed childbearing and the increasing age of mothers (Cottreau et al. 2019; Kobayashi et al. 2019; Korenaga & Tewari 2020). The rising incidence of pregnancy-associated cancer has become more pronounced, necessitating a comprehensive understanding of its impact on maternal and perinatal outcomes, mothers' experiences within the healthcare system, and associated mental health challenges.

The management of pregnancy-associated cancer presents significant complexities, creating a uniquely challenging scenario for expectant mothers and developing foetuses during pregnancy and for mothers and children during the postpartum period (Andersson et al. 2015; Hepner et al. 2019). Physiological changes and common symptoms during pregnancy can obscure subtle signs of pregnancy-associated cancer, often leading to delayed diagnosis and disease progression to more advanced stages (Botha, Rajaram & Karunaratne 2018; Durrani, Akbar & Heena 2018; Eastwood-Wilshere et al. 2019). The limited availability of large-scale prospective studies hinders the establishment of standardised diagnostic and therapeutic protocols (Hepner et al. 2019; Maggen et al. 2019). Additionally, the rapidly evolving landscape of oncology treatment presents further challenges for the management of pregnancy-associated cancer. The integration of modern therapies necessitates careful evaluation of their pharmacokinetics, pharmacodynamics, and potential transmission through breast milk (Hepner et al. 2019; Silverstein et al. 2020; Wolters et al. 2021). Long-term follow-up studies are crucial for assessing the impact of these treatments on maternal and neonatal health (Hepner et al. 2019; Maggen et al. 2019; Wolters et al. 2021).

Cancer is the second leading cause of mortality among women of childbearing age (Eastwood-Wilshere et al. 2019; Jeremic et al. 2018; Lomia et al. 2018), and it poses additional challenges when diagnosed during pregnancy or the postpartum period. Pregnancy-associated cancer profoundly affects women and their families (Stafford, Sinclair, Gerber, Collins, et al. 2021). Despite advances in treatment and management strategies, certain aspects of pregnancy-associated cancers require careful attention. Psychological, emotional, and mental health stress has been documented in previous studies (Harrison 2013; Henry et al. 2012; Kuswanto et al. 2018; Leung, Bryant & Stafford 2020) alongside the complexities of having young children and unemployment, which significantly affect the mental health

of patients and their partners (Catania, Sammut Scerri & Catania 2019). The burden of pregnancy-associated cancer extends beyond physical health and encompasses the arduous task of making critical decisions regarding pregnancy and cancer treatment. Therefore, it is crucial to investigate the complex interplay between pregnancy, cancer, and various physical, psychological, and familial factors to provide comprehensive care for the affected women and their families.

This introductory chapter presents a comprehensive overview of pregnancy-associated cancers and provides a context for this thesis. It outlines the definitions and epidemiology of pregnancy-associated cancer, examines the characteristics of pregnancies and births in Australia, and explores cancer and maternal care models within the Australian healthcare system. This chapter concludes by presenting the thesis's research aims, questions, significance, and structure, laying the foundation for subsequent chapters.

1.2 Epidemiology of pregnancy-associated cancer

Pregnancy-associated cancer is defined as a diagnosis of cancer during pregnancy or 12 months postpartum (Andersson et al. 2015; Cottreau et al. 2019; Dahling et al. 2009; Eastwood-Wilshere et al. 2019). The subsequent sections present a comprehensive analysis of the epidemiology of pregnancy-associated cancer.

1.2.1 Prevalence of pregnancy-associated cancer

Cancer occurs in approximately one in every 1,000 pregnancies, and the prevalence of pregnancy-associated cancer is increasing due to delayed childbearing (Eastwood-Wilshere et al. 2019; Esposito et al. 2021; Hepner et al. 2019). A population-based linkage study conducted in Australia revealed that approximately two-thirds of pregnancy-associated cancer cases were diagnosed postpartum, with the likelihood of developing pregnancy-associated cancer being directly proportional to advancing maternal age (Lee et al. 2012). Although cancer during pregnancy is considered rare, it accounts for approximately 0.07% to 0.1% of all malignant tumours (Hepner et al. 2019).

The most prevalent malignancies associated with pregnancy are melanoma, breast cancer, and cervical cancer (Cottreau et al. 2019; Eibye, Kjær & Mellekjær 2013; Hepner et al. 2019; Parazzini et al. 2017). Certain malignancies, such as melanoma, lung cancer, and haematopoietic cancer, have a higher

tendency to metastasise to the placenta, posing significant risks to both the mother and foetus (Hepner et al. 2019). Melanoma is of particular concern because it is responsible for one-third of pregnancy-associated malignancies worldwide (Hepner et al. 2019; Zagouri et al. 2016). Less common types of pregnancy-associated cancer include colorectal, ovarian, endocrine and thyroid cancer, and Hodgkin's lymphoma and leukaemia (Andersson et al. 2015; Dahling et al. 2009).

1.2.2 Incidence of pregnancy-associated cancer worldwide

The incidence of pregnancy-associated cancer is gradually increasing with substantial variation in the literature. Several studies have reported increasing incidence rates in different countries. A recent large retrospective population-based cohort study conducted in China estimated the incidence of pregnancy-associated cancer is 2.63 per 1,000 pregnancies (Yu et al. 2023). This finding aligns with the broader global trend of an increasing incidence. For instance, in Australia, the incidence rose from 112.3 to 191.5 per 100,000 women giving birth between 1994 and 2007 (Lee et al. 2012). In Korea, the incidence rate increased from 76.5 to 312 per 100,000 women giving birth between 1995 and 2013 (Min Hee et al. 2016). Similarly, in the USA, the incidence increased from 75 to 173 per 100,000 women giving birth between 2002 and 2012 (Cottreau et al. 2019). In Denmark, the estimated incidence increased from 5.4% to 8.3% or 89.6 per 100,000 women giving birth between 1977 and 2006 (Eibye, Kjær & Mellekjær 2013). These studies collectively underscore a consistent upward trend in the occurrence of pregnancy-associated cancer across various regions.

The incidence and type of pregnancy-associated cancers show significant geographical variation. Cervical cancer is the most common malignancy (36%) in Japan (Kobayashi et al. 2019), and melanoma is the most common malignancy (31%) during pregnancy in Europe (Sacchetto et al. 2018; Zelin et al. 2020). The incidence of melanoma is considerably lower in Asian countries than in Western countries (Ribero et al. 2017; Still & Brennecke 2017). Notably, in China, the incidence of thyroid cancer during pregnancy has increased by 12% in the past 20 years (Kobayashi et al. 2019; Yu et al. 2023).

Additional studies have highlighted the diversity of pregnancy-associated cancers. In Canada, the incidence of pregnancy-associated non-Hodgkin lymphoma has increased from 4.44 to 7.17 per 100,000 births over nine years (El-Messidi, Patenaude & Abenhaim 2015). Although colorectal is rare, research from Petruzzelli et al. (2020) and Yang et al. (2021) has documented an incidence rate of 1 in 13,000 pregnancies (Petruzzelli et al. 2020; Yang & Han 2021). In Korea, thyroid cancer is the most

frequently diagnosed cancer in pregnant women, a trend attributed to routine ultrasound screening that facilitates early detection (Kobayashi et al. 2019). Despite these variations, breast cancer has consistently emerged as the predominant pregnancy-associated cancer worldwide (Alfasi & Ben-Aharon 2019; Durrani, Akbar & Heena 2018; Galati et al. 2023; Maxwell et al. 2019).

1.2.3 Pregnancy-associated cancer incidence in Australia

Previous research suggests that the incidence of pregnancy-associated cancer in Australia has been rising over recent decades (Bannister-Tyrrell et al. 2015; Lee et al. 2012; Sullivan et al. 2022).

An increase in maternal age in Australia, as in many other parts of the world, may be linked to a higher risk of pregnancy-associated cancers such as breast cancer and melanoma (Bannister-Tyrrell et al. 2015; Safi et al. 2021).

Among pregnancy-associated cancers in Australia, melanoma is the most common, accounting for 33.3% of cases, followed by breast cancer (21%) and thyroid cancer (19.6%)(Lee et al. 2012). In Australia, the incidence of melanoma during pregnancy and the postpartum period is 45 per 100,000 births (Lee et al. 2012; Still & Brennecke 2017). Melanoma diagnosed at a later stage presents a higher risk of metastasis due to its potential to spread through the skin membrane (Bannister-Tyrrell et al. 2015; Still & Brennecke 2017). The incidence of gestational breast cancer (GBC) ranges from 6.8 to 7.5 per 100,000 births (Safi et al. 2021; Sullivan et al. 2022). Breast cancer during pregnancy is a significant concern because of its impact on both maternal and foetal health, and these statistics highlight the growing importance of understanding and managing pregnancy-associated cancer in the context of increasing maternal age and evolving healthcare challenges in Australia.

1.3 Risk factors for pregnancy-associated cancer

Factors associated with pregnancy-associated cancer remain largely unexplored. However, advanced maternal age is consistently identified as one of the most significant risk factors for pregnancy-associated cancer (Eastwood-Wilshire et al. 2019; Monteiro et al. 2019; Safi et al. 2021; Wolters et al. 2021). The likelihood of developing cancer during pregnancy is expected to increase as the risk of most malignancies increases with age (Ruiz et al. 2017; Troisi et al. 2018). This risk factor has often been

linked to the increasing trend of delayed childbearing in recent years (Eastwood-Wilshere et al. 2019; Maggen et al. 2019; Wolters et al. 2021).

In Australia, the proportion of women giving birth aged 35 years or older increased from 13% in 1991 to 26% in 2019 (Australian Institute of Health and Welfare 2021). This demographic change parallels findings from a population-based study in New South Wales (1994–2008), which reported a significant increase in pregnancy-associated cancer from 112.3 to 191.5 per 100,000 maternities, 14% driven by increasing maternal age. (Lee et al. 2012). Similarly, a more recent study reported that women aged 35 years or older are at an increased risk of gestational breast cancer (Safi et al. 2021). It is important to note that the increased incidence of pregnancy-associated cancer in older women may not solely be due to delayed childbearing. Instead, it reflects a natural increase in cancer risk with age.

Other contributing factors may also be linked to the first pregnancy being at an older age (Monteiro et al. 2019; Ruiz et al. 2017). The association between older maternal age and hormone-sensitive cancers, such as breast, ovarian, and endometrial cancers, has been well documented, as these cancers are more prevalent in older women (Kobayashi et al. 2019; Safi et al. 2021; Troisi et al. 2018). Family history has emerged as a potential risk factor for certain pregnancy-associated cancers (Ruiz et al. 2017; Samadder et al. 2020).

Although the pathophysiology of pregnancy-associated cancer is not fully understood, several hypotheses have been proposed. Hormonal changes, immunological suppression, increased permeability, pregnancy-associated growth factors, and vascularisation during pregnancy or the postpartum period may accelerate tumour growth (Hepner et al. 2019; Ho, Cassano-Bailey & Czaykowski 2012; Proussaloglou, Blanco & Siziopikou 2023).

1.4 Healthcare system and pregnancy-associated cancer care models in

Australia

The healthcare system and models of care refer to the organisation and delivery of healthcare services. It is essential to understand these aspects because they affect how women with pregnancy-associated cancer receive treatment and support. This section explores pregnancies and births in Australia, the importance of the health system and models of care influencing women's outcomes. It discusses how the healthcare system impacts the management of pregnancy-associated cancer.

1.4.1 Pregnancies and births in Australia

In 2019, Australia recorded 303,054 live births, 2,183 stillbirths (7.2 per 1,000 births), and 714 neonatal deaths (2.4 per 1,000 births) (Australian Institute of Health and Welfare 2021). In the Australian context, stillbirth is defined as the loss of a pregnancy at or beyond 20 weeks of gestation or a birth weight of at least 400 g, whereas neonatal death refers to death occurring within the first 28 days of life (Centre for Epidemiology and Evidence 2019). Although the general trend in birth rates in Australia has been declining over the past decade, there has been a notable increase in births among women of older maternal age (35 years and over), reflecting broader demographic and social changes such as delayed childbearing and changes in fertility preferences (Australian Bureau of Statistics 2024; Australian Institute of Health and Welfare 2021).

The demographic profile of mothers in Australia showed that a significant majority (64.1%) were native-born, with a considerable proportion originating from overseas countries, notably India (5.4%), China (3.2%), and New Zealand (2.8%) (Australian Institute of Health and Welfare 2021). In Australia, most women (64%) give birth vaginally; however, the rate of caesarean sections remains notably high and is steadily increasing, now accounting for 36% of all births (Australian Institute of Health and Welfare 2021 ; Dahlen et al. 2023). From 1991 to 2017, the rate of caesarean deliveries in Australia significantly increased, while the incidence of vaginal births without medical intervention declined during the same period (Australian Institute of Health and Welfare 2019; Dahlen et al. 2023).

Furthermore, the demographic composition of pregnant women in Australia includes a notable representation of Indigenous and overseas-born mothers (Hennegan, Redshaw & Miller 2014; Sanjida et al. 2022) . Of all births in this dataset, 4.8% of births were to women who identified as Indigenous (Aboriginal and/or Torres Strait Islander) (Australian Institute of Health and Welfare 2021). This aligns with national data, which shows approximately 6.0% of babies are identified as Indigenous at birth, reflecting identification by either parent (Australian Institute of Health and Welfare 2021). This diverse cultural landscape can significantly influence pregnancy incidence and management, as cultural beliefs and access to healthcare services vary widely across groups (Hennegan, Redshaw & Miller 2014; Sanjida et al. 2022). Providing culturally appropriate and safe maternal care is especially critical for Indigenous and overseas-born mothers, who may encounter unique challenges in navigating the

healthcare system during pregnancy, particularly when faced with a cancer diagnosis (Dahlen et al. 2023; Kildea et al. 2016; Sanjida et al. 2022).

1.4.2 Healthcare system in Australia

Australia's healthcare system is renowned for its comprehensive coverage, accessibility, and quality of care, combining the public and private sectors to serve diverse populations (Department of Health 2019; Donato & Scotton 2020). The system aims to ensure all Australians have access to necessary healthcare services. The federal, state and territory governments jointly fund Australia's healthcare system (Australian Institute of Health and Welfare 2021 ; Donato & Scotton 2020).

Public Healthcare: Medicare

Medicare is Australia's national public health insurance scheme, established in 1984 and funded through taxation (Callander & Fox 2018; Macri 2016). It provides free or subsidised healthcare services for Australian citizens, permanent residents and some temporary residents. Medicare coverage includes general practitioner (GP) visits, specialist consultations (public system), diagnostic tests, and treatment in public hospitals (Australian Institute of Health and Welfare 2021 ; Callander & Fox 2018). Public hospital care is funded through the National Health Reform Agreement (NHRA) and not directly through the Medicare Benefits Schedule (MBS)(Macri 2016). An individual's Medicare status determines their entitlement to free public hospital care, which is available to Australian citizens, permanent residents, and others eligible under the system. Medicare also subsidises some medical services provided by private practitioners. Additionally, the Pharmaceutical Benefits Scheme (PBS) subsidises the cost of prescription medications, making many essential drugs more affordable for patients (Australian Institute of Health and Welfare 2021 ; Macri 2016)

Private Healthcare

Alongside the public system, private healthcare plays a significant role in Australia's healthcare system (Australian Institute of Health and Welfare 2021 ; Donato & Scotton 2020; Thomson 2020). Private health insurance offers additional coverage, including access to private hospitals, choice of doctors, and reduced waiting times for elective surgeries. It also includes services not typically included in Medicare, such as dental care, physiotherapy, and optical services. Private health insurance in Australia is optional, but the government encourages its uptake through various policies, such as Medicare Levy Surcharge, which penalises higher-income earners without private cover; Lifetime

Health Cover loading, which increases premiums for those who join later in life; and Private Health Insurance Rebate, which offers financial incentives to reduce the cost of premiums (Australian Bureau of Statistics 2024; Thomson 2020).

Primary and Specialist Care

Generally, GPs provide primary care in Australia and serve as patients' first point of contact (Baker, Britt & Harrison 2020). Through specialist referrals, GPs become crucial for preventative care, chronic disease management, and care coordination. The healthcare system promotes a model of continuous, comprehensive, and coordinated care, particularly for managing chronic illnesses (Baker, Britt & Harrison 2020). Specialist care is accessible through referrals from GPs, ensuring that patients receive expert diagnosis and treatment for specific conditions (Macri 2016). Specialists operate in public and private sectors, with services ranging from cardiology and oncology to dermatology and obstetrics (Australian Bureau of Statistics 2024; Australian Institute of Health and Welfare 2021 ; Macri 2016; Thomson 2020).*Hospital Services*

Australia's hospital system includes public and private hospitals that offer services ranging from emergency care to elective surgeries and specialised treatments. Public hospitals provide free or low-cost treatment to patients under Medicare, whereas private hospitals cater to patients with private health insurance (Australian Institute of Health and Welfare 2021 ; Callander & Fox 2018).

Obstetric and cancer care models in Australia

In Australia, obstetric care is delivered through both public and private healthcare systems, offering a range of care models including midwifery-led continuity of care, general practitioner shared care, and specialist obstetrician-led care (Baker, Britt & Harrison 2020; Callander & Fox 2018; Thomson 2020). Women with low-risk pregnancies are often managed by midwives or general practitioners, while those with complex needs, such as pregnancy-associated cancer, are typically referred to tertiary-level maternity hospitals where maternal-foetal medicine specialists coordinate care (Australian Bureau of Statistics 2024; Australian Institute of Health and Welfare 2021 ; Baker, Britt & Harrison 2020; Macri 2016; Thomson 2020). Obstetric clinical pathways are standardised protocols designed to guide care for various pregnancy-related conditions (e.g., gestational diabetes, preeclampsia), but they rarely accommodate the complexities of cancer treatment during pregnancy (Baker, Britt & Harrison 2020; Hunter et al. 2019). These pathways tend to focus on maternal and foetal health monitoring, routine antenatal screening, and delivery planning, and do not typically include coordinated oncology input unless initiated by individual clinicians (Baker, Britt & Harrison 2020; Hunter et al. 2019; Wolters et al.

2021). This gap underscores the siloed nature of care delivery between obstetrics and oncology, where treatment plans are often developed in parallel rather than collaboratively (Esposito et al. 2021; Wolters et al. 2021).

Cancer care in Australia presents a unique challenge, necessitating coordination across multidisciplinary teams within a dual healthcare system encompassing both public and private sectors (Hunter et al. 2019; Walpole et al. 2019). Multidisciplinary teams are a foundational element of oncology care, designed to bring together a range of specialists to collaboratively plan treatment, conduct comprehensive case discussions, make patient management decisions, and monitor clinical progress (Boisen & Balslev 2016; Walpole et al. 2019). This multidisciplinary cancer care model involves collaboration among oncologists (medical, surgical and radiation oncologists) obstetricians, paediatricians, psycho-oncologists, mental health professionals, social workers and allied health professionals such as dietitians and physiotherapists (Hunter et al. 2019; Walpole et al. 2019). In the context of pregnancy-associated cancer, multidisciplinary care becomes even more complex due to the involvement of additional maternal and neonatal health services (Eastwood-Wilshere et al. 2019; Silverstein et al. 2020). In such cases, obstetricians, maternal-foetal medicine specialists, neonatologists, and midwives are often integrated into multidisciplinary meetings (Hunter et al. 2019; Walpole et al. 2019). They are all working together to develop personalised care plans that balance maternal cancer treatment with foetal health and well-being (Hunter et al. 2019; Walpole et al. 2019). This approach ensures all aspects of patient care are coordinated, and treatment strategies are carefully tailored to the unique circumstances of each case (Amant et al. 2019; Royal College of Obstetricians and Gynaecologists 2023; Sorouri et al. 2023; Walpole et al. 2019). While multidisciplinary teams are widely regarded as essential to high-quality maternal cancer care, the empirical evidence supporting their effectiveness remains limited. Their implementation across clinical settings is inconsistent, and key barriers continue to hinder optimal functioning for maternal cancer care (Eastwood-Wilshere et al. 2019; Hunter et al. 2019; Silverstein et al. 2020).

Australia's public and private healthcare services offer different levels of access to maternity and cancer care (Donato & Scotton 2020; Hunter et al. 2019). Approximately 75% of Australian women give birth in the public system, where cancer care in public hospitals integrates treatments, such as chemotherapy, radiotherapy, and surgery, within a united care plan (Callander & Fox 2018; Hunter et al. 2019; Macri 2016). This integrated approach promotes continuity of care but can result in longer waiting times, leading some patients to pursue private care for expedited access (Macri 2016). However, private health services in Australia are fragmented. While private hospitals offer quicker access to specific treatments (e.g., surgery, radiotherapy) and the option to select specialists, they

typically lack a fully integrated approach to cancer care (Macri 2016). Patients receiving care in private facilities may face logistical challenges in coordinating treatments across different locations and often incur significant out-of-pocket costs despite having private insurance (Christine et al. 2017; Hunter et al. 2019). The differences between the public and private systems illustrate broader challenges in achieving consistent, coordinated care for cancer patients across the healthcare continuum.

For women with pregnancy-associated cancer, this fragmentation is particularly concerning due to the complexity and rising incidence requiring hospitalisation. Breast cancer, the second most common pregnancy-associated cancer in Australia, accounts for 72.2% of hospital admissions among pregnant cancer patients (Lee et al. 2012). This high burden underscores the urgent need for improved care coordination and comprehensive support systems (Hunter et al. 2019).

In Australia, the Optimal Care Pathway Program aimed to enhance cancer care quality and address disparities in patient outcomes (Bergin et al. 2020). While this initiative has enhanced care for many types of cancer, there remains a significant gap in the management and comprehensive care for women with pregnancy-associated cancer (Hunter et al. 2019; Stafford et al. 2022). The absence of national guidelines tailored explicitly to oncological care during pregnancy and the postpartum period presents substantial challenges in delivering coordinated and consistent care (Australian Bureau of Statistics 2024; Hunter et al. 2019; Stafford et al. 2022). Without standardised national protocols, the treatment of pregnancy-associated cancer is often highly individualised. This can result in fragmented care pathways in which treatment decisions are made based on the unique circumstances of each patient, leading to inconsistencies in care delivery.

The absence of a standardised and systemic approach to pregnancy-associated cancer raises important questions regarding the overall outcomes for both mothers and their babies. Balancing cancer treatment with pregnancy-related care often places women in a difficult position due to the need to make complex decisions that weigh the health and well-being of women and their unborn children. Cancer treatments, such as chemotherapy, radiation, or surgery, may pose risks to foetal development, while delaying treatment could compromise the mother's prognosis. Additionally, the emotional toll of managing a dual focus on survival and pregnancy outcomes, coupled with the physical demands of both conditions, can be overwhelming. These challenges underscore the importance of exploring how existing care models address the unique needs of women with pregnancy-associated cancer, including coordinated multidisciplinary approaches, tailored treatment plans that prioritise both maternal and neonatal outcomes and women's mental health support.

1.5 Aims, objectives, research question and significance of thesis

1.5.1 Aims

To explore the impacts and maternal, perinatal and neonatal outcomes following a pregnancy-associated cancer diagnosis.

1.5.2 Research objectives

The objectives of the thesis are:

1. To investigate the maternal outcomes for women diagnosed with pregnancy-associated cancer.
2. To investigate the perinatal and neonatal outcomes for babies born to women with pregnancy-associated cancer.
3. To explore the impact of pregnancy-associated cancer on communication between women and healthcare providers, including oncology and obstetric teams.
4. To explore women's mental health and well-being needs following a diagnosis of pregnancy-associated cancer.
5. To identify opportunities to enhance the care provided to women diagnosed with pregnancy-associated cancer.

1.5.3 Research questions

To achieve the above aim and objectives, this thesis will answer six (6) research questions as follows:

1. What are the maternal outcomes for women with pregnancy-associated cancer?
2. What are the perinatal and neonatal outcomes for babies born to women with pregnancy-associated cancer?
3. Do perinatal outcomes for babies born to women with cancer during pregnancy differ based on exposure to systemic cancer treatment in utero?
4. What are women's experiences of communication with their healthcare providers following a diagnosis of pregnancy-associated cancer?
5. What are the mental health impacts for women diagnosed with pregnancy-associated cancer?
6. What kinds of information or services would enhance patient experiences for women with pregnancy-associated cancer?

1.5.4 Significance of the thesis

The growing incidence of pregnancy-associated cancer over the past two decades underscores the urgent need for comprehensive research that addresses not only the clinical outcomes but also the experiences of women diagnosed with pregnancy-associated cancer (Eastwood-Wilshere et al. 2019; Safi et al. 2023; Stafford, Sinclair, Gerber, Collins, et al. 2021). Despite this growing need, the existing literature remains fragmented, often focusing narrowly on specific cancer types or isolated aspects of care (Akalin & Pinar 2016; Aurast et al. 2023; Hunter et al. 2019). This thesis seeks to bridge these gaps by providing a holistic exploration of pregnancy-associated cancer, encompassing maternal and neonatal outcomes, the impact of systemic therapies, and women's healthcare experiences.

Pregnancy introduces added complexity to cancer management (Eastwood-Wilshere et al. 2019; Faccio et al. 2020; Roberts & Andrewes 2022). The physiological changes and unique medical considerations required during pregnancy and the postpartum period complicate diagnosis, treatment, and care pathways for women with pregnancy-associated cancer (Silverstein et al. 2020; Zagouri et al. 2016). Managing cancer alongside the needs of a developing foetus or newborn presents significant challenges for both healthcare providers and pregnant women (Stafford, Sinclair, Gerber, Collins, et al. 2021; Stafford et al. 2022). The delicate balance between optimal cancer treatment and safeguarding maternal and foetal health expands the complexity of care.

Although the scope of this thesis is ambitious, it is carefully structured to offer a robust understanding of the critical issues related to pregnancy-associated cancer. By integrating quantitative analyses of maternal and neonatal outcomes with qualitative insights into women's interactions with healthcare professionals and the mental health impacts of diagnosis, this study sheds light on the multifaceted nature of cancer management during pregnancy. The goal is to generate evidence-based recommendations to guide healthcare professionals to deliver person-centred care, improve clinical outcomes, and enhance women's and babies' overall well-being. This thesis specifically focuses on examining the physical, psychosocial, and mental health impacts of pregnancy-associated cancer on women, as these domains align with the available data and research questions. While social, economic, and spiritual impacts are acknowledged in the broader literature, they fall outside the scope of this research.

The findings of this study will contribute to the development of more effective clinical guidelines, service improvements, and supportive care strategies for women diagnosed with pregnancy-associated cancer.

1.6 Thesis structure

The structure of this thesis is outlined as follows

Chapter 1 Provides background information about pregnancy-associated cancer, the prevalence and incidence of pregnancy-associated cancer, pregnancies and births in Australia, the health system, maternity care and the cancer care model in Australia. In addition, it describes the aims, objectives, research question and significance of this study.

Chapter 2 Reviews the current international literature on epidemiological data, management and maternal and neonatal outcomes after being diagnosed with pregnancy-associated cancer. This chapter also reviewed women's experiences regarding mothering, quality of life, communication with health care professionals and impact on mental health after their diagnosis.

Chapter 3 Describes this study's methodology, theoretical framework and methods. Details of the study aim, design, population, recruitment, data collection and analysis procedures, and ethical considerations are also provided.

Chapter 4 Presents Study 1, Incidence and maternal and neonatal outcomes following pregnancy associated colorectal cancer (PACRC): A population-based linked data study. This study aimed to describe the incidence of pregnancy-associated colorectal cancer (PACRC) in New South Wales (NSW), Australia and examine the perinatal outcomes of women with PACRC and their babies. This study has been published in the *Journal of Obstetrics and Gynaecology Research*.

Chapter 5 Presents Study 2, Perinatal outcomes for infants exposed to systemic treatment during gestation: A systematic review and meta-analysis. This study explored the available evidence relating to whether perinatal outcomes for babies born to women with cancer during pregnancy differ based on whether they are exposed to systemic cancer treatment (chemotherapy, hormonal therapy, immunotherapy) in utero. This study has been published in *BMJ Open*.

Chapter 6 Presents Study 3, Women's perspectives on communication following the diagnosis of gestational or postpartum cancer: A qualitative study. This study aimed to understand women's

perspectives on communication with healthcare providers (HCPs) following a pregnancy-associated cancer diagnosis. This study has been published in *Midwifery*.

Chapter 7 Presents Study 4 Cancer diagnosis during pregnancy and the postpartum period: Impact on well-being and mental health. This study aimed to explore the mental health and well-being of women diagnosed with pregnancy-associated cancer to enhance mental healthcare in this vulnerable group. This study has been published in *Women's Reproductive Health*.

Chapter 8 Discussion: This chapter discusses the implications of the findings of this thesis in the context of previous research, identifies the study's limitations, and highlights important issues relevant to the research aims and objectives. This chapter also identifies areas for future research. This chapter also discusses the literature results and provides recommendations for clinical practice and future research.

Chapter 9 Conclusions: This chapter summarises the key findings, discusses their implications and provides recommendations for clinical practice and future research. It also reflects on the thesis's overall contribution to the pregnancy-associated cancer research field.

1.7 Chapter summary

This chapter provides background knowledge on pregnancy-associated cancer, its prevalence and incidence, the healthcare system in Australia, the pregnancy-associated cancer care model, and the established research aim, research questions, and thesis structure. The next chapter (Chapter 2) will provide a review of the literature on the coexistence of pregnancy-associated cancer and the main issues associated with the diagnosis, management, and experiences of women after diagnosis with pregnancy-associated cancer.

Chapter 2: Literature review

2.1 Chapter introduction

This chapter provides a narrative literature review intended to summarise current knowledge and context on pregnancy-associated cancer. It examines key themes, including the rising global incidence of pregnancy-associated cancer, its impact on affected women and their families, the diagnostic, therapeutic, and management challenges during care, and the associated maternal and neonatal outcomes. Given the relatively limited availability of research in this area, the purpose of this review is not to provide a formal systematic synthesis but to draw on existing evidence to highlight the complexities of pregnancy-associated cancer care. Importantly, this chapter identifies key gaps in the literature that inform the aims, research questions, and significance of this thesis, particularly regarding clinical outcomes, care experiences, and mental health impacts for women diagnosed with pregnancy-associated cancer.

2.2 Literature search

To inform this narrative literature review, a broad search of peer-reviewed publications was conducted across key databases, including PubMed, Medline, Scopus, ProQuest, Cochrane Library, and Google Scholar. Search terms included combinations of “pregnancy-associated cancer,” “gestational cancer,” “maternal outcomes,” “neonatal outcomes,” “mental health,” “healthcare experiences,” and related terms. Additional sources were identified through reference lists and authoritative national and international cancer organisations. To inform this narrative literature review, a broad search of peer-reviewed publications was conducted across key databases, including PubMed, Medline, Scopus, ProQuest, Cochrane Library, and Google Scholar. Search terms included combinations of “pregnancy-associated cancer,” “gestational cancer,” “maternal outcomes,” “neonatal outcomes,” “mental health,” “healthcare experiences,” and related terms. Additional sources were identified through reference lists and authoritative national and international cancer organisations. In this review, ‘authoritative websites’ were defined as official government health agencies, recognised professional organisations (e.g., Cancer Council Australia, Royal Australian and New Zealand College of Obstetricians and Gynaecologists), and international health bodies (e.g., WHO). The grey literature search was not conducted systematically but was informed by the candidate’s awareness of key organisations and publications relevant to pregnancy-associated cancer and maternal healthcare. While this approach

may introduce some selection bias, the aim was to include major national guidelines and widely cited policy documents to supplement the peer-reviewed evidence

The purpose of this search was not to undertake a formal, systematic or scoping review, but to identify relevant literature that provides context for this thesis. Selected studies were prioritised based on relevance to the research questions, inclusion of maternal or neonatal outcomes, or exploration of women's experiences and healthcare services. A summary of the search strategy and terms is provided in Appendix 1.

2.2.1 Literature overview

The literature review incorporated diverse sources, including cohort studies, case-control studies, case series, systematic reviews, and clinical guidelines for obstetric management. The review is organised around key thematic areas relevant to this thesis: the rising global incidence of pregnancy-associated cancer, its clinical and psychosocial impact on women and their families, the diagnostic, therapeutic, and management challenges it poses, and the maternal and neonatal outcomes associated with these diagnoses.

This review provides a broader understanding of pregnancy-associated cancer. Some studies have focused on common types of pregnancy-associated cancer, such as breast cancer (Johansson et al. 2019; Lundberg et al. 2024), whereas other studies examined more complex cases, such as pregnancy-associated colorectal cancer (Amarjothi et al. 2019; Kocián et al. 2019). Certain studies focus exclusively on cancer diagnosis during pregnancy, which is also known as gestational cancer, and their associated outcomes (Aurast et al. 2023; Greiber et al. 2022; Safi et al. 2021; Sullivan et al. 2022). At the same time, some studies examine cancer diagnoses either during pregnancy or within 12 months postpartum, known as pregnancy-associated cancer (Cottreau et al. 2019; Eastwood-Wilshere et al. 2019). Given the limited research in this field, this literature review included studies addressing both categories to provide a more comprehensive understanding of the topic.

Some studies have undertaken comparative analyses between healthy pregnant women and those diagnosed with pregnancy-associated cancer, highlighting differences in maternal and neonatal outcomes (Andersson et al. 2015; Chen et al. 2018; Maggen et al. 2019), while other studies have focused exclusively on women with pregnancy-associated cancer, with a particular emphasis on examining the outcomes following exposure to systemic therapies (Garcia Morillo & Cubillo 2021;

Zagouri et al. 2016; Zubor et al. 2018). Furthermore, emerging qualitative research has explored the psychosocial and mental health impact of pregnancy-associated cancer on women and their families, as well as their experiences of healthcare services and communication with healthcare professionals (Leung, Bryant & Stafford 2020; Stafford, Sinclair, Gerber, Saunders, et al. 2021; Stafford et al. 2022). As pregnancy-associated cancer is rare and lacks available research, this multifaceted approach ensures that the review gathers the full spectrum of clinical experiences and evidence. This approach provides a robust foundation for understanding and addressing the complexities involved in the management of pregnancy-associated cancer, highlighting the differences in treatment approaches and care strategies.

2.3 Pregnancy-associated cancer: challenges and complexities

Pregnancy-associated cancer presents complex diagnostic and management challenges that differ significantly from cancer care in non-pregnant populations (Borowska-Waniak et al. 2023; Folsom & Woodruff 2020). Treatment decision-making requires careful balancing of maternal health needs with foetal safety, particularly regarding the timing and choice of systemic therapies (Eastwood-Wilshere et al. 2019; Silverstein et al. 2020; Wolters et al. 2021).

While treatment options are limited during pregnancy, a wider range of therapeutic approaches becomes available when the woman is not pregnant (Borowska-Waniak et al. 2023; Folsom & Woodruff 2020; Pereg, Koren & Lishner 2008). Although treatment guidelines increasingly support multidisciplinary approaches, evidence remains limited regarding optimal care pathways, especially for rarer cancers or advanced disease stages during pregnancy (Borowska-Waniak et al. 2023; Eastwood-Wilshere et al. 2019; Pereg, Koren & Lishner 2008)

Furthermore, the psychosocial and emotional impact of pregnancy-associated cancer is profound. Women report significant psychological distress, shaped not only by the life-threatening nature of their illness but by the additional responsibility of safeguarding their unborn child (Ferrari et al. 2018; Harrison 2013). Unlike non-pregnant women, who can focus solely on their own health, pregnant women face the dual emotional burden of managing both maternal and foetal well-being (Kozu, Masujima & Majima 2020; Voulgaris, Pentheroudakis & Pavlidis 2011). This dual responsibility complicates decision-making and exacerbates emotional distress, creating treatment dilemmas distinct from those encountered in non-pregnant cancer diagnoses (Borowska-Waniak et al. 2023; Ferrari et al. 2018; Harrison 2013). Despite emerging recognition of the mental health burden, research

into tailored psychosocial interventions and mental health supports for this population remains scarce (Kozu, Masujima & Majima 2020; Roberts & Andrewes 2022). Overall, the literature highlights the urgent need for research that not only clarifies clinical management strategies but also addresses the underexplored psychological and emotional needs of women facing pregnancy-associated cancer.

2.3.1 The global incidence of pregnancy-associated cancer is on the rise

Previous studies have reported that the incidence of pregnancy-associated cancer has increased in recent years, raising significant concern, particularly among younger women during the reproductive period (Capozza et al. 2024; Eastwood-Wilshere et al. 2019; Javitt 2023). These concerns include the complexities of balancing maternal cancer treatment with foetal health, the potential impact of cancer therapies on pregnancy outcomes, the emotional and psychological toll on young mothers and their families, the risks of delayed cancer diagnosis due to pregnancy-related physiological changes, and the long-term implications for both maternal and child health (Capozza et al. 2024; Eastwood-Wilshere et al. 2019; Javitt 2023). This rise in incidence may be attributed to delayed childbearing associated with advanced maternal age and advances in diagnostic techniques that have led to cancer detection during pregnancy or the postpartum period (Botha, Rajaram & Karunaratne 2018; Korenaga & Tewari 2020; Parazzini et al. 2017; Safi et al. 2021; Wolters et al. 2021).

International research has documented this increasing trend, though incidence rates vary globally (Cottreau et al. 2019; Eibye, Kjær & Mellemkjær 2013; Lee et al. 2012; Min Hee et al. 2016). In Australia, the incidence of pregnancy-associated cancer rose markedly between 1994 and 2007, increasing from 112.3 to 191.5 cases per 100,000 maternities. (Lee et al. 2012). In Korea, the rate rose from 76.5 to 312 per 100,000 women giving birth between 1995 and 2013 (Min Hee et al. 2016). Similarly, in the United States, the incidence increased from 75 to 173 per 100,000 women giving birth from 2002 to 2012 (Cottreau et al. 2019). In Denmark, estimates show an increase from 5.4% to 8.3%, or 89.6 per 100,000 women giving birth, between 1977 and 2006 (Eibye, Kjær & Mellemkjær 2013).

Studies conducted in Italy did not observe an increasing trend in the incidence of pregnancy-associated cancer from 2001 to 2012 and 2003 to 2015, suggesting possible geographic and healthcare system variation (Murgia et al. 2019; Parazzini et al. 2017). This discrepancy warrants further investigation of the potential contributing factors, such as regional variations in cancer screening, reporting practices, population demographics, and healthcare access that may be associated with a higher risk of pregnancy-associated cancer.

2.3.2 Women's experiences after diagnosis with pregnancy-associated cancer

Women diagnosed with cancer during pregnancy, or the postpartum period encounter a range of experiences throughout the care and management process. These experiences encompass physical, emotional, mental health and psychological challenges, shaped by interactions with healthcare providers, treatment decisions, and the complexities of balancing maternal and foetal health needs.

Cancer care and communication support

Pregnancy-associated cancer care is complicated because there may be a conflict between the care of the mother and the impact of treatment on the foetus, especially in advanced stages of malignant disease (Hepner et al. 2019; Kobayashi et al. 2019; Zubor et al. 2018). This dual focus brings about various physical, emotional, and psychological challenges that often shape women's overall experience and perception of the care they receive. Some studies have suggested that multidisciplinary teamwork (including obstetricians, oncologists, paediatricians, and psychologists) may enhance mother and baby outcomes (Hepner et al. 2019). However, many questions remain about the provision of care for pregnancy-associated cancer, particularly when it involves uncommon cancers such as colorectal or pancreatic cancer. Very few studies have been conducted to determine maternal cancer care and experiences. Providing adequate cancer care remains challenging because of limited knowledge and understanding of how to best support women with pregnancy-associated cancer (Amarjothi et al. 2019; Boyd et al. 2012; Esposito et al. 2024).

Effective communication between HCPs and women is a critical component of cancer care, particularly in pregnancy-associated cancer (Hurren et al. 2023; Stafford et al. 2022). Women with pregnancy-associated cancer face unique and complex physical and emotional challenges as they manage both the health and well-being of their unborn children (Ferrari et al. 2018; Leung, Bryant & Stafford 2020). In navigating these complexities, compassionate communication from HCPs is essential, ensuring that women feel informed, supported, and involved in decision-making throughout their treatment (Hurren et al. 2023; Roberts & Andrewes 2022). Previous research has highlighted that communication is pivotal to women's experience with cancer care (Hurren et al. 2023; Kozu, Masujima & Majima 2020; Prades et al. 2014; Shim et al. 2016).

Women feel overwhelmed by the complexity of information surrounding their diagnosis, treatment options, and potential risks to their babies when they are diagnosed with pregnancy-associated cancer (Ferrari et al. 2018; Roberts & Andrewes 2022). Healthcare providers must carefully tailor their communication strategies to meet the unique needs of pregnant women, balancing the delivery of critical information with sensitivity to the emotional and psychological challenges these patients face (Hurren et al. 2023).

Inadequate communication can lead to heightened anxiety, confusion, and a sense of powerlessness in women with pregnancy-associated cancer (Roberts & Andrewes 2022). Women often face uncertainty about outcomes for both them and their babies, which can exacerbate their fear and distress (Ferrari et al. 2018; Roberts & Andrewes 2022). Open, transparent, and empathetic communication has been shown to improve patient satisfaction, enhance adherence to treatment plans, and build trust between patients and providers (Garcia Morillo & Cubillo 2021; Hurren et al. 2023; Kozu, Masujima & Majima 2020). Cancer care and communication support are integral to ensuring positive experiences among women diagnosed with pregnancy-associated cancer (Hammarberg et al. 2018; Roberts & Andrewes 2022).

The literature highlights a significant gap in the research on the experiences of mothers receiving cancer care during pregnancy or the postpartum period, particularly regarding the role of communication in shaping these experiences (Hammarberg et al. 2018; Hurren et al. 2023; Stafford, Sinclair, Gerber, Collins, et al. 2021; Stafford et al. 2022). Few studies have explored the critical importance of communication and specific services that can enhance the overall experience of women diagnosed with pregnancy-associated cancer (Hammarberg et al. 2018; Hurren et al. 2023; Kozu, Masujima & Majima 2020; Roberts & Andrewes 2022).

Addressing this gap is crucial because effective communication is integral to patient safety, building trust, and ensuring women feel supported throughout treatment. To optimise outcomes for women diagnosed with pregnancy-associated cancer, it is essential to adopt a woman-centred approach supported by multidisciplinary management and effective communication that addresses the unique needs and challenges women face during this highly challenging period (Giusti et al. 2020; Maggen et al. 2019; McCormack & McCance 2006; Silverstein et al. 2020). Therefore, it is essential to conduct further research on the cancer care and communication needs of women with pregnancy-associated cancer to gather more data for improving future counselling and management of both prenatal and postnatal care.

Women's priorities and needs during and after cancer treatment

The unique challenges of a pregnancy-associated cancer diagnosis require a thorough understanding of the priorities and support needs of affected women. Their concerns often extend beyond traditional cancer treatment and encompass emotional, psychological, and practical needs.

One of the primary concerns for women diagnosed with pregnancy-associated cancer is the health and safety of their foetus (Hammarberg et al. 2018; Leung, Bryant & Stafford 2020). This can lead to difficult decisions, such as delaying cancer treatment like chemotherapy or other systemic therapies until the second or third trimester when the risks to the foetus are lower (Esposito et al. 2016; Ngu & Ngan 2016). Women often strongly prefer receiving clear and consistent information about how different treatment options may impact foetal health, highlighting the importance of effective communication from HCPs (Hammarberg et al. 2018; Hurren et al. 2023).

Research indicates that women undergoing pregnancy-associated cancer treatment emphasise the importance of personalised care and shared decision-making; they prefer to be actively involved in treatment decisions and seek clear explanations about the risks and benefits of various options (Hori & Suzuki 2021; Linkeviciute et al. 2024; Mahmoodi & Sargeant 2019; Wolters et al. 2021). Shared decision-making fosters a sense of control and empowerment during an overwhelming and distressing experience (Aslani 2013; Mahmoodi & Sargeant 2019). Women with pregnancy-associated cancer seek individualised treatment plans that consider both their personal preferences and the unique requirements of their pregnancy (Garcia Morillo & Cubillo 2021; Roberts & Andrewes 2022; Stafford, Sinclair, Gerber, Collins, et al. 2021; Voulgaris, Pentheroudakis & Pavlidis 2011). However, the extent to which these tailored plans are successfully implemented can vary significantly.

Women's priorities extend beyond the immediate treatment period, with many expressing concerns about breastfeeding, the long-term effects of cancer treatment on both their health and their baby's health, fears of cancer recurrence, and future pregnancies (Faccio et al. 2020; Gorman et al. 2015; Leung, Bryant & Stafford 2020; Vanstone et al. 2021). They highly value ongoing support from their healthcare providers, including regular follow-up care and transparent information on fertility preservation options and future reproductive health.

Women diagnosed with pregnancy-associated cancer have a range of priorities that extend beyond the immediate concerns of cancer treatment. Their need encompasses the safety of their unborn child,

desire for personalised care, shared decision-making, and post-treatment support. Addressing these priorities requires a holistic, multidisciplinary approach from HCPs to ensure these women receive the comprehensive support they need during this challenging time.

2.3.3 Impact of pregnancy-associated cancer diagnosis on women

A diagnosis of pregnancy-associated cancer profoundly affects women's quality of life, encompassing the physical, emotional, psychological, and social dimensions (Burke et al. 2017; Sekse et al. 2019). The simultaneous management of pregnancy or caring for a newborn alongside cancer introduces complex challenges that can diminish women's overall well-being (Faccio et al. 2020).

The physical impact of cancer treatment during pregnancy often affects women's quality of life. Treatments, such as chemotherapy, surgery, and radiation, can result in nausea, pain, and other side effects that limit physical functioning and further reduce women's ability to engage in daily activities (Faccio et al. 2020; Hofman et al. 2007). Physical impairments, including decreased mobility and increased reliance on others for basic tasks, can significantly reduce quality of life and make routine tasks more challenging (Burke et al. 2017).

Although advancements in treatment and management have improved clinical outcomes, several critical aspects remain insufficiently addressed, particularly in mental health, psychological and social domains (Roberts & Andrewes 2022; Stafford, Sinclair, Gerber, Collins, et al. 2021). The literature highlights the complex and multifaceted nature of these challenges, which include psychological stress, the added responsibilities of caring for a newborn along with other young children, and the economic strain resulting from unemployment, all of which can significantly affect the mental health of both women and their partners (Faccio et al. 2020; Gotze et al. 2017; Salonen et al. 2011). The burden of pregnancy-associated cancer extends beyond the physical implications of the disease, encompassing the psychological distress associated with simultaneously managing pregnancy and cancer treatment. Women may experience anxiety related to the potential effects of treatment on both their health and the well-being of their foetus. This dual challenge and the overall strain on family dynamics further exacerbate the emotional toll (Ferrari et al. 2018; Leung, Bryant & Stafford 2020).

Impact on women's mental health

The mental health impact of a pregnancy-associated cancer diagnosis on mothers extends well beyond the initial diagnosis, influencing their well-being throughout pregnancy and the postpartum period (Ferrari et al. 2018; Roberts & Andrewes 2022). Research indicates that these women often experience significant anxiety, depression, and fatigue, particularly concerning the health of their unborn children, who may be exposed to chemotherapy or other systemic therapies (Faccio et al. 2020; Ferrari et al. 2018; Henry et al. 2012; Leung, Bryant & Stafford 2020; Roberts & Andrewes 2022). The dual burden of managing cancer while pregnant can lead to a sense of loss of control, which exacerbates stress and emotional distress (Faccio et al. 2020; Leung, Bryant & Stafford 2020). These concerns are compounded by fear of cancer recurrence and the safety of future pregnancies, creating a complex emotional landscape as they navigate the transition to motherhood while simultaneously confronting a life-threatening illness (Faccio et al. 2020; Gorman et al. 2015; Stafford, Sinclair, Gerber, Collins, et al. 2021; Vanstone et al. 2021).

This is even more difficult for women with young children and newborns (Salonen et al. 2011). The literature suggests that these women face significant difficulties in providing emotional and mental support to their children while simultaneously managing their health as cancer patients and primary caregivers (Salonen et al. 2011; Semple & McCaughan 2013). Additionally, the emotional disconnect some women feel from their pregnancy as they focus on cancer treatment can prevent them from embracing the anticipation and joy often associated with pregnancy. Instead, they may experience feelings of sadness, isolation, or guilt due to the illness and its treatment (Faccio et al. 2020; Vanstone et al. 2021). Due to physical limitations, emotional exhaustion, and the demands of treatment, women may find themselves withdrawing from social interactions, leading to feelings of loneliness (Stafford, Sinclair, Gerber, Collins, et al. 2021). This social withdrawal can further diminish their overall quality of life, reducing access to emotional support (Vanstone et al. 2021).

Unfortunately, mental health experiences for women with pregnancy-associated cancer remain under-researched, leaving a significant gap in understanding and support (Faccio et al. 2020; Leung, Bryant & Stafford 2020; Stafford, Sinclair, Gerber, Collins, et al. 2021). This gap underscores the need for further research to explore the adjustment and coping strategies employed by these women, particularly those diagnosed with cancer during pregnancy or postpartum, to better understand how to support them and their families effectively.

Impacts on partner or spouse

The diagnosis and treatment of pregnancy-associated cancer may also have profound implications for partners or spouses who often face challenges. While there is an extensive body of research exploring the impact of cancer diagnoses on partners and family members in the general oncology population, studies specifically examining the experiences of partners or spouses of women diagnosed with pregnancy-associated cancer are extremely limited (Vandenbroucke, Han, et al. 2017). Therefore, insights from the broader cancer caregiving literature are drawn upon here to help understand potential challenges faced by partners in the context of pregnancy-associated cancer (Akyüz et al. 2008; Drabe et al. 2013; Möllerberg et al. 2016). A recent study conducted in Malta found that cancer diagnoses in female partners or spouses place additional burdens on male partners as they struggle to balance work, domestic responsibilities, and caregiving duties (Catania, Sammut Scerri & Catania 2019). This study further highlighted the psychological stress experienced by male partners, particularly the emotional strain caused by their partner's fear of disease recurrence. This stress can negatively impact the well-being and mental health of the entire family including children (Catania, Sammut Scerri & Catania 2019).

The emotional burden of cancer can significantly affect the dynamics and quality of a couple's relationship, leading to increased stress and tension (Akyüz et al. 2008; Drabe et al. 2013; Vandenbroucke, Han, et al. 2017). Research suggests that open communication, social support, and psychological resilience (hardiness) are critical factors that can improve the quality of life of patients and their partners (Badr 2017; Senneseth et al. 2017). Although there is substantial research on caregiving in the general oncology population, many studies focus on specific cancer types or age groups and often exclude divorced or widowed spouses and single-parent families (Catania, Sammut Scerri & Catania 2019; Senneseth et al. 2017) and the literature on the impact of pregnancy-associated cancer diagnoses on partners is extremely limited. By addressing these areas, future research can provide critical insights into managing the psychological and mental health impacts of pregnancy-associated cancer on the entire family, ultimately improving their overall well-being and quality of life.

2.3.4 Management of pregnancy-associated cancer

Clinical management of pregnancy-associated cancer is complex because of the lack of evidence-based approaches and logistical challenges involved in the treatment of pregnancy-associated cancer. These challenges become even more definite when managing advanced or rare pregnancy-associated

cancers, such as colorectal, pancreatic, head and neck, or oral cancers (Boyd et al. 2012; Cordeiro & Gemignani 2017; Figueiró-Filho et al. 2019; Munteanu et al. 2019; Ouh, Cho & Na 2020). The primary focus in managing pregnancy-associated cancer is to ensure the safety of both the mother and baby throughout the diagnosis and treatment process (De Haan et al. 2018). However, the lack of comprehensive data, particularly regarding the impact of novel anticancer medications for pregnancy-associated cancer, poses significant obstacles to the development of standardised treatment and management protocols (Eastwood-Wilshire et al. 2019; Silverstein et al. 2020; Wolters et al. 2021). A multidisciplinary approach is critical for effectively managing pregnancy-associated cancer, which requires the collaboration of HCPs from various specialties, including obstetrics, oncology, paediatrics, and psychology. Integrating diverse expertise is essential to address the complex medical and psychosocial needs of women with pregnancy-associated cancer (Greiber et al. 2022; Hepner et al. 2019; Melan et al. 2017; Silverstein et al. 2020).

2.3.5 Diagnosis of pregnancy-associated cancer

The diagnosis of cancer during pregnancy presents significant challenges and often leads to delays in diagnosis. The timing of diagnosis is variable, occurring at any point during pregnancy or the postpartum period. The following section provides a detailed analysis of the findings in the literature.

Delays in diagnosis

The literature consistently highlights significant delays in diagnosing pregnancy-associated cancer, which can be attributed to a combination of patient-related and systemic challenges. Patient-related aspects include the misinterpretation of cancer symptoms as pregnancy discomfort, which can lead to delays in seeking medical attention (Johansson et al. 2019; Kocián et al. 2019; Silverstein et al. 2020). This issue is particularly pronounced in rare cancers such as colorectal or gastric cancer, where symptoms may overlap with typical pregnancy-related changes (Kocián et al. 2019; Shemer et al. 2022). Additionally, the natural focus on the developing foetus and a general lack of awareness of cancer symptoms during pregnancy further exacerbate these delays (Johansson et al. 2019).

Routine prenatal screening and care are primarily focused on monitoring and managing the health of both the mother and the foetus during pregnancy. Routine healthcare for the mother is overlooked outside the pregnancy-specific context, which can sometimes lead to missed or delayed cancer diagnoses (Johansson et al. 2019). Moreover, clinicians hesitate to perform radiologic or invasive

diagnostic procedures during pregnancy due to a lack of specific evidence-based guidelines, further delaying the diagnosis (Botha, Rajaram & Karunaratne 2018; Hepner et al. 2019; Vandecaveye et al. 2021; Woitek et al. 2016).

A study by Sekine et al. (2018) found that while prenatal checkups in Japan contribute to the early detection of gynaecological cancers, there are still notable delays in diagnosing non-gynaecological cancers during pregnancy (Sekine et al. 2018). For instance, early detection of melanoma by identifying pigmented lesions during pregnancy is possible. However, diagnosis is often delayed due to limited awareness among clinicians and patients and insufficient screening protocols (Hepner et al. 2019; Still & Brennecke 2017). Therefore, an early diagnosis remains a significant challenge.

Previous research has suggested that HCPs often misattribute cancer symptoms to pregnancy-related discomforts, such as nausea, vomiting, abdominal pain, and altered bowel habits, resulting in diagnostic delays and poorer outcomes (Amarjothi et al. 2019; Constantin et al. 2023; Hepner et al. 2019; Hussain et al. 2018; Munteanu et al. 2019). Furthermore, studies indicate that many cancer cases during pregnancy are diagnosed at advanced stages because of missed warning signs and a general lack of suspicion among HCPs, who may not initially consider cancer in young, otherwise healthy pregnant women (Amarjothi et al. 2019; Hepner et al. 2019; Kocián et al. 2019; Rogers et al. 2022). This tendency contributes significantly to delays in diagnosis.

According to previous studies, cancer is less frequently diagnosed during pregnancy than postpartum. Studies by Ives et al. (2005) and Lee et al. (2012) reported that two-thirds of pregnancy-associated cancers are diagnosed within the first year postpartum rather than during pregnancy (Ives, Saunders & Semmens 2005; Lee et al. 2012). This observation is further validated by a large Swedish study, which found a significant delay in cancer diagnosis during pregnancy, with 54% of cases being diagnosed postpartum compared to just 4% to 7% diagnosed during pregnancy (Andersson et al. 2015). The physiological changes associated with pregnancy can obscure cancer symptoms, often resulting in missed or delayed diagnoses that are only identified during the postpartum period (Kocián et al. 2019; Silverstein et al. 2020).

Timing of diagnosis

The literature reveals a distinct pattern in the timing of cancer diagnoses during pregnancy, with higher rates observed in the third trimester than in the earlier stages, suggesting that cancer may be more challenging to detect in the initial stages of pregnancy (Amarjothi et al. 2019; Andersson et al. 2015;

Johansson et al. 2019; Predescu D et al. 2020). Andersson et al. (2015) noted that cancer diagnoses are most frequently made in the third trimester, indicating an increased likelihood of detection as the pregnancy progresses (Andersson et al. 2015). This increased likelihood in the third trimester suggests that as pregnancy advances, both patients and clinicians may become more attuned to symptoms that could indicate cancer. Conversely, cancer diagnosis is less common in the first trimester, potentially because the focus is primarily on typical pregnancy symptoms, which may obscure early cancer indicators and delay detection.

The timing of diagnosis also varies according to the cancer type. For instance, colon and endocrine cancers are more commonly diagnosed in the second trimester, potentially due to symptom onset aligning with physical changes that prompt further investigation (Amarjothi et al. 2019; Andersson et al. 2015; Predescu D et al. 2020). These findings underscore the complexity of cancer diagnosis during pregnancy and highlight the importance of heightened awareness and tailored diagnostic approaches at each stage of gestation.

Challenges in the diagnostic approach to pregnancy-associated cancer

A systematic and thorough physical examination combined with a proactive approach to additional diagnostic investigations in pregnancy is challenging (Maggen et al. 2019; Wolters et al. 2021). Comprehensive physical examination can be complicated for detecting colorectal cancer, gynaecological cancers (such as ovarian or cervical cancer), and other abdominal and pelvic cancers during pregnancy due to the anatomical changes caused by the enlarging uterus (Hepner et al. 2019; Kocián et al. 2019; Munteanu et al. 2019; Silverstein et al. 2020), but diagnosing early-stage cancers such as melanoma or breast cancer may be relatively more straightforward during pregnancy. Nevertheless, an expert clinical eye is essential for early detection and accurate diagnosis. Serum tumour markers have potential value in the diagnosis and monitoring of cancer, such as ovarian cancer, but their effectiveness is limited during pregnancy due to substantial physiological fluctuations in serum levels, which can lead to variability in diagnostic accuracy (Han et al. 2012; Michalczyk & Cymbaluk-Płowska 2021).

Imaging modalities such as ultrasonography and magnetic resonance imaging (MRI) are universally recommended and safe methods for diagnosing and determining pregnancy stages in all trimesters (Botha, Rajaram & Karunaratne 2018; Hepner et al. 2019; Silverstein et al. 2020; Vandecaveye et al. 2021). USG is particularly beneficial because it poses no risk to the foetus. However, its diagnostic accuracy in detecting deep pelvic or abdominal tumours, such as colorectal or ovarian cancers, may be

limited by the operator's skill and the progression of pregnancy (Maggen et al. 2019; Michalczyk & Cymbaluk-Płowska 2021; Yang & Han 2021).

MRI is often preferred for more detailed imaging, especially in cancer staging, as it does not expose the foetus to ionising radiation. However, the use of gadolinium-based contrast agents during MRI requires careful consideration due to potential foetal risks, and it is generally avoided unless necessary (Botha, Rajaram & Karunaratne 2018; Eastwood-Wilshere et al. 2019; Maggen et al. 2019; Silverstein et al. 2020). For staging purposes, chest radiography with proper abdominal shielding is recommended for various types of pregnancy-associated cancers, particularly those that may involve or spread to the lungs, such as colorectal, breast or ovarian cancer. This procedure can be safely performed during pregnancy with minimal radiation exposure to the foetus (Eastwood-Wilshere et al. 2019; Hepner et al. 2019; Jha et al. 2022; Silverstein et al. 2020).

The application of computed tomography (CT) and mammography should be cautiously limited to situations where the clinical benefits substantially outweigh the potential risks, particularly in non-emergency, elective scenarios (Hepner et al. 2019; Silverstein et al. 2020). Additionally, invasive diagnostic procedures, including biopsies (lymph node biopsy or bone marrow biopsy to diagnose lymphoma or leukemia), fine-needle aspiration for breast cancer, and lumbar puncture, can be performed safely during pregnancy with the use of appropriate sedation techniques to minimise risk (Eastwood-Wilshere et al. 2019; Hepner et al. 2019; Silverstein et al. 2020). This cautious yet comprehensive approach to diagnostic evaluation promptly identifies and manages cancer, optimising outcomes for both the mother and foetus while minimising potential risks associated with diagnostic procedures during pregnancy. (Botha, Rajaram & Karunaratne 2018).

2.3.6 The most common treatment protocols for pregnancy-associated cancer

The treatment protocols for pregnancy-associated cancer present distinct challenges that set them apart from the management of other cancers while adhering to the standard approach of individualised care and multidisciplinary team planning. These treatment protocols are highly individualised and depend on various factors, including the type and stage of cancer as well as the trimester of pregnancy, which present significant challenges due to the limited availability of treatment data from retrospective studies (Hepner et al. 2019; Maggen et al. 2019; Niu, Li & Mueller 2019;

Wolters et al. 2021). It requires a delicate balance, aiming to maximise the therapeutic benefits for the mother while minimising potential risks to the foetus.

This balance is particularly challenging in malignant tumours or advanced-stage cancers, which require more aggressive treatments than benign neoplasms, which are non-cancerous (Liu et al. 2015; Niu, Li & Mueller 2019). The diagnosis of malignant disease during pregnancy is often delayed, and the prognosis is poor (Kobayashi et al. 2019; Ulrikh et al. 2022). Immediate follow-up examinations are crucial for early detection of malignant tumours during pregnancy or postpartum, with treatment not delayed unless necessary (Kobayashi et al. 2019; Ulrikh et al. 2022). In contrast, managing benign tumours, which do not have malignant potential, tends to be less complex during pregnancy and postpartum, often allowing for more conservative approaches (Liu et al. 2015; Niu, Li & Mueller 2019).

Notably, modern medical treatments have advanced to the point where pregnant women can receive cancer therapy with outcomes comparable to those of non-pregnant women, allowing for childbirth without significant complications (Garcia Morillo & Cubillo 2021). The guiding principle in the treatment of cancer in pregnant women is to maintain an equivalent standard of care provided to non-pregnant patients while prioritising the well-being of both the mother and the foetus (Zagouri et al. 2016). However, ethical dilemmas often arise in clinical decisions that affect the mother and newborn's future. A recent study emphasised that oncological treatments must carefully balance the mother's and child's risks and benefits. This underscores the need for a nuanced approach that considers the ethical complexities inherent in these cases (Schwab, Anic & Hasenburg 2021).

Although the management of pregnancy-associated cancer is challenging, particularly for advanced or malignant diseases, advances in treatment protocols have made it possible to administer effective therapies during pregnancy or the postpartum period. Nonetheless, ongoing research and ethical deliberation are essential to continue improving the outcomes for both mothers and their offspring.

Surgical treatment for pregnancy-associated cancer

The timing of surgical intervention for cancer during pregnancy is carefully determined by weighing the potential risks to both the mother and foetus (Eastwood-Wilshere et al. 2019; Hepner et al. 2019; Maggen et al. 2019). Evidence suggests that anaesthetic and surgical procedures are safest during pregnancy, especially during the second trimester, achieving favourable maternal oncologic outcomes with minimal harm to the foetus (Eastwood-Wilshere et al. 2019; Hepner et al. 2019; Maggen et al. 2019; Upadya & Saneesh 2016). Van Calsteren et al. (2010) reported that approximately 65.7% of

women diagnosed with cancer during pregnancy underwent surgery (Van Calsteren et al. 2010). Although there is a low risk of miscarriage during the first trimester, surgery should not be delayed if necessary for the mother's health (Figueiro-Filho et al. 2018; Hepner et al. 2019). This recommendation is based on the understanding that delaying essential surgical interventions can lead to cancer progression, thereby compromising both maternal and foetal outcomes. Previous studies also highlighted concerns that major abdominal or pelvic surgeries during pregnancy, especially pregnancy-associated colorectal cancer, might carry higher risks of complications and morbidities, necessitating careful consideration and planning (Aytac et al. 2016; Hepner et al. 2019; Kobayashi et al. 2019; Kocián et al. 2019; Peccatori et al. 2013).

Radiation treatment for pregnancy-associated cancer

Radiotherapy, which utilises high doses of radiation ranging from 40 to 70 Gy, is a standard cancer treatment method (Dauer et al. 2012). However, during pregnancy, its application is typically avoided owing to the potential harm to the foetus, as the dose is significantly higher than that used in diagnostic procedures (Dauer et al. 2012; Kal & Struikmans 2005; Mazzola et al. 2019). Despite these concerns, there are certain urgent clinical situations, such as spinal cord compression, central nervous system metastasis, and the need to treat specific cancers, where the use of radiotherapy before delivery may be warranted (Chen et al. 2008; Peccatori et al. 2013). Several factors, including the total radiation dose and proximity of the treatment area to the foetus, influence the extent of foetal radiation exposure during treatment (Mazzola et al. 2019). To mitigate the associated risks, protective measures, such as the use of shielding and maintaining an appropriate distance from the foetus, are essential (Dauer et al. 2012; Mazzola et al. 2019).

Although radiotherapy may be feasible for treating cancers in areas such as the head, neck, arms, or legs, with minimal risk to the foetus (Mazzola et al. 2019; Needleman & Powell 2016). It is generally not recommended for cancers of the abdomen or pelvis, where the risk of foetal exposure is significantly higher (Mazzola et al. 2019; Pereg, Koren & Lishner 2008). In such cases, consideration of pregnancy termination may arise as a complex and ethically challenging decision (Fenig et al. 2001; Mazzola et al. 2019). Radiotherapy remains a critical approach for pregnancy-associated cancer treatment, and its use during pregnancy requires careful consideration of its risks and benefits.

Chemotherapy and other systemic therapy for pregnancy-associated cancer

Systemic therapy for pregnancy-associated cancer includes chemotherapy, hormonal therapy, and monoclonal antibodies (Silverstein et al. 2020). However, the administration of therapeutic agents during pregnancy is associated with adverse effects on the growing foetus (Capozza et al. 2024; Hepner et al. 2019; Maggen et al. 2019; Yu et al. 2023). These risks are especially pronounced with chemotherapy administered during the first trimester, a critical period of organogenesis (Momen et al. 2017; Schuurman et al. 2019; Zubor et al. 2018). Several studies have underscored the dangers of administering chemotherapy in the first trimester, highlighting its potential to cause severe foetal anomalies (Esposito et al. 2016; Kobayashi et al. 2019; Momen et al. 2017). However, some studies have suggested that foetal complications during this period may not always be directly attributable to chemotherapy, as genetic factors also play a critical role in congenital anomalies (Han et al. 2013; Momen et al. 2017).

Specific chemotherapeutic agents, such as methotrexate, dacarbazine, cyclophosphamide, and cytarabine, are of particular concern due to their high teratogenic potential (Azim, Peccatori & Pavlidis 2010; Dawson et al. 2014; Selig et al. 2012). Additionally, targeted agents, such as trastuzumab, and hormonal treatments, such as tamoxifen, are discouraged during pregnancy because of teratogenicity concerns (Azim, Peccatori & Pavlidis 2010; Lambertini, Peccatori & Azim 2015).

Chemotherapy administered after the first trimester is generally considered safer (Garofalo et al. 2017; Hepner et al. 2019; Kobayashi et al. 2019). Data regarding the use of taxane-based chemotherapy during pregnancy are reassuring, with studies indicating no significant increase in adverse maternal or foetal outcomes when administered after the first trimester (Azim, Peccatori & Pavlidis 2010; Cardonick et al. 2012; Ferrigno Guajardo et al. 2024; Zagouri et al. 2013). However, current evidence is limited, and more long-term follow-up studies are needed to comprehensively assess these agents' impact on foetal development. Administering chemotherapy 3-4 weeks before delivery is recommended to prevent haematological toxicity, which could lead to maternal and neonatal infections and bleeding complications (Dekrem, Van Calsteren & Amant 2013; Hepner et al. 2019).

Although chemotherapy may be associated with some effects, such as preterm delivery, low birth weight, and intrauterine growth restriction, most women prefer to continue their pregnancy rather than terminate it, as highlighted by several studies (Abdalla et al. 2017; Abdel-Hady et al. 2012; Danet et al. 2018). The association between preterm birth and chemotherapy, long-term neurological,

cardiotoxic, and psychological effects in children remain poorly understood (Dekrem, Van Calsteren & Amant 2013; Framarino-dei-Malatesta et al. 2015; Framarino-dei-Malatesta, Sammartino & Napoli 2017; Kobayashi et al. 2019).

A recent multicentre observational study from China found that women who received chemotherapy established a statistically significant reduction in mortality rates compared to those who did not (Yp et al. 2019). These findings suggest that chemotherapy may contribute to improved survival outcomes for women diagnosed with cancer during pregnancy without adversely impacting child mortality or developmental outcomes. This is reassuring; however, concerns are particularly pronounced when systemic treatment is required for a rare or advanced stage of cancers such as pregnancy-associated colorectal cancer, which has unique management challenges during pregnancy (Aytac et al. 2016; Kocián et al. 2019). Chemotherapy is a critical component of treating advanced or metastatic colorectal cancer. After the first trimester, it is considered safer, and treatment options like 5-Fluorouracil (5-FU) and Oxaliplatin, often used in combination (e.g., FOLFOX), can be administered with careful monitoring (Frydenberg et al. 2020; Kozai et al. 2022; Makoshi et al. 2015; Rogers, Dasari & Eng 2016). These regimens are effective in managing colorectal cancer while minimising risks to the foetus. However, currently, there is no standardised, evidence-based guideline for managing pregnancy-associated colorectal cancer due to its complex and variable nature; most of the studies are single case studies and require further research (Rogers, Dasari & Eng 2016; Rogers et al. 2022).

Despite these challenges, evidence supports the effectiveness of systemic therapies, including taxane-based chemotherapy and anthracyclines, in improving maternal oncologic outcomes without causing significant harm to the foetus (Azim, Peccatori & Pavlidis 2010; Ferrigno Guajardo et al. 2024; Framarino-dei-Malatesta, Sammartino & Napoli 2017; Zheng et al. 2017). These findings discourage practices such as pregnancy termination or early delivery in pregnant women with cancer, emphasising that treatment can be safely managed in many cases to support both maternal and foetal health (Capozza et al. 2024; De Haan et al. 2018; Esposito et al. 2016; Ferrigno Guajardo et al. 2024).

Although these findings are promising, further research is required. Current studies are limited by their retrospective nature, small sample size, and lack of generalisability (Hepner et al. 2019; Maggen et al. 2019; Silverstein et al. 2020). Most therapies used to treat cancer during pregnancy are classified as teratogens, primarily based on findings from animal studies. However, assessing their safety in humans is challenging because of the rarity of cancer during pregnancy and the ethical considerations surrounding clinical trials in this population (Hepner et al. 2019; Silverstein et al. 2020). Long-term data collection on children exposed to chemotherapy in utero and the exploration of novel targeted

therapies for pregnant women diagnosed with cancer are crucial for advancing the understanding and management of pregnancy-associated cancer.

2.3.7 Maternal outcomes

The clinical characteristics and maternal outcomes of pregnancy-associated cancer vary significantly, depending on the type of cancer and its management. A retrospective cohort study by Min Hee et al. (2016) conducted between 1995 and 2013 revealed substantial variability across maternal characteristics, gestational age at diagnosis, cancer type, stage, symptoms and signs, cancer treatment, pregnancy management, and subsequent perinatal and maternal outcomes, including the maternal mortality rate (Min Hee et al. 2016). Notably, 49.3% of women delivered prematurely, and the overall maternal mortality rate was 31%. Despite these challenges, 79.3% of women decided to continue their pregnancies, underscoring the need for timely diagnosis and carefully tailored management strategies to improve maternal outcomes (Min Hee et al. 2016).

Maternal outcomes during pregnancy tend to be more favourable for common cancers, such as melanoma, cervical, and breast cancers, than for less common cancers, such as pancreatic, head and neck, bone, or oral cancers (Boyd et al. 2012; Maxwell et al. 2019; Simoes et al. 2018). However, evidence indicates that women with pregnancy-associated cancer tend to experience worse obstetric outcomes than those without a cancer diagnosis (Maxwell et al. 2019; Simoes et al. 2018). These adverse outcomes include significantly higher risks of thromboembolic events, with an adjusted odds ratio (AOR) of 6.50 (95% CI 3.5–12.1) reported in the cancer-in-pregnancy group compared to women without cancer (Greiber et al. 2021). Additionally, the odds of severe maternal morbidities, including acute abdomen, acute renal failure, and hysterectomy, were markedly elevated, with an AOR of 5.07 (95% CI 3.72–6.90) in the gestational cancer group and an AOR of 1.55 (95% CI 1.16–2.09) in the postpartum cancer group, compared to women without cancer (Safi et al., 2023; Esposito et al., 2021; Walters et al., 2024) (Safi et al. 2023). Additionally, women with pregnancy-associated cancer are at an increased risk of antenatal hospitalisation, planned preterm births, labour induction, caesarean section deliveries, and prolonged hospital stays due to various complications (Esposito et al. 2021; Greiber et al. 2021; Lee et al. 2012; Safi et al. 2023; Walters et al. 2024).

A recent population-based study from the USA further highlighted the increased risks for gestational diabetes, preeclampsia, eclampsia, obstructed labour, and caesarean delivery among women diagnosed with benign or malignant tumours during pregnancy (Niu, Li & Mueller 2019). Similarly, a

recent cohort study by Greiber et al. (2022) found that cancer during pregnancy increases the risk of induced abortion and planned premature births (Greiber et al. 2022). Despite these risks, evidence suggests no significant long-term maternal complications following cancer treatment during pregnancy or the postpartum period (Greiber et al. 2022; Maggen et al. 2019; Maxwell et al. 2019). Moreover, advancements in antenatal treatments, such as chemotherapy, have improved maternal outcomes in recent years (De Haan et al. 2018; Yp et al. 2019).

Breastfeeding outcomes for women undergoing cancer treatment during pregnancy or the postpartum period present additional challenges. Stopenski et al. (2017) found that chemotherapy during pregnancy often led to decreased milk supply, resulting in breastfeeding difficulties (Stopenski et al. 2017). Furthermore, breastfeeding is frequently discouraged when systemic treatments continue postpartum due to limited safety data and concerns about potential neonatal complications (Ngu & Ngan 2016; Wolters et al. 2021). These findings emphasise the need for further research to assess the impact of cancer treatment on breastfeeding practices and neonatal health.

In addition to physical and clinical challenges, pregnancy-associated cancer imposes significant emotional and mental health burdens on affected women. Despite the complexity of the care involved, few studies have addressed the healthcare experiences of women diagnosed with cancer during pregnancy or postpartum (Boyd et al. 2012; Figueiro-Filho et al. 2018; Vanstone et al. 2021). Therefore, further research is crucial to evaluate maternal experiences to improve maternal outcomes during this challenging period. **Table 2.2** shows studies on maternal outcomes observed between 2010 and 2023.

Table 2.2 Studies on maternal outcomes observed between 2010 and 2023

Author/Year	Country	Sample	Study	Maternal Outcome
Lee et al. (2012)	Australia	N=1798	Population-based cohort study	Women with cancer diagnosed during pregnancy had high rates of labour induction (28.5%), caesarean section (40.0%) and planned preterm birth (19.7%).
Shim et al. (2016)	Korea	N=87	Retrospective cohort study	80% of women continued their pregnancy. Early diagnosis was associated with improved maternal outcomes.
Stopenski et al. (2017)	USA	N=96	Cohort study	Breastfeeding difficulties, including inadequate breast milk supply, are common after chemotherapy.
Simoes et al. (2018)	Germany	N=25	Retrospective single-institution study	Breast cancer diagnosis in the postpartum period was associated with a poorer prognosis.
Niu et al. (2019)	USA	N=13156 (benign) N=707 (malignant)	Population-based cohort study	Maternal outcomes may be associated with gestational diabetes, preeclampsia/eclampsia, obstructed labour, and caesarean delivery.
Yp et al. (2019)	China	N=118	Observational study	Chemotherapy reduces the mortality rate in pregnant women with (1:9 vs 26:23, P=0.016) cancer but is associated with an increased rate of caesarean delivery (84.7% vs 52.5%, P=0.001) compared to those not exposed to chemotherapy
Esposito et al. (2021)	Italy	N=831	Population-based cohort study	Pregnancy-associated cancer was associated with labour induction or planned delivery.
Greiber et al. (2022)	Denmark	N=1068	Cohort study	Pregnancy-associated cancer is associated with an increased risk of induced abortion (24.8% vs. 20.0%) and planned preterm birth (11.8% vs. 1.3%) compared to pregnancies without cancer.
Safi et al. (2023)	Australia	N=2373	Populational-based observational study	Women with pregnancy-associated cancer are more likely to have serious maternal complications, such as acute abdominal and acute renal failure, which were significantly higher compared to no cancer group.

Maternal prognosis and survival following pregnancy-associated cancer

The prognosis and survival outcomes for women diagnosed with pregnancy-associated cancer vary significantly across studies, highlighting the complexity of the condition and the multiple factors influencing these outcomes. Generally, pregnancy itself does not adversely affect maternal prognosis when compared to non-pregnant patients matched by age, cancer stage, and treatment regimens unless there is an urgent need for cytotoxic treatment during the first trimester, which poses additional risks (Pereg, Koren & Lishner 2008; Van Calsteren & Amant 2014).

Stensheim et al. (2009) found that pregnancy-associated cancer diagnoses did not increase the risk of mortality, with the notable exception of melanoma, where pregnant women exhibited a worse prognosis than non-pregnant women (Stensheim et al. 2009). However, contrasting findings were reported by Jones et al. (2017), who observed no significant differences in the prognosis between pregnant and non-pregnant women diagnosed with melanoma, indicating the need for further investigation (Jones et al. 2017). Regarding gynaecological malignancies, current evidence suggests that pregnancy does not adversely affect prognosis (Korenaga & Tewari 2020). Similarly, studies on breast cancer and lymphoma have also found no significant differences in prognosis between pregnant and nonpregnant women (Evens et al. 2013; Johansson et al. 2019; Lundberg et al. 2024). Recent research indicates that modern medical treatments can effectively manage cancer during pregnancy, resulting in outcomes comparable to those in the non-pregnant population and enabling childbirth without significant adverse sequelae (Garcia Morillo & Cubillo 2021; Lundberg et al. 2024).

However, the survival rates and prognosis in women with pregnancy-associated cancer can vary significantly depending on the cancer type, stage, and the presence of metastasis. Pregnant women with advanced malignant diseases generally have a poorer prognosis (Amarjothi et al. 2019; Kobayashi et al. 2019). Hepatocellular carcinoma during pregnancy is associated with a high risk of maternal mortality (Marasciulo et al. 2024). In contrast, colorectal cancer presents a similar prognosis and survival rate to that of the general population despite often being diagnosed at a more advanced stage (Aytac et al. 2016; Dahling et al. 2009). However, the small sample sizes in these studies limit the ability to draw definitive conclusions, and further broad-scale research is necessary.

2.3.8 Neonatal and children's long-term outcomes

The impact of pregnancy-associated cancer extends beyond maternal health and has significant implications for neonatal and long-term outcomes in children. The interplay between maternal cancer treatment and foetal development raises concerns about potential adverse effects on neonates, including preterm birth, low birth weight, and neonatal intensive care unit (NICU) admissions (De Haan et al. 2018). While immediate outcomes, such as survival rates and neonatal complications, have been well documented, the long-term health, developmental, and psychological effects on children exposed to cancer treatments in utero remain poorly understood.

Neonatal outcomes following pregnancy-associated cancer

Cancer treatment during pregnancy has been associated with a range of adverse neonatal outcomes, including preterm birth, low birth weight, low Apgar scores, small for gestational age (SGA), neonatal distress, and admissions to the neonatal intensive care unit (NICU) (De Haan et al. 2018; Garofalo et al. 2017; Maggen et al. 2019; Momen et al. 2018). Among these, preterm birth has been consistently identified as the most common adverse neonatal outcome in women diagnosed with cancer during pregnancy (De Haan et al. 2018; Esposito et al. 2021; Garofalo et al. 2017; Maggen et al. 2019; Momen et al. 2018; Shechter Maor et al. 2019; Sullivan et al. 2022).

De Haan et al. (2018) reported a notably high incidence of preterm births (48%) among women diagnosed with any type of cancer during pregnancy (De Haan et al. 2018). Furthermore, a recent study found an even higher incidence of preterm births (83.8 %) among women exposed to chemotherapy during pregnancy than those who were not exposed (Capozza et al. 2024). Few other recent studies also reported that, apart from preterm birth and foetal growth restriction, there were no significant complications for neonates following cancer treatment during pregnancy (Esposito et al. 2021; Maxwell et al. 2019; Saad et al. 2023; Shechter Maor et al. 2019).

Prematurity remains a significant global health concern, as it is a leading contributor to neonatal mortality and morbidity (De Haan et al. 2018; Harrison & Goldenberg 2016; Lataifeh et al. 2011). Lu et al. (2017) found that the risk of neonatal death for infants born to women with cancer during pregnancy was nearly three times higher than that for those born to women without cancer, primarily due to prematurity (Lu et al. 2017). A nationwide cohort study in Denmark supported these findings,

indicating that pregnancy-associated cancer increases the risk of planned preterm birth, leading to higher rates of neonatal morbidity and mortality (Greiber et al. 2022).

The association between NICU admission and preterm birth has been well-documented across several extensive cohort studies for women diagnosed with cancer during pregnancy (De Haan et al. 2018; Garofalo et al. 2017). However, the frequency of NICU admission may also vary for different cancers. For instance, De Haan et al. (2018) reported that infants born to women with gastrointestinal cancers had the highest NICU admission rates. In contrast, those born to women with gestational thyroid, abdominal, or cervical cancers had the lowest rates of NICU admission (De Haan et al. 2018). Further large-scale and longitudinal studies are necessary to draw definitive conclusions regarding the risks and neonatal outcomes associated with cancer treatment during pregnancy. **Table 2.3** shows studies on neonatal outcomes observed between 2011 and 2024.

Table 2.3 Studies on neonatal outcomes observed between 2011 and 2024

Author/Year	Country	Sample	Study	Neonatal Outcomes
Abdel-Hady et al. (2012)	Egypt	N=118	Prospective study	Chemotherapy exposure during the second and third trimesters in utero causes minimal morbidity to the unborn foetus.
Amant et al. (2012)	Belgium, Netherlands, Czech Republic	N=114	An observational study	Prematurity was common and was associated with impaired cognitive function following chemotherapy exposure. However, cardiac and central nervous system functions were unaffected.
Cardonick et al. (2015)	USA	N=57	Cohort study	There were no significant cognitive or behavioural differences between chemotherapy-exposed and non-exposed groups of children.
Garofalo et al. (2017)	Italy	N=59	Retrospective study	There was an increased rate of preterm birth and small for gestational age neonates, but it was not statistically significant.
Lu et al. (2017)	Sweden	N=984	Cohort	Maternal cancer during pregnancy is linked to an increased risk of rare but severe outcomes, such as stillbirth and neonatal mortality.
DeHaan et al. (2018)	INCIP (16 countries of EUROPE)	N=1170	Descriptive cohort study	Babies exposed to chemotherapy were more likely to be small for gestational age and require NICU admission compared to those not exposed.
Momen et al. (2018)	Denmark	N=5523365	Population-based register study	The findings indicate a link between pregnancy-associated cancers and adverse birth outcomes in the offspring.
Esposito et al. (2021)	Italy	N=831	Population-based study	Pregnancy-associated cancer was associated with iatrogenic preterm delivery.
Greiber et al. (2022)	Denmark	N=1068	Cohort	Planned premature birth and neonatal morbidity and mortality were common for babies exposed to chemotherapy.
Lundberg et al. (2024)	Sweden	N=880	Population-based matched study	Planned preterm births were more common.
Capozza et al. (2024)		N=37	Observational study	There is an increased risk of prematurity and small for gestational age after chemotherapy exposure.

Children's long-term outcomes following pregnancy-associated cancer

The long-term outcomes of children exposed to chemotherapy or other systemic cancer treatments in utero remain an area of limited research with a notable scarcity of published data. Few previous studies showed that children born to mothers diagnosed with cancer during pregnancy exposed to chemotherapy in utero had no significant differences in cognitive, behavioural, general, and neurological development and school performance in early childhood compared with those born to healthy mothers (Amant et al. 2015; Cardonick et al. 2015). Moreover, early studies by Nulman et al. (2001) and Aviles et al. (2001) reported normal neurological development and the absence of long-term congenital, neurological, or psychological abnormalities in children whose mothers were treated for malignancies during pregnancy (Avilés & Neri 2001; Nulman et al. 2001), including those exposed during the first trimester (Avilés & Neri 2001).

Additionally, studies have shown that in-utero exposure to anthracyclines is not associated with cardiac dysfunction, further supporting the notion that chemotherapy may not have significant short-term adverse effects on growth, cognitive function, or cardiac health in children (Amant et al. 2012; Avilés & Neri 2001; Murthy et al. 2014). A recent study by Vandenbroucke et al. (2017) supports these findings, suggesting that chemotherapy exposure in utero does not significantly affect future neurocognition or long-term health issues (Vandenbroucke, Verheecke, et al. 2017). Similarly, Passera et al. (2019) concluded that in-utero exposure to chemotherapy, including anthracyclines and cyclophosphamide, did not affect foetal brain growth. However, these studies primarily focused on short-term outcomes, highlighting the critical need for more extensive research on the long-term effects (Passera et al. 2019). However, a very recent study by Van Assche et al. (2022) emphasised that maternal stress and reduced mother-infant bonding associated with postpartum cancer treatment may adversely affect children's cognitive and behavioural development (Van Assche et al. 2022). This finding suggests that increased support and attention are necessary to foster cognitive and behavioural growth in children exposed to such stressors (Van Assche et al. 2022).

Despite generally reassuring findings, concerns persist regarding the potential risks of secondary malignancies, infertility, and psychiatric issues in children exposed to chemotherapy in utero. For example, in utero, exposure to cyclophosphamide has been linked to long-term carcinogenicity, based on a limited number of cases (Avilés & Neri 2001; Cardonick et al. 2010; Peres et al. 2001). Additionally, Chen et al. (2018) found that parental cancer, particularly life-threatening cancers, might increase the risk of psychiatric disorders in children (Chen et al. 2018). In conclusion, although current evidence

suggests that the short-term effects of in-utero exposure to chemotherapy and other systemic therapies may be minimal, there remains a significant gap in our understanding of long-term outcomes. This underscores the need for continued research, mainly longitudinal studies, to comprehensively assess the potential risks and ensure that children exposed to these treatments receive appropriate monitoring and care throughout their development.

2.4 Gaps in the literature

The review of existing literature reveals several critical gaps in understanding and managing pregnancy-associated cancer.

The rising incidence of pregnancy-associated cancers remains poorly understood. Although advanced maternal age is often cited as a contributing factor, the interplay of other potential factors, such as environmental, genetic, and healthcare-related influences, warrants further investigation. Research on pregnancy-associated cancers has predominantly focused on common cancers, such as breast cancer, with minimal attention given to rarer malignancies, including colorectal cancer (Boyd et al. 2012; Kocián et al. 2019; Munteanu et al. 2019; Rogers et al. 2022). Standardised clinical guidelines for managing these rare cancers during pregnancy or the postpartum period are lacking.

Limited research has been conducted on the effects of novel anticancer medications administered during pregnancy, particularly concerning maternal and neonatal outcomes following systemic treatment (Capozza et al. 2024; Hepner et al. 2019; Maggen et al. 2019). Current evidence is predominantly derived from expert opinions and small-sample studies, such as case-control, cohort, and single-case studies, which are prone to confounding factors. Large-scale studies and clinical trials involving pregnant women are urgently needed to evaluate the safety and efficacy of new therapies, including targeted treatments and immunotherapies, and to develop robust evidence-based guidelines for pregnancy-associated cancer management.

Limited research has addressed quality of life, emotional well-being, and psychological impacts on women diagnosed with cancer during pregnancy or postpartum. The interplay between cancer treatment, pregnancy, and motherhood remains underexplored, creating a gap in the understanding of how to provide appropriate support to these women (Faccio et al. 2020). The quality of communication between HCPs and women diagnosed with pregnancy-associated cancer has received

insufficient attention. Studies have rarely explored how effective communication with HCPs can enhance patient experience and outcomes. Furthermore, research identifying services that could improve the overall care experience during pregnancy and postpartum is lacking (Hammarberg et al. 2018; Stafford, Sinclair, Gerber, Collins, et al. 2021). The mental health impacts of pregnancy-associated cancer are under-researched, with a limited focus on the psychological distress and emotional toll of managing cancer during pregnancy or postpartum (Leung, Bryant & Stafford 2020). Targeted studies examining the mental health assessments of affected women and interventions are needed to address these challenges.

This review highlights the substantial limitations of existing research on pregnancy-associated cancer, emphasising the critical need for future studies. Future research is required to understand the healthcare experiences of pregnant women with cancer, the long-term effects of treatment, and the psychosocial and emotional dimensions of this condition. Addressing these gaps will support the development of comprehensive clinical guidelines and tailored support strategies for vulnerable populations.

2.5 Rationale for the thesis

Recent studies have highlighted a notable increase in the incidence of pregnancy-associated cancer. Despite this trend, significant gaps persist in the comprehensive documentation of pregnancy-associated cancer diagnoses, maternal and neonatal outcomes, management strategies, and experiences of women navigating both obstetric and cancer care. Additionally, there is limited understanding of the impact of this pregnancy-associated cancer diagnosis on the quality of life and mental health. This thesis sought to address these gaps by exploring critical areas, including maternal and neonatal outcomes following systemic therapy exposure, the incidence and outcomes of pregnancy-associated colorectal cancer, and the broader impact of pregnancy-associated cancer on women's quality of life, mental health, and healthcare experiences in obstetric and oncology settings.

Pregnancy-associated colorectal cancer (PACRC) is specifically highlighted in this research because it presents unique diagnostic and management challenges compared to other common pregnancy-associated cancers, such as breast or cervical cancer (Alkhamis et al. 2020; Petruzzelli et al. 2020; Siegel, Naishadham & Jemal 2012; Xu, Kong & Shen 2018). Colorectal cancer is the third most common cause of cancer-related mortality in women and the seventh most common type of cancer during pregnancy

(Alkhamis et al. 2020; Petruzzelli et al. 2020; Siegel, Naishadham & Jemal 2012; Xu, Kong & Shen 2018). Due to limited robust evidence and clinical guidelines, the diagnosis and treatment of PACRC are particularly challenging as symptoms such as abdominal pain, rectal bleeding, and changes in bowel habits often overlap with normal physiological changes of pregnancy (Khodaverdi, Kord Valeshabad & Khodaverdi 2013; Kocián et al. 2019; Petruzzelli et al. 2020). The increasing incidence of colorectal cancer among young adults, partly linked to delayed childbearing, further underscores the need to understand its clinical implications, management complexities, and outcomes (Kocián et al. 2019; Petruzzelli et al. 2020; Yang & Han 2021).

The decision to focus on PACRC in Study 1 was therefore made to address an underexplored and clinically complex area where evidence is especially limited. Most existing data come from case reports and small series, insufficient for informing evidence-based practice. By specifically investigating maternal and neonatal outcomes in PACRC, this thesis contributes much-needed epidemiological evidence to an area where clinical uncertainty is particularly high. While subsequent studies in this thesis address pregnancy-associated cancer more broadly, the focused attention in Study 1 responds to an identified evidence gap and provides critical insights into one of the more diagnostically challenging cancer types encountered in pregnant populations.

This thesis contributes to a more nuanced understanding of the complexities surrounding pregnancy-associated cancer, focusing on maternal and neonatal outcomes and the lived experiences of women navigating a dual diagnosis. This thesis employs a multi-method approach integrating quantitative and qualitative studies (detailed in Chapter 3) to address these gaps comprehensively.

This thesis contains four critical studies, combining a large-scale epidemiological linked data study, systematic review and meta-analysis, and in-depth qualitative interviews to explore pregnancy-associated cancer holistically. This multifaceted approach ensures a robust investigation of clinical outcomes, healthcare experiences, and mental health impacts, contributing to the evidence base needed to improve management strategies and patient care.

2.6 Chapter summary

This chapter reviewed the current literature on pregnancy-associated cancer, focusing on its incidence, maternal and neonatal outcomes, and women's overall experiences. It highlighted significant gaps in all these domains, emphasising the need for further research to address these critical areas. This chapter provided a foundational framework for the thesis by synthesising the existing evidence. It outlined the clinical significance of pregnancy-associated cancer, shedding light on its impact on both health outcomes and women's lived experiences. Furthermore, it identified key research gaps, which this thesis aims to address. The subsequent chapter, Chapter 3, details the methodology and methods employed in this research, building upon the gaps and areas of significance identified in the literature review.

Chapter 3: Methodology

3.1 Chapter introduction

In Chapter 2, the literature review established that although pregnancy-associated cancer remains rare, its incidence is steadily increasing (Cottreau et al. 2019; Eastwood-Wilshire et al. 2019). Chapter 2 also identified a significant research gap regarding long-term maternal, perinatal, and neonatal outcomes following exposure to systemic cancer treatments, as well as the experiences of women who were diagnosed with cancer during pregnancy or postpartum. It also highlights the need for further exploration of women's interactions with healthcare professionals, their quality of life, mental health and well-being impacts, and the services required to support them during and after their treatment (Ferrari et al. 2018; Stafford, Sinclair, Gerber, Collins, et al. 2021; Vanstone et al. 2021). The impact of pregnancy-associated cancer is profound, compromising women's ability to participate fully in life and necessitating improved communication and ongoing mental healthcare. This thesis addresses these research gaps by exploring women's experiences and needs in the context of pregnancy-associated cancer.

To address these gaps, this thesis adopts a multi-methods research design that applies distinct quantitative and qualitative studies to explore corresponding aspects of pregnancy-associated cancer. In a multi-methods approach, different research questions are addressed through separate, methodologically appropriate studies, each employing the design best suited for its specific aim (Marchisotti & Farias Filho 2022; Seawright 2016). Rather than integrating or combining data across paradigms, this approach embraces methodological pluralism, recognising that each component of the research is shaped by its own philosophical and methodological foundations (Esbjörn-Hargens 2006; Marchisotti & Farias Filho 2022; Seawright 2016).

This chapter outlines the overarching aim and research questions of the thesis, which serve as the foundation for selecting the separate but related quantitative and qualitative approaches. It also details the research design, study populations, data sources, data analytical techniques, and ethical considerations relevant to each study (Chapters 4, 5, 6, and 7). This chapter provides a coherent framework that ensures the thesis is logically structured, methodologically sound, and academically robust by clearly articulating the aims, questions, and rationale for each method.

3.2 Aims and research questions

3.2.1 Aims

To explore the impacts and maternal, perinatal and neonatal outcomes following a pregnancy-associated cancer diagnosis.

3.2.2 Research questions

To achieve the above aim and objectives, this thesis will answer six (6) research questions as follows:

1. What are the maternal outcomes for women with pregnancy-associated cancer?
2. What are the perinatal and neonatal outcomes for babies born to women with pregnancy-associated cancer?
3. Do perinatal outcomes for babies born to women with cancer during pregnancy differ based on exposure to systemic cancer treatment in utero?
4. What are women's experiences of communication with their healthcare providers following a diagnosis of pregnancy-associated cancer?
5. What are the mental health impacts for women diagnosed with pregnancy-associated cancer?
6. What kinds of information or services would enhance patient experiences for women with pregnancy-associated cancer?

3.3 Philosophical orientation: pragmatism

The overarching philosophical orientation of this thesis is grounded in pragmatism, which supports the use of multiple methods to address complex, real-world problems (Johnson & Onwuegbuzie 2004; Yvonne Feilzer 2010). Pragmatism acknowledges that both objective and subjective knowledge are valuable but prioritises practical problem-solving and the generation of actionable insights (Johnson & Onwuegbuzie 2004; Morgan 1998, 2007; Yvonne Feilzer 2010).

In this thesis, a pragmatic orientation informed the overall design by allowing for the use of both quantitative and qualitative methods in separate but complementary studies. Each methodological choice was driven by its appropriateness to answer a specific research question, rather than by a fixed philosophical allegiance. While these studies are conducted independently, they are unified by their

focus on producing meaningful knowledge to inform clinical practice and improve the care of women diagnosed with pregnancy-associated cancer.

3.4 Methodology and study design

3.4.1 Methodology

The methodology of a research study involves a systematic and theoretical analysis of the methods employed, shaped by an overarching philosophical framework and guiding assumptions (Creswell & Clark 2017). It reflects the researcher's understanding of knowledge (epistemology) and reality (ontology) and provides strategies for inquiry (Creswell & Clark 2017). This thesis adopts a multi-methods research design, applying both quantitative and qualitative approaches in separate, complementary studies to address distinct research questions related to pregnancy-associated cancer.

In a multi-methods framework, quantitative and qualitative components are not integrated into a unified design; rather, each method is selected for its suitability in addressing specific research aims and is underpinned by its philosophical orientation (Esbjörn-Hargens 2006; Marchisotti & Farias Filho 2022; Seawright 2016). This approach reflects methodological pluralism, recognising that complex health phenomena require both empirical measurement and exploration of subjective experience (Dupin & Borglin 2020; Esbjörn-Hargens 2006; Marchisotti & Farias Filho 2022; Seawright 2016).

The quantitative studies (Studies 1 and 2) are situated within a post-positivist framework, which assumes that while an objective reality exists, it can only be probabilistically understood through empirical investigation (Ryan 2018 (Adam 2013; Clark 1998; Morgan 2007; Ryan 2018)). Post-positivism builds on positivism's emphasis on observation and measurement but recognises that all knowledge is inherently fallible, provisional, and influenced by context (Adam 2013; Reed 2010). It acknowledges that research is shaped by limitations such as measurement error, researcher bias, and situational variability, and therefore emphasises the use of rigorous, transparent, and replicable methods to reduce but never fully eliminate these sources of uncertainty (Adam 2013; Clark 1998; Morgan 2007; Ryan 2018).

In this thesis, the quantitative studies focus on assessing maternal, perinatal, and neonatal outcomes using statistical methods, drawing on large-scale linked health data and a systematic review and meta-analysis. The associated ontology is objectivism, which holds that measurable phenomena exist independently of human perception (Nasution 2018). However, consistent with post-positivist thinking, these analyses also acknowledge the importance of critical interpretation, recognising that clinical and

social factors shape the meaning and implications of empirical findings. The goal is not to claim absolute truths but to generate robust, contextually informed evidence that can meaningfully contribute to clinical guidelines, health policy, and public health practice.

The qualitative aspects of this study, which explore women's experiences of pregnancy-associated cancer, are grounded in an interpretivist framework. Interpretivism is a philosophical research approach that emphasises understanding individuals' subjective meanings and experiences within their specific social and cultural contexts (Alharahsheh & Pius 2020; Ryan 2018). This approach focuses on the complexity and subjectivity of social phenomena, aiming to explore how individuals create and make sense of their realities (Alharahsheh & Pius 2020; Creswell & Clark 2017; Ryan 2018). Using an interpretivism approach is valuable for addressing research questions focused on women's experiences with cancer during pregnancy and the postpartum period, as it allows for a deeper exploration of how their own lives and social contexts shape their understanding and responses to pregnancy-associated cancer.

The ontology of this framework is subjectivism, which holds that reality is socially constructed and varies among individuals. By adopting qualitative methods such as interviews, this study captures the depth and nuance of each woman's experience, aiming to explore how they construct and understand their reality. This perspective is crucial for understanding the lived experiences of women diagnosed with pregnancy-associated cancer and for identifying how their needs can be addressed in healthcare settings. A phenomenological approach was employed in the qualitative studies in this thesis, aiming to understand the lived experiences of women diagnosed with pregnancy-associated cancer (Emiliussen et al. 2021; Neubauer, Witkop & Varpio 2019). This method seeks to uncover commonalities across these subjective experiences, enhancing understanding of the phenomenon. Thematic analysis was employed to identify semantic themes that reflect the explicit content of the data (Braun & Clarke 2006, 2021; Byrne 2022). By adhering to these rigorous guidelines, this study ensures the trustworthiness and credibility of its findings, ultimately contributing to a more comprehensive understanding of the phenomenon.

By employing separate quantitative and qualitative studies aligned with distinct research aims, this thesis draws on the strengths of multiple methodological approaches. However, it does not seek to integrate or merge these approaches under a single mixed-methods framework. Instead, it uses them in parallel to provide a broad, multifaceted examination of the clinical outcomes and lived experiences associated with pregnancy-associated cancer (Morse 2003; Schoonenboom & Johnson 2017). This methodological pluralism allows the thesis to address complex research questions from multiple perspectives, generating evidence relevant to both clinical practice and patient-centred care.

3.4.2 Rationale for this research

The scarcity of qualitative and quantitative data on pregnancy-associated cancer in Australia and limited international data underscores the need for a comprehensive investigation (Capozza et al. 2024; Fotheringham et al. 2024; Pereg, Koren & Lishner 2008; Stafford, Sinclair, Gerber, Collins, et al. 2021). A multi-methods research design provides a robust framework for addressing this gap, by applying different but complementary methods to explore distinct aspects of the research problem (Dupin & Borglin 2020; Esbjörn-Hagens 2006; Marchisotti & Farias Filho 2022; Seawright 2016).

A single research approach is insufficient to understand a complex issue like pregnancy-associated cancer, which requires broad epidemiological data and an understanding of individual lived experience (Ferrari et al. 2018; Mertens 2015; Silverstein et al. 2020; Stafford, Sinclair, Gerber, Collins, et al. 2021; Wolters et al. 2021).

The quantitative component of this thesis used linked data to examine large-scale epidemiological trends, incidence rates, and maternal and neonatal outcomes. The systematic review further synthesises existing research on pregnancy-associated cancer, ensuring a rigorous evaluation of data related to perinatal outcomes following exposure to systemic treatment in utero. These quantitative studies generate generalisable, population-level insights into clinical outcomes, contributing important evidence to inform clinical guidelines and healthcare practice.

The qualitative component of this thesis employed in-depth interviews with women diagnosed with pregnancy-associated cancer. These narratives offer valuable insights into women's experiences, interactions with HCPs, and the mental health impact of their diagnosis. This qualitative exploration humanises the data, capturing nuances and emotional dimensions that quantitative methods cannot.

By applying multiple, methodologically distinct approaches, this thesis examines both the statistical patterns and subjective experiences associated with pregnancy-associated cancer. Although the quantitative and qualitative studies are conducted independently, together their findings are intended to inform clinical guidelines and improve healthcare practices, ultimately supporting effective healthcare and policy interventions for women facing this complex condition (Dupin & Borglin 2020; Esbjörn-Hagens 2006; Marchisotti & Farias Filho 2022; Seawright 2016).

3.4.3 Study design

This thesis employs a multi-methods research design, applying distinct quantitative and qualitative approaches to examine corresponding aspects of pregnancy-associated cancer. The quantitative component includes two studies: a population-based linked data study and a systematic review and meta-analysis. These studies investigate large-scale epidemiological trends, maternal and neonatal outcomes, and the effects of systemic cancer treatment on perinatal outcomes. The qualitative component consists of in-depth semi-structured interviews with women diagnosed with pregnancy-associated cancer, focusing on their experiences of communication with HCPs and the mental health impacts of their diagnosis.

Each study was designed to address specific research questions using the most appropriate methodological approach. The quantitative studies generate generalisable, population-level insights into clinical outcomes, while the qualitative studies provide a rich, in-depth understanding of women's lived experiences. Although the samples and data sources differ, the studies are unified by a shared aim to enhance understanding of the clinical outcomes and women's experiences after being diagnosed with pregnancy-associated cancer.

The weighting of the research

The weighting of the studies reflects the emphasis placed on each component to address research objectives and questions effectively. Equal weighting is given to both the quantitative and qualitative components of this research. The quantitative studies establish the scope and magnitude of the clinical issues. In contrast, the qualitative data provide detailed narratives of women's interactions with HCPs and their emotional responses to the diagnosis of pregnancy-associated cancer. This balanced application of methods ensures that both clinical patterns and personal perspectives are adequately considered, enhancing the practical relevance of the findings for healthcare service delivery and policy development.

Timing of methods

The multi-methods research design employed in this thesis follows a sequential structure in which the quantitative studies were conducted first, followed by the qualitative studies. While the findings from the quantitative phase helped highlight areas requiring further exploration, the two components remained analytically independent, with no attempt to merge data or integrate findings across

paradigms. Instead, each methodological strand contributes complementary forms of evidence, together offering a broader, multidimensional understanding of pregnancy-associated cancer.

In this thesis, Study 1 utilised quantitative data to provide large-scale insights into the epidemiological trends of pregnancy-associated colorectal cancer (PACRC) in Australia, highlighting critical areas such as birth interventions and maternal and neonatal outcomes. However, the absence of treatment data in Study 1 highlighted the need for further quantitative investigation. Study 2, a systematic review and meta-analysis addressed this gap by examining the perinatal outcomes for babies born to women with cancer in pregnancy exposed to systemic cancer treatment in utero.

Although independently designed, the qualitative studies explored themes that aligned with clinical concerns highlighted in the earlier quantitative studies. Studies 3 and 4 involved in-depth semi-structured interviews with women diagnosed with pregnancy-associated cancer, either during pregnancy or postpartum. These studies explored women's experiences of communication with healthcare providers and the mental health impacts of their diagnosis.

By applying methodologically distinct but thematically aligned studies, this thesis offers a comprehensive exploration of pregnancy-associated cancer. Each study contributes unique insights relevant to clinical practice and healthcare delivery, collectively addressing both measurable health outcomes and the lived experiences of affected women.

3.5 Study methods

This thesis comprises four distinct studies, including two quantitative investigations focused on maternal, neonatal, and perinatal outcomes and two qualitative studies that explore women's perspectives on communication with HCPs and the impact of mental health and well-being on women diagnosed with pregnancy and the postpartum period.

Study 1: Incidence and maternal and neonatal outcomes following pregnancy-associated colorectal cancer: A population-based linked data study

This study focuses on the incidence and maternal and neonatal outcomes following pregnancy-associated colorectal cancer (PACRC). This population-based linked data study seeks to quantify the incidence rates and compare the health outcomes of affected women and their infants with those of a control group.

Study design

A population-based cohort study was conducted using linked data from NSW Health. NSW Health manages and funds public and private hospitals, including emergency care facilities. The network has a range of inpatient and outpatient services across rural, regional, and metropolitan NSW (with a population of 8.2 million), including over 200 public and private hospitals (NSW Health 2024). The study comprised all women who gave birth between 1 January 1994 and 31 December 2013 in the NSW public and private sectors. Birth is defined as all live births and stillbirths at least 20 weeks of gestation or at least 400 grams (g) of weight (Centre for Epidemiology and Evidence 2019).

The study groups included all women who gave birth and were diagnosed with colorectal cancer during pregnancy (gestational CRC group) and those who were diagnosed within one year postpartum (postpartum CRC group). The comparison group included women who gave birth without cancer diagnosed during pregnancy or within one year postpartum.

The following linked datasets were used: Perinatal Data Collection (PDC), NSW Cancer Registry (NSWCR), NSW Admitted Patient Data Collection (APDC), Register of Congenital Conditions (RoCC), Perinatal Death Review (PDR), Register of Births, Deaths, and Marriages (RBDM), and the Cause of Death Unit Record File (COD URF)(CHeReL. 2019a, 2019b). Details of all these linked datasets are provided in **Appendix 2**.

Women with any other type of cancer diagnosed during pregnancy or within the one-year postpartum period were excluded.

Outcome measures

The maternal outcomes included pregnancy and birth management, such as induction of labour and mode of birth (spontaneous vaginal birth, instrumental birth, or caesarean section), maternal complications (gestational hypertension and gestational diabetes) and severe maternal complications. Gestational hypertension refers to a new diagnosis of hypertension after 20 weeks of gestation with or without preeclampsia. The decision to combine the two types of pregnancy-associated hypertension stems from the fact that the variable containing information before 2006 encompassed both of these types (CHeReL. 2019a). Severe maternal complications are reflected by the severe maternal morbidity outcome indicator (MMOI), a composite measure developed by Roberts et al. (2008) (Roberts et al. 2008). The MMOI was developed using a validated list of 14 ICD10 diagnosis

codes (such as cardiac arrest, cerebral oedema, and disseminated intravascular coagulopathy) and 11 Australian Classification of Health Interventions (ACHI) ICD10 procedure codes (such as assisted ventilation, hysterectomy and dialysis). Perinatal outcomes included perinatal deaths (stillbirth or neonatal deaths), preterm birth (birth before 37 completed weeks), small for gestational age (SGA), low birth weight (LBW<2500 g), Apgar at 5 min, admission to ICU (admission to Special Care Nursery or Neonatal Intensive Care for 4 hours or more), the diagnosis of congenital conditions and, severe neonatal adverse outcomes. Severe neonatal adverse outcomes are reflected by the Neonatal Adverse Outcome Indicator (NAOI), a composite measure developed by Lain et al. (2012) (Lain et al. 2012). The NAOI was developed using a validated list of 12 ICD10 diagnosis codes (such as respiratory distress syndrome, seizure, and intraventricular haemorrhage) and seven ACHI ICD10 procedures (such as resuscitation, blood transfusion and mechanical ventilation). An explanation of MMOI and NAOI composite measures is presented in **Appendix 3**. Maternal and neonatal outcome measures and associated linked data sources are presented in **Table 3.1**.

Table 3.1 Maternal and neonatal outcome measures and associated linked data sources

Maternal outcomes	
Dataset	Specific measures
Perinatal data collection (PDC)	Pregnancy and birth management (Induction of labour and mode of birth such as spontaneous vaginal, instrumental, or caesarean section) Maternal complications (gestational hypertension, gestational diabetes) and Severe maternal complications (cardiac arrest, cerebral oedema and disseminated intravascular coagulopathy)
Admitted patient data collection (APDC)	Detailed patient information, including procedure and diagnosis during hospital stays
Registry of births, deaths, and marriages (RBDM)	Birth and death registration, including maternal, perinatal and neonatal deaths, as well as parent/child details
NSW cancer registry (NSWCR)	Demographics, cancer diagnosis, staging, histological grading and metastatic spread and cause of death of all people in NSW
Perinatal outcomes	
Dataset	Specific measures
Perinatal data collection (PDC)	All births, including live births and stillbirths (at least 20 weeks of gestation or 400 g birth weight) Severe neonatal complications (respiratory distress syndrome, seizure, and intraventricular haemorrhage)
Admitted patient data collection (APDC)	Preterm birth (<37 weeks), low birth weight (lbw < 2500 g), Apgar score at 5 minutes, admission to ICU (special care nursery or neonatal intensive care for 4 hours or more)
Perinatal death review (PDR)	Stillbirth or neonatal deaths
Register of congenital conditions (RoCC)	Diagnosed congenital condition during pregnancy or birth
Cause of death unit record file (COD URF)	Coded death data form by the Australian Bureau of Statistics (ABS)

Data analysis

Descriptive statistics were used to report nominal variables (counts and percentages). Continuous variables are presented as mean and standard deviation (SD). One-way ANOVA was used to compare the difference in mean maternal age between the study and the comparison group. The Chi-square test was used to examine the differences in categorical variables between the study and control groups. Poisson regression models without and with adjustment for maternal age were used to estimate the annual increase in the incidence rate each year.

The likelihood of adverse maternal and infant outcomes was compared between the study and control groups using Generalised Estimating Equation (GEE) models. The results of the univariable and multivariable models were reported as adjusted odds ratios (AOR) with corresponding 95% confidence intervals for each variable. Confounders included maternal age, country of birth, remoteness, parity, history of CS, plurality, timing of antenatal care, smoking during pregnancy, place of birth, pre-existing diabetes, pre-existing hypertension, chronic kidney disease, and cardiovascular disease before pregnancy (**Chapter 4, Table 4.4**).

Kaplan-Meier curves and log-rank tests were used to compare the survival of women with pregnancy-associated colorectal cancer. Data analysis was performed using Statistical Package for Social Sciences (SPSS) version 27.

Study 2: Perinatal outcomes for infants exposed to systemic treatment during gestation: a systematic review and meta-analysis

The aim of this systematic review and meta-analysis was to explore the effects of systemic cancer treatment on perinatal outcomes for infants, comparing those exposed to therapy with those who were not. This review seeks to address key research questions regarding the potential risks and impacts of systemic cancer therapy on the perinatal health of infants, offering insights to guide clinical decision-making and improve care for affected women and their babies.

Study design

This systematic review focuses exclusively on quantitative studies to investigate perinatal outcomes following a diagnosis of gestational cancer. Studies were selected for inclusion based on the PECO framework (Population, Exposure, Comparator, Outcome), which guided the development of the review question and inclusion criteria. The population (P) consisted of women diagnosed with cancer during pregnancy. The exposure (E) included women who received systemic cancer treatment during

pregnancy, such as chemotherapy, targeted therapy, or a combination of these. The comparator (C) group comprised women diagnosed with cancer during pregnancy who did not receive systemic cancer treatment. The outcomes (O) considered for inclusion were perinatal outcomes, including spontaneous abortion, pregnancy termination, intrauterine growth restriction (IUGR), stillbirth, neonatal mortality, preterm birth (<37 weeks), Apgar score at 5 minutes, small for gestational age (SGA), low birth weight, congenital anomalies, neonatal intensive care unit (NICU) admission, and long-term infant outcomes such as cognitive or academic performance

This systematic review and meta-analysis included both cohort and case-control studies. Peer-reviewed full-text articles published in English that met the search criteria were included. Systematic reviews, case studies, animal studies, letters, abstracts, seminar reviews, and editorials were excluded from the analysis.

Search methods for the identification of studies

Information sources and search strategy

MEDLINE and EMBASE via OVID, COCHRANE, CINAHL, and Google Scholar databases were searched for articles published between January 2001 and March 2023. These dates were chosen to prioritise studies relevant to current treatment regimens and clinical context. The search terms are presented in **Appendix 4**.

Searching other resources

The reference lists of all included studies were searched for further relevant publications. In addition, a paediatric endocrinologist was contacted and played a crucial role as a content expert to provide expertise and insights for this research. He was contacted to gather additional information, help interpret the review's findings, and ensure the accuracy and relevance of the study.

Study records

Study Selection

Two investigators independently screened the titles and abstracts returned from the searches and removed ineligible records. The full texts of the remaining records, comprising those that appeared to meet the inclusion criteria and those where eligibility was uncertain after title and abstract review, were accessed and reviewed by the same two investigators to decide which records to include in the review. A third investigator resolved any discrepancies between the two investigators.

Data collection

Two investigators independently extracted the relevant data using a standardised electronic data extraction form (see **Appendix 5**). Where possible, the study authors were contacted to provide any missing information. Further discussion with a third investigator resolved any disagreement between the two investigators.

Data analysis

For this systematic review and meta-analysis, raw data were extracted from all eligible studies reporting on perinatal outcomes following systemic cancer treatment during gestation. The analysis focused on dichotomous outcomes, including spontaneous abortion, stillbirth, birthweight <10th percentile (small for gestational age, or SGA), intrauterine growth restriction (IUGR), and preterm birth (<37 completed weeks of gestation).

A Bayesian random-effects model was employed to estimate pooled odds ratios (ORs) and corresponding 95% confidence intervals (CIs). This modelling approach was selected to account for between-study heterogeneity, which was anticipated due to variation in cancer types, patient populations, treatment protocols, and outcome definitions across the included studies. The Bayesian framework allowed for the incorporation of prior information and provided more robust estimates under conditions of clinical and methodological heterogeneity.

The prior distributions were defined as follows: a normal distribution with a mean of 0 and standard deviation of 10 for the intercept, and a half-Cauchy distribution with a scale of 1 for the standard deviation of the random effects. Four Markov Chain Monte Carlo (MCMC) chains were run with 4,000 iterations per chain, including a burn-in period of 1,000 iterations.

Forest plots were generated for individual studies; however, pooled estimates were not presented in cases where none of the included studies reported adjusted odds ratios. This decision was made to

avoid generating potentially biased pooled estimates from unadjusted data. All analyses were conducted using R statistical software (version 4.4.3; R Core Team, 2025).

Study 3: Women's perspectives on communication following the diagnosis of gestational or postpartum cancer: A qualitative study, and

Study 4: Cancer diagnosis during pregnancy and the postpartum period: Impact on well-being and mental health

A qualitative approach was employed for Study 3 and Study 4. Study 3 examined women's communication experiences with their treating healthcare professionals. It also sought to identify any communication gaps and to explore the services that enhanced women's experiences during treatment. The study also considered what additional support services women felt could have been beneficial during their diagnosis and treatment. Study 4 explored the impact of pregnancy-associated cancer on women's mental health and well-being. The aim was to understand the mental health challenges that women faced and the support they received.

Studies 3 and 4 used the same sample, consisting of women diagnosed with cancer during pregnancy or in the postpartum period. The inclusion and exclusion criteria for participant selection and procedure were the same for both studies, ensuring consistency in the examined population.

Study design

An individual semi-structured interview approach was used for studies 3 and 4, as it is particularly suited for exploring topics that need to be better understood (Cohen & Crabtree 2008). The primary goal of qualitative research is to gain an in-depth understanding of how individuals interpret and give meaning to their experiences and the social and cultural contexts in which these experiences occur. This approach focuses on exploring the complexities of human behaviour and its underlying reasons rather than simply quantifying them (Creswell 2013).

Participants and procedure

The eligibility criteria comprised all women in Australia diagnosed with pregnancy-associated cancer. Other eligibility criteria required that participants be at least 18 years of age at the time of recruitment, be able to speak and read English, possess psychological and cognitive capacity to provide informed consent, and actively participate in the interviews.

After obtaining ethical approval (UTS; HREC REF NO. ETH19-4526) for the project, participants were recruited via national advertisements on popular social media platforms (Facebook, Twitter, and Instagram) and established community networks (such as Cancer Council NSW, Cancer Council Victoria, Breast Cancer Network Australia, Mummy's Wish group, and Bub Hub). These communities allowed the study to be shared on their websites, and potential participants could access the study details, eligibility criteria, and the researcher's contact information. Interested women were encouraged to reach the study team via email. Subsequently, potential participants were provided with a participant information sheet and consent form. Once informed consent was obtained, the study team scheduled interview appointments. Seventeen women who met the inclusion criteria were interviewed over a period from March 2021 to July 2022.

Initially, Studies 3 and 4 intended to recruit women diagnosed with cancer during pregnancy. However, following challenges in recruitment between late pregnancy and the early postpartum period, a protocol amendment was submitted and approved (see **Appendix 7**). The amended criteria expanded eligibility to include women diagnosed with cancer during pregnancy and 12 months postpartum. This change allowed for the inclusion of women whose cancer diagnoses occurred shortly after childbirth (up to 12 months of birth), enabling the research to capture critical insights into how pregnancy, early motherhood, and cancer care intersect in real-world settings.

While this shift expanded the study's scope, the core aim of exploring the lived experience of women navigating cancer in close temporal proximity to pregnancy remained intact. During data collection and analysis, diagnostic timing was carefully noted, and emergent themes were compared across subgroups (during pregnancy or post-partum) to ensure analytic clarity and internal consistency. No thematic discrepancies were found that would compromise the interpretive integrity of the findings.

Among the participants, 11 resided in metropolitan areas, while six lived in regional areas. Sixteen women had attained a tertiary-level education, and one had completed high school education. Most women (58.8%) were diagnosed during the postpartum period, aged 35 to 44 years. The remaining participants (41.1%) were diagnosed during pregnancy, aged 25 to 34 years. Further details regarding the participant characteristics are presented in **Tables 6.1** and **7.1** in **Chapters 6 and 7**.

Data collection

Semi-structured interviews were conducted with individuals, allowing us to concentrate on essential issues for participants and gain insight into their experiences (DeJonckheere & Vaughn 2019). The research team developed an interview guide specifically designed to explore women's experiences of care during pregnancy and postpartum, the communication practices of healthcare professionals, and potential services that enhanced women's experiences.

Two experienced qualitative researchers conducted the interviews, which were administered via phone. The average duration of the interviews was 50 minutes. Audio recordings of the interviews were made with permission from the participants, and noteworthy nonverbal responses such as crying or laughing were also captured. The confidentiality and anonymity of the participants were maintained, and information was identifiable only to the interviewer.

Data Analysis

In these qualitative studies, all interviews were transcribed verbatim, capturing the spoken content and the nuances of speech, such as "umms" and "ahhs", to represent women's experiences authentically. The data were subjected to inductive reflexive thematic analysis, following Braun and Clarke's methodological guidelines (Braun & Clarke 2021). This approach was selected to thoroughly explore women's lived experiences and facilitate the emergence of rich themes grounded in their narratives.

The six stages outlined by Braun and Clarke were meticulously followed during the thematic analysis process to ensure methodological accuracy, including familiarisation, code generation, theme development, reviewing and refining themes, defining themes, and report writing (Braun & Clarke 2021; Byrne 2022). This structured approach enhances the methodological rigour of the analysis and promotes a comprehensive understanding of the data.

Interviews were listened to repeatedly, transcribed, and field notes were taken. The interview transcripts were then imported into NVivo 12 Pro, where the initial coding of the data was conducted. Themes and relevant quotes emerged from the coded data. Continuous discussions and consultations with the supervisor were undertaken to review and finalise the identified themes and associated quotes. Through this repetitive process, the researchers explored individual and shared perspectives and uncovered patterns within and across women's narratives.

In these qualitative studies, a phenomenological approach was employed to understand the lived experiences of women diagnosed with pregnancy-associated cancer (Emiliussen et al. 2021; Neubauer, Witkop & Varpio 2019). Thematic analysis in this context focuses on identifying semantic themes that reflect the explicit content of the data and capturing the broader implications of participants' narratives (Braun & Clarke 2006, 2021; Byrne 2022). By adhering to these rigorous guidelines, the trustworthiness and credibility of the findings were ensured, providing valuable insights into the complexities of living with cancer during pregnancy or postpartum.

3.6 Methodological Rigour and Trustworthiness

Given the multi-method design of this thesis, the rigour of each methodological component is addressed separately in alignment with its respective paradigm.

For the quantitative studies (Studies 1 and 2), rigour was ensured through the use of validated datasets, appropriate statistical modelling (including adjustments for confounders), and transparent reporting of inclusion criteria and outcome measures. Data quality and validity were enhanced through the use of population-level administrative health data and systematic methods for data extraction and synthesis.

For the qualitative studies (Studies 3 and 4), trustworthiness was maintained through strategies aligned with qualitative quality standards. These included prolonged engagement with the data, independent coding and analysis, reflexive thematic analysis, and consultation with supervisors throughout the coding process. Researcher reflexivity was maintained through journaling and memo-writing during analysis, ensuring transparency and minimising bias in interpretation (Bordia & Crossman 2021). The study adhered to the criteria of credibility, confirmability, and dependability and ensured transparency through detailed documentation of the research process (Karcher, McCuaig & King-Hill 2024; Peddle 2022).

As this is a multi-method rather than mixed-methods thesis, the studies were conducted and analysed independently; therefore, no claims of data or analytic integration are made. Instead, the separate findings contribute complementary insights into pregnancy-associated cancer.

3.7 Data management and storage

All data, including audio recordings, signed consent forms, and transcripts, were securely stored on a password-protected computer belonging to the researcher during data collection and analysis. A comprehensive research data management plan was implemented in compliance with the *Australian Code for the Responsible Conduct of Research* (Michelle et al. 2020). This plan utilised Stash for the ongoing management and storage of data, ensuring safety, confidentiality, and compliance with ethical standards. The data will be retained for five years from the date of publication. After this retention period, all data will be securely destroyed following the protocols for the disposal of confidential information, ensuring complete confidentiality and adherence to ethical guidelines.

3.8 Ethical consideration

3.8.1 Ethics approval

Ethical approval for study 1 was obtained from the NSW Population and Health Services Research Ethics Committee (reference HREC/17/CIPHS/11).

Before participant recruitment, the UTS Human Research Ethics Committee obtained ethical approval for Studies 3 and 4 (REF No. ETH19-4526). The original project recruited women diagnosed with cancer during pregnancy. During the recruitment process, several women who had been diagnosed with cancer in the postpartum period expressed an interest in participating in the study. An amendment was submitted to the UTS Human Research Ethics Executive Review Committee to include these women in the study. The committee reviewed and approved the amendments (UTS HREC; REF No. ETH20-5565), confirming that the modifications complied with the NHMRC National Statement on Ethical Conduct in Human Research (2007).

Ethical approval for studies 1, 3 and 4 is provided in **Appendix 7**.

3.8.2 Informed consent

For Study 1, a retrospective population-based linkage study utilising pre-collected administrative data, a waiver of consent was granted. The rationale for this waiver was that the involvement of participants presented a negligible risk as the research focused on events that had already occurred. Data on women's cancer diagnoses and birth outcomes were collected previously, and no interventions were

administered to the participants as part of the study. Furthermore, no identifiable information was used, and only aggregated data were published to protect the participant's privacy.

For Studies 3 and 4, potential participants were provided with a detailed participant information sheet outlining the study's aims, confidentiality measures, and the topic's sensitive nature. The consent process emphasised voluntary participation, giving participants sufficient time to ask questions. They were informed of their right to withdraw at any time without consequence. Additional support resources were offered due to the topic's sensitive nature, and participants were encouraged to engage in the interview at a pace and setting that was comfortable for them. The advertisement for the study, participant information sheet, interview guidelines, and consent form are included in **Appendix 8**.

3.8.3 Potential risks and mitigation strategies

The primary risk for participants was the potential for emotional distress. Receiving a cancer diagnosis during or shortly after pregnancy is challenging, and discussing these experiences can evoke strong emotional reactions. Additionally, some participants may have experienced pregnancy loss, stillbirth, or the death of their baby shortly after birth, which could also be distressing. Another consideration was the inconvenience posed to the participants by taking time out of their schedule to participate in the study.

To address these concerns, each interview was conducted with sensitivity and care to minimise potential distress. Distress protocols were established for each study, prioritising participants' well-being. Participants were provided with information on available support services multiple times, including on the Participant Information Sheet and Consent Form, at the beginning of each data collection session and upon completion.

3.9 Chapter summary

This chapter outlined the philosophical foundations, methodological choices, ethical considerations, and quality assurance strategies underpinning this thesis. The research is structured as a multi-method study, with each component tailored to address a specific question relating to maternal and neonatal outcomes and women's lived experiences following pregnancy-associated cancer. The following chapters present each study in detail, offering distinct but complementary insights to inform healthcare and policy development.

The following chapters will describe these studies in depth.

Chapter 4: Incidence, and maternal and neonatal outcomes following pregnancy-associated colorectal cancer: A population-based linked data study

4.1 Publication

The results of this chapter have been published as follows:

Farhana, S., Frawley, J., Safi, N., Anazodo, A., Zalcborg, J. R., & Sullivan, E. A. (2024). Incidence, and maternal and neonatal outcomes following pregnancy-associated colorectal cancer: A population-based linked data study. *The Journal of Obstetrics and Gynaecology Research*, 2025-01, Vol. 51 (1), p.e16149-n/a.

4.2 Chapter introduction

The rising incidence of pregnancy-associated cancer, the complexities involved in its management, and its role as a significant contributor to mortality among women of childbearing age are highlighted in Chapter 1. Chapter 2 also underscores the limited research available on maternal and neonatal outcomes following a diagnosis of pregnancy-associated cancer, establishing the significance of this study. This chapter introduced the first and second research questions: "*What are the maternal outcomes for women with pregnancy-associated cancer?*" and "*What are the perinatal and neonatal outcomes for babies born to women with pregnancy-associated cancer?*" Given the broad and under-researched nature of pregnancy-associated cancer, further investigation is imperative. This study specifically focused on the incidence of pregnancy-associated colorectal cancer (PACRC) in New South Wales (NSW), Australia, and examined the maternal and neonatal outcomes associated with this condition. The increasing occurrence of colorectal cancer in younger adults, especially women in the reproductive period, further underscores its growing impact, highlighting the urgent need for comprehensive research and targeted interventions (Alkhamis et al. 2020; Stoffel & Murphy 2020; Troisi et al. 2018). This study aimed to provide population-based evidence on the trends and outcomes of PACRC, offering valuable insights to inform clinical practice and public health strategies.

4.3 Background

Cancer is the second leading cause of death among women of childbearing age (Eastwood-Wilshere et al. 2019). The incidence of pregnancy-associated cancer, which is defined as cancer diagnosed during pregnancy or within one year of delivery, is increasing due to delayed childbearing (Lee et al. 2012; Predescu D et al. 2020). Although colorectal cancer (CRC) in pregnancy (gestational colorectal cancer) is rare, the incidence rate is still 1 in 13,000 pregnancies (Samadder et al. 2020; Yang & Han 2021). Colorectal cancer is the third most common cause of mortality in women and the seventh most common type of cancer in pregnancy (Alkhamis et al. 2020; Petruzzelli et al. 2020). Furthermore, the manifestation of colorectal cancer in younger adults underscores its significant impact and reinforces the need for comprehensive attention and intervention (Alkhamis et al. 2020; Aytac et al. 2016).

The early symptoms and signs of CRC, such as fatigue, iron deficiency anaemia and change in bowel habits, might be overlooked as they mimic changes commonly related to pregnancy (Khodaverdi, Kord Valeshabad & Khodaverdi 2013; Petruzzelli et al. 2020). As a result, patients may be diagnosed with more advanced CRC cancer with an ensuing worse prognosis, especially during pregnancy or postpartum (Alkhamis et al. 2020; Aytac et al. 2016; Yang & Han 2021). Very few studies have explored pregnancy-associated colorectal cancer (PACRC), and the majority of these have been case studies or small case series.

Our study aimed to estimate the incidence of PACRC in NSW, Australia. We examined the pregnancy and birth outcomes for women with colorectal cancer and their infants and compared the overall survival outcomes for women diagnosed with gestational CRC and postpartum CRC.

4.4 Methods

We conducted a population-based cohort study using linked data from NSW Health. NSW Health is responsible for managing and funding both public and private hospitals, including emergency care. Its network has a range of inpatient and outpatient services across rural, regional, and metropolitan NSW (with a population of 8.2 million), including over two hundred public and private hospitals (NSW Health 2024). The study comprised all women who gave birth between 1 January 1994 and 31 December 2013 in the NSW public and private sector. Birth is defined as all live births and stillbirths of at least 20 weeks gestation or at least 400 grams (g) birthweight (Centre for Epidemiology and Evidence 2019).

The study groups included all women who gave birth and were diagnosed with colorectal cancer during pregnancy (gestational CRC group) and those who were diagnosed within one year postpartum (postpartum CRC group). The comparison group included women who gave birth without cancer diagnosed during pregnancy or within one year postpartum.

We used the following linked datasets: Perinatal Data Collection (PDC), the NSW Cancer Registry (NSWCR), NSW Admitted Patient Data Collection (APDC), the Register of Congenital Conditions (RoCC), Perinatal Death Review (PDR), Register of Births, Deaths and Marriages (RBDM), Cause of Death Unit Record File (COD URF) (CHeReL. 2019a, 2019b). Details of all these linked data sets are presented in **Appendix 2.**

Women with any other type of cancer diagnosed during pregnancy or within a one-year postpartum period were excluded.

4.4.1 Outcome measures

The maternal outcomes included pregnancy and birth management (induction of labour or mode of birth, either spontaneous vaginal birth, instrumental birth or caesarean section (CS), pregnancy complications (gestational hypertension and gestational diabetes) and severe maternal complications. In this study, gestational hypertension refers to a new diagnosis of hypertension after 20 weeks of gestation with or without preeclampsia. Two types of pregnancy-associated hypertension combined in this study (with or without preeclampsia) as hypertension variables prior to 2006, encompassing both types (CHeReL. 2019a). Severe maternal complications are reflected by the severe maternal morbidity outcome indicator (MMOI), a composite measure developed by Roberts et al. (2008) (Roberts et al. 2008). The MMOI was developed using a validated list of 14 ICD10 diagnosis codes (such as cardiac arrest, cerebral oedema, and disseminated intravascular coagulopathy) and 11 Australian Classification of Health Interventions (ACHI) ICD10 procedure codes (such as assisted ventilation, hysterectomy and dialysis). Perinatal outcomes included perinatal deaths (stillbirth or neonatal deaths), preterm birth (birth before 37 completed weeks), small for gestational age (SGA), low birth weight (LBW<2500 g), Apgar at 5 min, admission to ICU (admission to Special Care Nursery or Neonatal Intensive Care for 4 hours or more), the diagnosis of congenital conditions and, severe neonatal adverse outcomes. Severe neonatal adverse outcomes are reflected by the Neonatal Adverse Outcome Indicator (NAOI), a composite measure developed by Lain et al. (2012) (Lain et al. 2012). The NAOI was developed using a validated list of 12 ICD10 diagnosis codes (such as respiratory distress syndrome,

seizure, and intraventricular haemorrhage) and seven ACHI ICD10 procedures (such as resuscitation, blood transfusion and mechanical ventilation). Components of MMOI and NAOI are presented in **Appendix 3**.

4.4.2 Statistical analysis

We used descriptive statistics to report nominal variables (counts and percentages). Continuous variables were presented as mean and standard deviation (SD).

One-way ANOVA was used to compare the difference in mean maternal age between the study and the comparison group. The Chi-square test was used to examine the difference in categorical variables between the study and the comparison group. Poisson regression models without and with adjustment for maternal age were used to estimate the annual increase in the incidence rate each year. The likelihood of adverse maternal and infant outcomes was compared between the study and comparison groups using the Generalised Estimating Equation (GEE) models. The results of univariable and multivariable models were reported as adjusted odds ratios (AOR) with corresponding 95% confidence intervals for each variable. Confounders include maternal age, country of birth, remoteness, parity, history of CS, plurality, the timing of antenatal care, smoking during pregnancy, place of birth, pre-existing diabetes, pre-existing hypertension, chronic kidney disease and cardiovascular disease prior to pregnancy (**Table 4.4**).

Kaplan-Meier curves and log-rank tests were used to compare the survival of women with pregnancy-associated colorectal cancer. Data analysis was undertaken using Statistical Package for Social Sciences (SPSS) version 27.

Kaplan-Meier curves and log-rank tests were used to compare the survival of women with pregnancy-associated colorectal cancer. Data analysis was undertaken using Statistical Package for Social Sciences (SPSS) version 27.

4.5 Results

There were 22 women diagnosed with colorectal cancer during pregnancy (gestational CRC group), 101 women diagnosed within one year postpartum (postpartum CRC group), and 1,786,078 women included who gave birth with no cancer diagnosis during pregnancy or within one year postpartum.

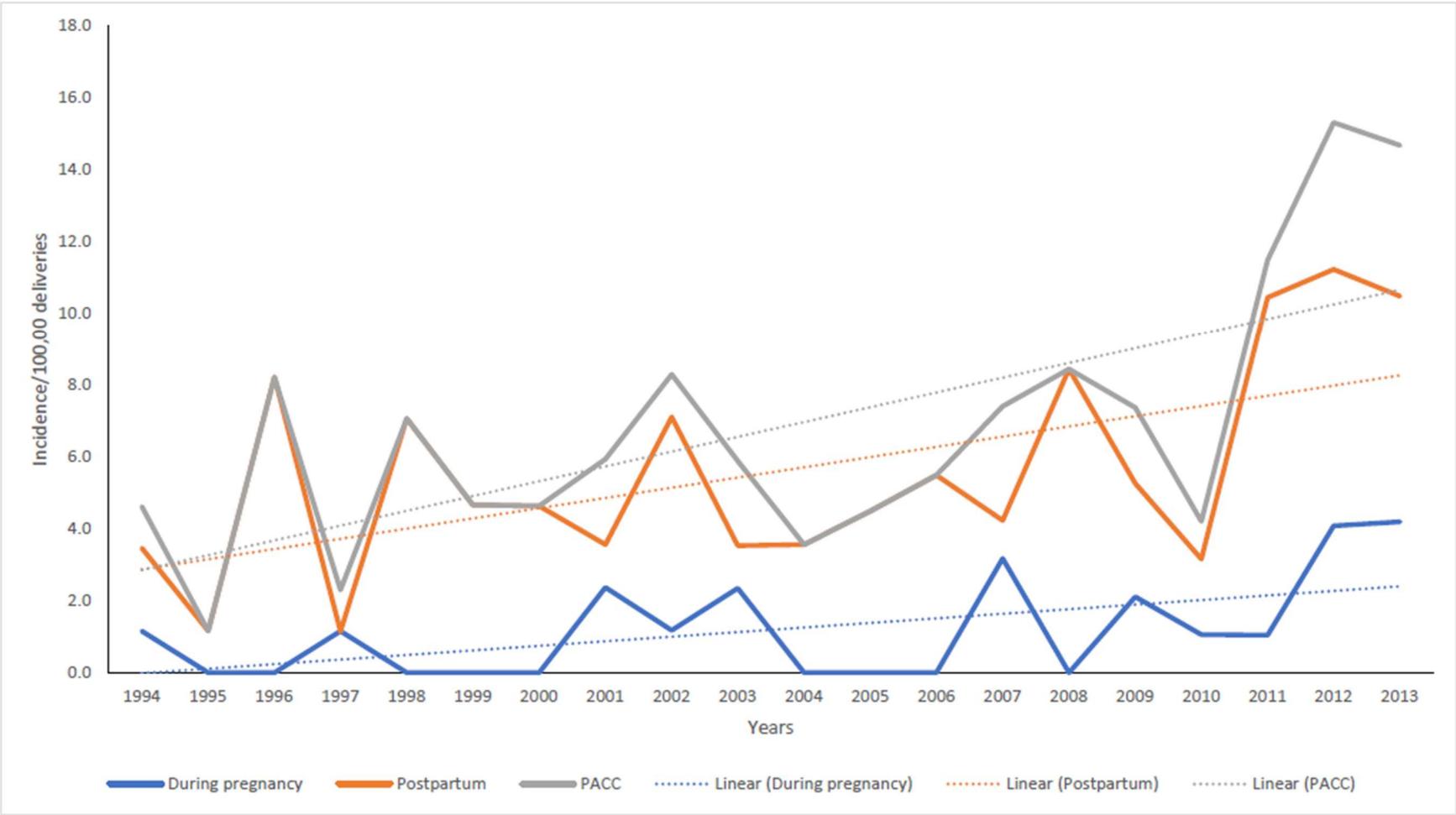
4.5.1 Incidence

We estimated the crude incidence rate of PACRC in NSW from 1994 to 2013 as 6.9 (95% CI 5.7-8.2) per 100,000 women giving birth (**Figure 4.1**). The incidence of PACRC increased from 4.6 per 100,000 women giving birth in 1994 to 14.7 per 100,000 women giving birth in 2013. This represents a significant increase of 6.6% each year (95%CI 3.2%-10.0%, p-value <0.001), and after adjusting for maternal age, the incidence significantly increased by 5.8% each year (95%CI 2.4%-9.3%, p-value=0.001).

The crude incidence rate of gestational CRC during the study period was 1.2 (95% CI 0.8 – 1.8) per 100,000 women giving birth. The incidence of gestational CRC increased from 1.2 per 100,000 women giving birth in 1994 to 4.2 per 100,000 women giving birth in 2013. This represents a significant increase of 12.5% each year (95% CI 3.4% – 22.3%, p-value = 0.006), and after adjusting for maternal age, the incidence significantly increased by 12.3% each year (95% CI 3.3 % – 22.2%, p-value = 0.007).

The crude incidence rate of postpartum CRC was 5.6 (95% CI: 4.6 – 6.8) per 100,000 women giving birth. The incidence of postpartum CRC increased from 3.5 per 100,000 women giving birth in 1994 to 10.5 per 100,000 women giving birth in 2013. This represents a significant increase of 5.4% each year (95% CI: 1.8% – 9.2%, p-value = 0.003), and after adjusting for maternal age, the incidence significantly increased by 4.5% each year (95% CI: 0.9 % – 8.3%, p-value = 0.014).

Figure 4.1 Crude and age-standardised incidence of pregnancy-associated colorectal cancer in NSW (1994-2013)



4.5.2 Maternal characteristics

Maternal demographic characteristics are presented in **Table 4.1**. The mean age of women with gestational CRC and postpartum CRC was 30.4 years (SD=6.7) and 32.3 years (SD=4.8), respectively, whereas the mean age of women with no cancer was 29.6 years (SD=5.6). The mean age of women diagnosed with postpartum CRC was significantly higher than women giving birth with no cancer; the mean difference was 2.7 years (95% CI: 1.42-4.03).

A significantly higher proportion of women in the PACRC group were older (35 or over) than women in the no-cancer group (34.1% vs 19.7%, $p < 0.001$). A higher proportion of first-time mothers were women with gestational CRC compared to women with no cancer (68.2% vs 41%, $p < 0.01$).

4.5.3 Cancer characteristics

Data on cancer stages for women with pregnancy-associated colorectal cancer (PACRC) were available for 101 (82.1%) women. Among women with PACRC and a known cancer stage, 34 (33.7%) were localised, 38 (37.6%) were regional, and 29 (28.7%) were diagnosed with distant metastasis. Of all women with PACRC, 82 (66.7%) were diagnosed with colon cancer, and 41 (33.3%) women were diagnosed with rectal, sigmoid or anal cancer during the gestational and postpartum period (**Table 4.2**).

Among the 123 cases examined, the most prevalent histological type was adenocarcinoma (NOS), with 57 patients, while neuroendocrine tumour G1 (NET G1) had 32 cases. The data provides valuable insights into the histological diversity of carcinoma cases during pregnancy and postpartum. **Table 4.3** presents the distribution of histology codes for different types of carcinomas between the gestational and postpartum periods.

4.5.4 Maternal complications

Table 4.4 shows birth interventions and maternal complications. The odds of severe maternal complications, as reflected by MMOI, were significantly higher for women diagnosed with gestational CRC compared to women with no cancer (AOR 29.27, 95% CI: 11.18-76.63). The odds of MMOI were also higher for women diagnosed with postpartum CRC compared to women with no cancer (AOR 2.79, 95% CI: 1.12 - 6.97). Additionally, women diagnosed with postpartum CRC had significantly higher odds of gestational hypertension compared to women with no cancer (AOR 1.89, CI:1.06-3.35) (**Table 4.4**).

Table 4.1 Demographic characteristics

Factors	Gestational	Postpartum	no-PAC	Total
	N (%)	N (%)	N (%)	N (%)
Total	22(100.0)	101(100.0)	1786078 (100.0)	1786201(100.0)
Age group				
< 30	11(50.0)	26(25.7)	863125(48.3)	863162(48.3)
30 - 34	5(22.7)	39(38.6)	570119(31.9)	570163(31.9)
35 - 39	4(18.2)	29(28.7)	292292(16.4)	292325(16.4)
>= 40	2(9.1)	7(6.9)	59829(3.3)	59838(3.4)
Unknown	0(0.0)	0(0.0)	713(0.0)	713(0.0)
Country of birth				
Australia	15(68.2)	74(73.3)	1263082(70.7)	1263171(70.7)
Overseas	7(31.8)	27(26.7)	522996(29.3)	523030(29.3)
Remoteness				
Major Cities	17(77.3)	82(81.2)	1356994(76)	1357093(76)
Inner Regional	3(13.6)	17(16.8)	305696(17.1)	305716(17.1)
Outer Regional	2(9.1)	2(2.0)	91655(5.1)	91659(5.1)
Remote or very remote	0(0.0)	0(0.0)	13262(0.7)	13262(0.7)
Unknown	0(0.0)	0(0.0)	18471(1.0)	18471(1.0)
Parity				
0	15(68.2)	35(34.7)	732969(41)	733019(41.0)
>=1	7(31.8)	66(65.3)	1052856(58.9)	1052929(58.9)
Unknown	0(0.0)	0(0.0)	253(0.0)	253(0.0)
History of CS^a				
Yes	3(15.0)	17(19.1)	194555(13.5)	194575(13.5)
No	17(85)	68(76.4)	1226196(85.1)	1226281(85.1)
Unknown	0(0.0)	4(4.5)	20917(1.5)	20921(1.5)
Plurality				
Singleton	20(90.9)	97(96.0)	1759408(98.5)	1759525(98.5)
Multiple birth	2(9.1)	4(4.0)	26670(1.5)	26676(1.5)
Antenatal care				
< 14 weeks	15(68.2)	77(76.2)	1203102(67.4)	1203194(67.4)
14 - 20 weeks	4(18.2)	14(13.9)	384915(21.6)	384933(21.6)
> 20 weeks	2(9.1)	7(6.9)	170828(9.6)	170837(9.6)
Unknown	1(4.5)	3(3.0)	27233(1.5)	27237(1.5)
Smoking during pregnancy				
Yes	2(9.1)	13(12.9)	276270(15.5)	276285(15.5)
No	19(86.4)	88(87.1)	1504790(84.3)	1504897(84.3)
Unknown	1(4.5)	0(0.0)	5018(0.3)	5019(0.3)
Place of birth				
Tertiary hospital	8(36.4)	25(24.8)	490763(27.5)	490796(27.5)
Private hospital	5(22.7)	29(28.7)	388892(21.8)	388926(21.8)
Public hospital	9(40.9)	47(46.5)	906420(50.7)	906476(50.7)
Unknown	0(0.0)	0(0.0)	3(0.0)	3(0.0)
Pre-existing hypertension				
Yes	0(0.0)	1(1)	15723(0.9)	15724(0.9)

No	22(100)	100(99)	1770355(99.1)	1770477(99.1)
Pre-existing diabetes				
Yes	0(0.0)	0(0.0)	10037(0.6)	10037(0.6)
No	22(100)	101(100)	1776041(99.4)	1776164(99.4)
CKD^{bc}				
Yes	0(0.0)	1(1.4)	6402(0.6)	6403(0.6)
No	18(100)	70(98.6)	1077957(99.4)	1078045(99.4)
CVD^{bd}				
Yes	0(0.0)	8(11.3)	28534(2.6)	28542(2.6)
No	18(100)	63(88.7)	1055825(97.4)	1055906(97.4)

^aData were available from 1998 onwards, ^bData were available from Jul 2001 onwards, ^cHospital admission due to chronic kidney disease prior to pregnancy, ^dHospital admission due to cardiovascular disease prior to pregnancy

Table 4.2 Cancer characteristics

Factors	Gestational	Postpartum	Total
Total	22	101	123
Age at diagnosis			
< 25	4(18.2)	4(4.0)	8(6.5)
25 - 39	7(31.8)	18(17.8)	25(20.3)
30 - 34	5(22.7)	34(33.7)	39(31.7)
35 - 39	4(18.2)	37(36.6)	41(33.3)
≥ 40	2(9.1)	8(7.9)	10(8.1)
Cancer group			
Colon	11(50)	71(70.3)	82(66.7)
Rectum, rectosigmoid and anus	11(50)	30(29.7)	41(33.3)
Stage of cancer			
Localised	7(31.8)	27(26.7)	34(27.6)
Regional	6(27.3)	32(31.7)	38(30.9)
Distant	3(13.6)	26(25.7)	29(23.6)
Unknown	6(27.3)	16(15.8)	22(17.9)

Table 4.3 Summary of histological diagnosis for both study groups

Tumour histological classification	Gestational	Postpartum	Total
Carcinoma, NOS	2	0	2
Squamous cell carcinoma, NOS	1	4	5
Squamous cell carcinoma, keratinizing, NOS	0	1	1
Basaloid squamous cell carcinoma	0	1	1
Adenocarcinoma, NOS	6	51	57
Adenocarcinoma, intestinal type	1	0	1
Adenocarcinoma in adenomatous polyp	0	5	5
Neuroendocrine tumour G1 (NET G1)	9	23	32
Goblet cell adenocarcinoma/Goblet cell carcinoid	0	1	1
Adenocarcinoma in villous adenoma	0	3	3
Adenocarcinoma in tubule villous adenoma	1	7	8
Mucinous cystadenocarcinoma, NOS	0	1	1
Mucinous adenocarcinoma	2	4	6
Total	22	101	123

4.5.5 Obstetric management

Women with gestational CRC had significantly higher odds of birth intervention (induction or no labour CS) compared to women without cancer (AOR 4.39, 95% CI:1.5-12.84) (**Table 4.4**).

4.5.6 Women's survival outcome

There were no significant differences between the overall survival probability for the 123 women diagnosed during pregnancy and the postpartum period ($p=0.564$) (**Figure 4.2**). The all-cause mortality rate for women diagnosed with colorectal cancer during pregnancy and the postpartum period was 19.3 (95% CI: 6.1 -46.4) per 1,000 person-year and 26.2 (95% CI: 17.3 -38.1) per 1,000 person-years, respectively.

Among 123 women diagnosed with PACRC, 29 (23.6%) women died during the follow-up period. Of these 29 women, the majority ($n=21$, 72.4%) were staged at diagnosis with distant metastasis, followed by regional ($n=7$, 24.1%) and localised ($n=1$, 3.4%).

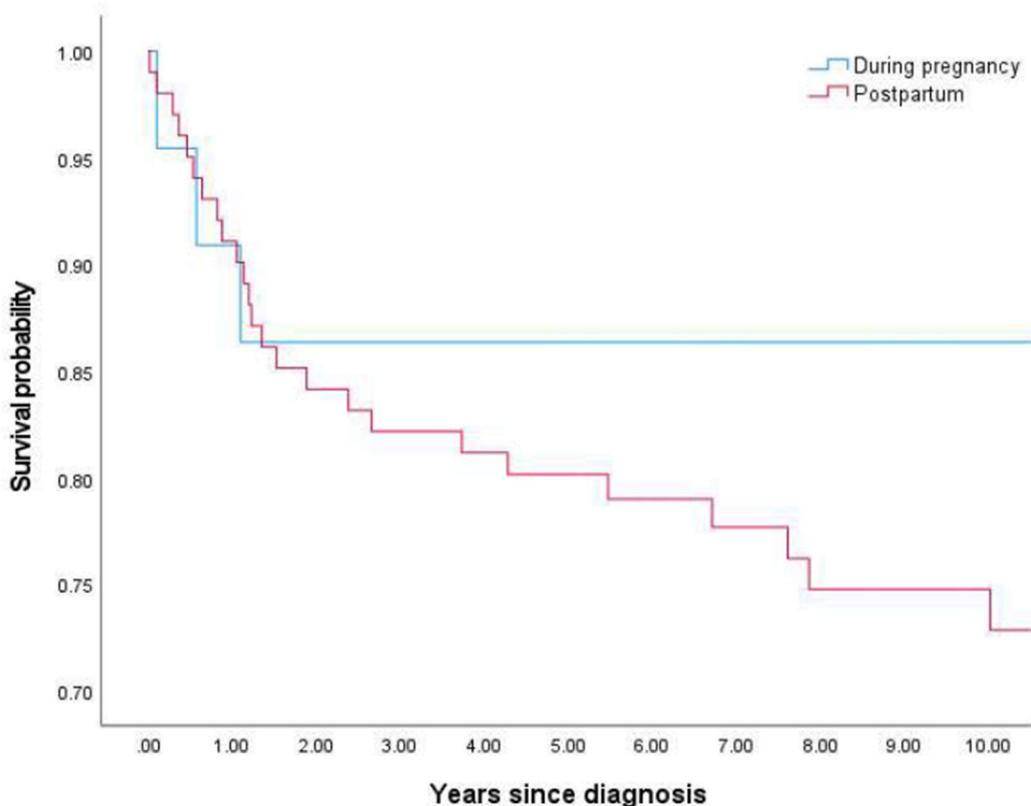
Of the 22 women with gestational CRC, four (18.2%) women had died by the end of the follow-up period. Of these women, three (75.0%) died within the first five years of cancer diagnosis and one over

ten years after cancer diagnosis. The cause of death for all four women was malignant neoplasm of the rectosigmoid junction.

Of the 101 women with postpartum CRC, 25 (24.8%) had died by the end of the follow-up period. Of those 20 (80.0%) women died within the first five years of cancer diagnosis, four (16.0%) died between five and ten years, and one died over ten years after a cancer diagnosis.

The principal causes of death in the 25 women with postpartum CRC included malignant neoplasm of an unspecified part of the colon (n=7, 28.0%), the rectosigmoid junction (n=5, 20.0%), the rectum (n=4, 16.0%), the sigmoid colon (n=2, 8.0%), the anal canal (n=1, 4%), other malignant neoplasm of the intestinal tract in for four women (16.0%), non-cancer related death for one women (4%) and an unknown cause of death for one women (4%).

Figure 4.2 Overall survival for gestational and postpartum colorectal cancer groups



4.5.7 Neonatal outcomes

There were 129 babies born to women with gestational CRC, 105 babies born to 101 women with postpartum CRC, and 1,795,978 babies born to women with no cancer. There were no perinatal deaths among babies born to women with gestational CRC and one (1%) perinatal death among babies born to women with postpartum CRC. The odds of perinatal death among babies born to women with postpartum CRC did not differ significantly from babies born to women with no cancer (AOR 0.89, 95% CI: 0.11-6.99) (**Table 4.5**).

The odds of preterm birth (< 37 weeks) were significantly higher in babies born to women with gestational CRC compared to babies born to women with no cancer (AOR 11.62, 95% CI:4.9-27.58). Similarly, the odds of planned preterm birth were higher in babies born to women with gestational CRC compared to babies born to women without cancer (AOR 9.91, 95% CI: 1.99-49.21). The higher rates of preterm birth were associated with a higher rate of admission to ICU in babies born to women with gestational CRC (50%) compared to babies born to women without cancer (16.4%) (AOR 3.96, CI:1.65-9.51) (**Table 4.5**).

There were no congenital abnormalities for babies born to women diagnosed with gestational CRC. However, the severe neonatal complications, as reflected by the NAOI, were higher for babies born to women diagnosed gestational CRC (40%) compared to babies born to women without cancer (5.2%) (AOR 8.65, CI:3.65-20.5) (**Table 4.5**). Among the children with severe neonatal complications in the gestational group, seven were diagnosed with respiratory distress syndrome of newborn, while one presented with transient tachypnoea of newborn and intracranial (nontraumatic) haemorrhage. Notably, all eight children necessitated ventilatory support/oxygen enrichment, with five requiring intravenous fluid (electrolyte/nutritional substance) and one needing the administration of packed cells.

Table 4.4 Obstetric morbidities, labour, and birth

Factors	Gestationa l N (%)	Postpartu m N (%)	no-PAC N (%)	Gestational^a AOR (95%CI)	Postpartum^a AOR (95%CI)
Total	22(100.0)	101(100.0)	1786078 (100.0)		
MMOI^{bc}					
Yes	8(44.4)	5(7.0)	26444(2.4)	29.27 (11.18 - 76.63)	2.79 (1.12 - 6.97)
No	10(55.6)	66(93)	1057915(97.6)		
Gestational diabetes					
Yes	2(9.1)	5(5.0)	81623(4.6)	1.78 (0.4 - 7.86)	0.98 (0.44 - 2.18)
No	20(90.9)	96(95)	1704455(95.4)		
Gestational hypertension					
Yes	1(4.5)	12(11.9)	109051(6.1)	0.45 (0.05 - 3.93)	1.89 (1.06 - 3.35)
No	21(95.5)	89(88.1)	1677027(93.9)		
Onset of labour					
Spontaneous	6(27.3)	51(50.5)	1088985(61)		
Induced	4(18.2)	29(28.7)	438995(24.6)	4.39 (1.5 -12.84) ^d	1.33 (0.91 -1.95) ^d
No labour	12(54.5)	21(20.8)	257643(14.4)		
Unknown	0(0.0)	0(0.0)	455(0.0)		
Type of delivery					
Vaginal	6(27.3)	58(57.4)	1140733(63.9)		
Instrumental vaginal	1(4.5)	8(7.9)	191746(10.7)		
Caesarean section	15(68.2)	35(34.7)	452709(25.3)	4.2 (1.72 -10.27) ^e	1.28 (0.91 - 1.80) ^e
Unknown	0(0.0)	0(0.0)	890(0.0)		
Discharge status (transferred)					
Yes	1(4.5)	6(5.9)	59176(3.3)	1.56 (0.21 - 11.73)	1.85 (0.76 - 4.49)
No	21(95.5)	95(94.1)	1726902(96.7)		

^aall outcomes are dichotomous in GEE models; ‘unknown’ category is combined with ‘no’ unless otherwise specified,

^bMaternal Morbidity Outcome Indicator (MMOI) occurred during pregnancy or within 42 days postpartum (14), ^cData were available from 2001 Jul onwards, ^d(Induced + no labour) vs. (spontaneous + unknown), ^eCS vs. (vaginal + instrumental vaginal + unknown).

Table 4.5 Neonatal outcomes (perinatal period)

Factors	Gestational N (%)	Postpartum N (%)	no-PAC N (%)	Gestational AOR (95%CI)^a	Postpartum AOR^a (95%CI)
Total	24(100.0)	105(100.0)	1813292 (100.0)		
Perinatal death					
Live>28days	24(100.0)	104(99.0)	1795978(99.0)		
Perinatal death	0(0.0)	1(1.0)	17059(0.9)	NA	0.89 (0.11 - 6.99)
Unknown	0(0.0)	0(0.0)	255(0.0)		
Gestational age at delivery					
<37 weeks	12(50.0)	15(14.3)	129637(7.1)	11.62 (4.9 - 27.58)	1.68 (0.89 - 3.18)
< 32 weeks	5(20.8)	5(4.8)	25244(1.4)		
32 - 36 weeks	7(29.2)	10(9.5)	104393(5.8)		
>= 37weeks	12(50.0)	90(85.7)	1683411(92.8)		
Unknown	0(0.0)	0(0.0)	244(0.0)		
Planned preterm^b					
Yes	6(25.0)	7(6.7)	43853(2.4)	9.91 (1.99 - 49.21) ^c	2.21 (0.92 - 5.32) ^c
No	6(25.0)	8(7.6)	85784(4.7)		
Not applicable	12(50.0)	90(85.7)	1683655(92.9)		
NAOI^{de}					
Yes	8(40.0)	7(9.1)	60062(5.2)	8.65 (3.65 - 20.5)	1.38 (0.60 - 3.17)
No	12(60.0)	70(90.9)	1093389(94.8)		
Low birthweight^e					
<2500g	11(45.8)	14(13.3)	103896(5.8)	12.92 (5.09 - 32.83)	2.14 (1.09 - 4.19)
>=2500g	13(54.2)	91(86.7)	1697220(94.2)		
Unknown	0(0.0)	0(0.0)	713(0.0)		
SGA^e					
Yes	1(4.2)	13(12.4)	184110(10.2)	0.33 (0.05 - 2.33)	1.41 (0.78 - 2.55)
No	23(95.8)	92(87.6)	1614179(89.6)		
Unknown	0(0.0)	0(0.0)	3540(0.2)		
LGA^e					
Yes	1(4.2)	12(11.4)	177888(9.9)	0.34 (0.03 - 3.89)	1.16 (0.67 - 2.00)
No	23(95.8)	93(88.6)	1620401(89.9)		
Unknown	0(0.0)	0(0.0)	3540(0.2)		
Apgar at 5min^e					
Less than 7	0(0.0)	1(1)	28820(1.6)	NA	0.56 (0.08 - 3.98) ^f
7 to 10	24(100.0)	104(99)	1767191(98.1)		
Unknown	0(0.0)	0(0.0)	5818(0.3)		
Admit to ICU^{eg}					
Yes	12(50.0)	27(25.7)	296258(16.4)	3.96 (1.65 - 9.51)	1.58 (1.02 - 2.44)
No	12(50.0)	78(74.3)	1504455(83.5)		
Unknown	0(0.0)	0(0.0)	1116(0.1)		
Length of stay^{eh}					
< 5 days	10(45.5)	62(66.7)	1185803(69.3)	1.57 (0.64 - 3.86)	0.90 (0.59 - 1.37)
5 or more	12(54.5)	31(33.3)	523106(30.6)		
Unknown	0(0.0)	0(0.0)	1698(0.1)		
Congenital conditionⁱ					
Yes	0(0.0)	0(0.0)	4765(1.6)	NA	NA
No	11(100)	31(100.0)	288073(98.4)		

^aall outcomes are dichotomous in GEE models; 'unknown' category are combined with 'no' unless otherwise specified. ^bIncluding labour induction and caesarean delivery without labour where main indications for caesarean section are not 'Failure to progress' or 'Fetal distress' preterm birth. ^cYes vs. (no + not applicable). ^dNeonatal Adverse Outcome Indicator (NAOI) identified from a birth record or in any hospital transfer admission prior to the first discharge home (Lain et al. 2012), ^eLive births only.^f(0 -3 + 4-6) vs. (7 – 10 + Unknown) ^gAdmission to Special Care Nursery (SC) or Neonatal Intensive Care unit (NICU) for 4 hours or more.^hOnly babies who were discharged home are included. ⁱRegister of Congenital Conditions are available for babies born in 2011 - 2013 only.

4.6 Discussion

This study found that although PACRC remains rare, the incidence has risen significantly by 6.6% yearly. This increasing trend persisted (Araujo et al. 2022; Saif 2005), even after adjusting for maternal age, and is consistent with several studies of an increasing incidence of PACRC over time (Aytac et al. 2016; Dahling et al. 2009; Samadder et al. 2020). A notable finding from this study is the increased interventions observed during childbirth for women with gestational CRC. Encouragingly, this study found no evidence of congenital anomalies or an elevated risk of perinatal death among babies born to women with PACRC. However, this study's results indicate a significantly higher rate of maternal and neonatal morbidities for women with gestational CRC than for women without cancer.

The incidence is on the rise

This study revealed a significant increase in the overall incidence of pregnancy-associated colorectal cancer (PACRC) over the 20-year study period (1994 to 2013), even after adjusting for maternal age. Even though advanced maternal age has been linked to this rise, this study's findings, consistent with previous research (Gens & Barbosa 2017; Samadder et al. 2020), suggest that it is not the only factor contributing to the increased incidence. Notably, the mean maternal age for women with gestational CRC in this study did not significantly differ from those without cancer, except for women with postpartum CRC, who were significantly older. This study hypothesises that the rise in incidence could be attributed to higher antenatal care uptake and improved cancer detection rates. However, this study's findings do not provide conclusive evidence regarding these potential contributing factors, necessitating further investigation into other plausible determinants. Previous research suggested that PACRC could be linked to various factors, including advanced maternal age, pregnancy-related growth factors, genetic predisposition and environmental influences (Predescu D et al. 2020; Samadder et al. 2020).

Additionally, there is an observed rise in PACRC cases among younger individuals, and different trends in the location of the cancers in pregnancy and postpartum are also worth noting. This increase may be attributed to factors not yet fully comprehended, potentially involving obesity and other unidentified lifestyle factors (Araujo et al. 2022; Ho, Cassano-Bailey & Czaykowski 2012; Predescu D et al. 2020; Samadder et al. 2020). The specific influence of these factors remains to be seen from this study, warranting further exploration to better understand the complex aetiology of PACRC.

Potential underdiagnosis during pregnancy

This study showed that the number of women diagnosed with postpartum CRC was almost five times those diagnosed with gestational CRC. This may be due to pregnancy delaying diagnosis and masking symptoms and signs. One recent study (Grass et al. 2019) found that two-thirds of women were diagnosed with CRC during the postpartum period despite having cancer-related symptoms (e.g., altered bowel habits and rectal bleeding) during pregnancy. Being younger (<45 years) and having symptoms similar to normal pregnancy contributes to a delay in the evaluation of gestational CRC. The diagnosis of gestational CRC poses a significant challenge for clinicians as it remains scarce, with an incidence rate of only 0.8 per 100,000 women giving birth (Amarjothi et al. 2019; Kocián et al. 2019) and potential underdiagnosis of gestational CRC may aggravate and worsen maternal conditions during postpartum (Aytac et al. 2016).

The diagnosis of gestational CRC introduces several complexities for healthcare teams. One notable challenge is the cautious approach towards conducting specific diagnostic tests during pregnancy, as there is a potential risk to the foetus. This hesitancy among healthcare providers may be influenced by limited clinical experience in managing this rare condition and the need for comprehensive data on optimal treatment and management approaches (Amarjothi et al. 2019; Kocián et al. 2019). Consequently, these uncertainties can contribute to delays in diagnosing and managing gestational CRC (Munteanu et al. 2019). Additionally, the practical considerations surrounding major surgical procedures, including the possibility of requiring a stoma (even temporarily), must be carefully considered when making decisions regarding the most appropriate course of action for pregnant individuals (Kocián et al. 2019; Predescu D et al. 2020).

This study's results suggest that women with gestational CRC are more likely to have severe MMOI than women with no cancer. Although women with postpartum CRC also had higher odds of adverse MMOI, their birth intervention (induction or no labour CS) was not significantly different from women with no cancer. Noting the rarity of PACRC and the commonality of presenting symptoms and signs of underdiagnosis of gestational CRC remains a challenge. In identifying this area, it is crucial to highlight the significance of incorporating antenatal guidelines for pregnant women, particularly in gestational CRC. These guidelines can play a vital role in emphasising the importance of early diagnosis and prompt treatment, ultimately aiming to reduce maternal morbidity associated with this condition. The Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) practice statements and guidelines provide evidence-based recommendations in antenatal care (Royal Australian and New Zealand College of Obstetricians and Gynaecologists 2023). They may serve as valuable references in developing comprehensive guidelines for gestational CRC management during pregnancy.

Increased delivery intervention and perinatal outcomes for babies

The obstetric management of gestational CRC is complex for clinicians who strive to maximise outcomes for the mother while minimising infant risks (Aytac et al. 2016; Munteanu et al. 2019). This study observed that women with gestational CRC had a higher rate of delivery intervention (induction or no labour CS) and planned preterm birth (<37 weeks) compared to women without cancer. Previous studies support these findings, indicating that women diagnosed with gestational CRC tend to have higher rates of preterm labour, caesarean sections (CS), and puerperal infections when compared to pregnant women without cancer (Dahling et al. 2009; Gens & Barbosa 2017). These studies hypothesised that women with CRC might be more susceptible to infections due to immune suppression, which could trigger an inflammatory reaction leading to preterm labour (Dahling et al. 2009; Gens & Barbosa 2017).

Additionally, vaginal delivery may heighten the risk of bleeding, and cancer-related immune suppression could increase the likelihood of complications such as infection, colon obstruction, perforation, and metastasis in women with gestational CRC compared to those without cancer (Gens & Barbosa 2017). Clinicians may be inclined to schedule preterm deliveries and CS for women with gestational CRC due to concerns about potential maternal and infant complications. Moreover, considerations about performing CRC resection during delivery may also influence decision-making (Dahling et al. 2009; Gens & Barbosa 2017; Longo et al. 2010). However, providing precise guidelines for women with gestational CRC during childbirth remains challenging. Obstetric management is highly individualised, considering factors such as the foetus's gestational age, the stage of cancer, and the maternal condition at the time of diagnosis (Dahling et al. 2009).

This study also found that there was a higher rate of preterm birth, admission to ICU, low birth weight (<2500 g) and NAOI for babies born to women with gestational CRC compared to women without cancer. This study included women diagnosed with cancer postpartum as a representation of undiagnosed cases during pregnancy, as literature suggests that the origin of postpartum cancer is likely to develop during pregnancy (Andersson et al. 2015; Lee et al. 2012; Silverstein et al. 2020). The lower rate of interventions in postpartum cases implies that intensive interventions during pregnancy are due to decisions around cancer management. The non-significant difference in the adverse neonatal outcomes between postpartum cancer cases and no cancer cases implies that cancer management, including timing and mode of birth and timing of initiation of cancer treatment, are the main factors affecting the neonatal outcome for babies born to women in the gestational group.

A higher rate of preterm birth and prematurity could be associated with NAOI. A study conducted by Kocián et al. (2019) revealed that women diagnosed with gestational colorectal cancer (CRC) experienced a higher incidence of iatrogenic preterm delivery than pregnant women without cancer. Most of these preterm deliveries were induced to expedite treatment initiation without compromising the foetus's well-being (Kocián et al. 2019). Premature delivery was

deemed necessary in certain situations, such as the need for postpartum therapy involving radiotherapy or surgery that could not be safely performed during pregnancy (Gens & Barbosa 2017; Kocián et al. 2019).

However, some cancer treatments are safer during pregnancy (Dahling et al. 2009; Kocián et al. 2019). Colon surgery to prevent disease progression may be an option before 20 weeks gestation as the uterus is still small (Dahling et al. 2009; Kocián et al. 2019). Among systemic cancer treatments, some (5-fluorouracil and oxaliplatin-based) are relatively safe to use during the second and third trimesters (Haggar et al. 2013; Kocián et al. 2019); therefore, clinicians may consider, if possible, initiating cancer treatment between the second and third trimesters and scheduling birth as close as possible to the 37th week of gestational age. Carefully considering the potential risks associated with preterm delivery is essential. Prematurity is recognised as the most common cause of neonatal morbidity and mortality, and it may contribute to developmental delay and neurodevelopmental impairment in the long term (Amant et al. 2015; Silverstein et al. 2020). The decision to proceed with preterm delivery in cases of gestational CRC should be made with meticulous consideration, weighing the benefits of early treatment initiation against the potential risks to the neonate's health and development.

Even though this study found a higher rate of NAOI for infants, reassuringly, there were no congenital anomalies and non-significant SGA for babies born to women with gestational CRC. Few recent studies also reported no adverse foetal outcome except prematurity and SGA, even in mothers diagnosed with advanced-stage metastasis (Gens & Barbosa 2017; Kocián et al. 2019; Yang & Han 2021). However, all those studies' sample sizes were very small, and the effect of the treatment, prognosis and maternal and neonatal outcomes still need to be noticeable (Kocián et al. 2019; Makoshi et al. 2015; Munteanu et al. 2019; Rogers, Dasari & Eng 2016).

According to Lee and Colleagues (2019), there was no difference in 5-year survival outcomes between pregnant women with colorectal cancer and non-pregnant women (Lee, Burge & Eastgate 2019). This was supported by another recent study (2020) that found overall survival was similar between women with colorectal cancer and non-pregnant women except for the advanced stage (Samadder et al. 2020). This study also showed similar survival outcomes for women with gestational CRC and postpartum CRC, suggesting that pregnancy did not significantly impact overall survival. This is reassuring for women and their clinicians regarding the prognosis of PACRC, enabling better planning for childbirth and postpartum care.

The disease burden is significant for women with PACRC and their families, challenges in optimising outcomes for women and their unborn children, and the psychological distress of simultaneously dealing with cancer and pregnancy. Further research is required to understand better the impacts of PACRC on maternal and neonatal outcomes after colorectal cancer management during pregnancy and the postpartum period.

4.7 Strengths and limitation

The strength of this study is that it is a population-based study spanning 20 years (1994-2013) and includes all women giving birth in NSW. However, the study needed more data on treatment for PACRC; therefore, this study could not provide a more in-depth review of maternal and neonatal outcomes related to treatment. The dataset's lack of information on early pregnancy loss limits analyses and may underrepresent the number of PACRC cases.

4.8 Conclusions

The incidence of PACRC has been rising over the last 20 years, even after adjusting for maternal age. Reassuringly, there were no congenital anomalies and perinatal deaths among babies of women with PACRC. However, the increase in birth interventions and higher maternal and neonatal morbidities among women with gestational CRC compared to women giving birth without cancer presents a complex challenge for healthcare practitioners, as there are still no precise guidelines for managing women diagnosed with PACRC. Further research is required with multidisciplinary collaboration to include women with a current PACRC diagnosis and treatment information to develop evidence-based protocols that address the healthcare needs of this vulnerable population.

4.9 Chapter summary

While this study provided valuable insights into the maternal and neonatal outcomes associated with pregnancy-associated colorectal cancer, the findings raised further questions regarding the clinical decision-making processes, particularly around the high rates of birth interventions and variations in care. The lack of individual-level treatment and communication data limited the ability to understand how clinical decisions were made and experienced by women. These gaps highlighted the need to explore women's subjective experiences and interactions with healthcare professionals, particularly around diagnosis, treatment planning, and delivery. These questions are explored in the qualitative interview study presented in Chapter 6.

Chapter 5: Perinatal outcomes for infants exposed to systemic treatment during gestation: A systematic review and meta-analysis

5.1 Publication

The results presented in this chapter have been published in the *BMJ Open* journal as follows: Sultana Farhana, Jane Frawley, Nadom Safi, Antoinette Anazodo, Richard G McGee, Marc Remond, Elizabeth A. Sullivan. 2024. Perinatal outcomes for infants exposed to systemic treatment during gestation: A systematic review and meta-analysis. *BMJ Open*, 2025-06, Vol. 15 (6), p.e08471.

5.2 Chapter introduction

Chapter 1 outlined that the incidence of pregnancy-associated cancer is on the rise, presenting complex challenges in its management. This complexity arises from the need to carefully balance the potential benefits of cancer treatment for the mother's survival against the risks that such treatment may pose to the developing foetus. This challenge underscores the critical importance of understanding how systemic cancer treatment affects maternal and foetal outcomes. Chapter 1 already established the significance of the research project and articulated the third research question: "Do perinatal outcomes for babies born to women with cancer during pregnancy differ based on exposure to systemic cancer treatment in utero?" Chapter 2 provides a comprehensive review of the current international literature on systemic therapy exposure in women diagnosed with cancer during pregnancy. This review highlights the frequent exclusion of pregnant women from therapeutic and preventive clinical trials, resulting in a considerable gap in the evidence regarding the safety and efficacy of systemic therapies for pregnant women and their offspring (Evans 2020; Shields & Lyerly 2013; Silverstein et al. 2020). This chapter aims to fill this gap by offering insights into these treatments' safety and potential risks, ultimately contributing to developing evidence-based guidelines for managing cancer during pregnancy.

5.3 Background

Cancer is a leading cause of mortality in women during their reproductive years (Eastwood-Wilshere et al. 2019; Garofalo et al. 2017), and the incidence of cancer diagnosed during pregnancy (gestational cancer) has been steadily increasing in recent decades (De Haan et al. 2018; Zagouri et al. 2016). This trajectory is primarily associated with the increasing age of women giving birth (Eastwood-Wilshere et al. 2019; Maggen et al. 2019; Wolters et al. 2021). Approximately one in every 1,000 pregnant women is diagnosed with cancer during pregnancy also known as gestational cancer (Hepner et al. 2019; Wolters et al. 2021), with breast cancer being the most common, comprising 21% of pregnancy-associated malignancies (Zubor et al. 2018). Cancer management during pregnancy is challenging because of the need to optimise women's outcomes while protecting the developing foetus (Zubor et al. 2018). Consequently, any treatment plan requires careful consideration of the mother's needs, alongside potential risks to

the foetus during pregnancy (De Haan et al. 2018). Generally, the most effective treatment, with the lowest risks to pregnancy and the foetus, is prioritised.

Systemic therapies for cancer management may include chemotherapy, hormonal therapy, non-cytotoxic therapy, and immunotherapy (Hepner et al. 2019). The administration of these therapeutic agents during pregnancy may be associated with adverse effects on the growing foetus, including congenital malformations and teratogenicity (Momen et al. 2018; Momen et al. 2017). Exposure during the first trimester is particularly risky for developing foetuses (Dekrem, Van Calsteren & Amant 2013; Garofalo et al. 2017; Momen et al. 2017). For this reason, the administration of any chemotherapeutic medication during pregnancy should be delayed until after 14 weeks of gestation (Garofalo et al. 2017; Hepner et al. 2019; Kobayashi et al. 2019). Even when chemotherapy is administered after this period, it increases the risk of stillbirth, preterm birth, prematurity, and intrauterine growth restriction (IUGR) (Capozza et al. 2024; De Haan et al. 2018; Garofalo et al. 2017).

Furthermore, it has been reported that the administration of chemotherapy in pregnancy as late as 3-4 weeks before giving birth may increase the risk of infections in mothers and foetuses and bleeding complications in mothers due to haematological toxicity (La Nasa, Gaughan & Cardonick 2019). In addition to the potential impact of in-utero chemotherapy exposure on perinatal outcomes for babies, it has been suggested that such exposure may be associated with long-term developmental consequences, especially cognitive and general development (Amant et al. 2015). However, at present, there is very limited evidence regarding the long-term outcomes of children who have been exposed to systemic therapy in utero (Amant et al. 2015; Cardonick et al. 2015).

Given the increasing incidence of gestational cancer and because it is not always possible to delay systemic therapy for women with gestational cancer until after they have given birth, foetal exposure to systemic therapy is increasing (Zhang et al. 2019). Hence, it is important for clinicians and patients to have a better understanding of perinatal outcomes associated with exposure to systemic therapy during pregnancy in women with cancer to inform critical treatment decisions.

This systematic review aimed to synthesise the available evidence relating to whether perinatal outcomes for babies born to women with cancer during pregnancy differ based on whether they are exposed to systemic cancer treatment (chemotherapy, hormonal therapy, immunotherapy) in-utero.

5.4 Methods

The methods and results of this systematic review and meta-analysis were reported following the "Preferred Reporting Items for Systematic Review and Meta-analysis Protocols" (PRISMA) guidelines (Page et al. 2021). The review aimed to address the following research question: "Do perinatal outcomes for babies born to women with cancer during pregnancy differ based on exposure to systemic cancer treatment in utero?"

5.4.1 Inclusion Criteria

Cohort and case-control studies were included. Systematic reviews, case studies, and animal studies were excluded. Peer-reviewed full-text articles published in English were included. Letters, abstracts, seminar reviews, and editorials were excluded from the analysis.

Studies included that reported both a study group (women with cancer during pregnancy who received systemic therapy) and a comparison group (women with cancer during pregnancy who did not receive systemic therapy).

5.4.2 Search methods for identification of studies

Information sources and search strategy

MEDLINE and EMBASE via OVID, COCHRANE, CINAHL, and Google Scholar were searched for all relevant articles published between January 2001 and March 2023. These dates were chosen to prioritise studies relevant to current treatment regimens and the clinical context. The search terms are presented in **Appendix 4**.

Searching other resources

The reference lists of the included studies were searched for additional relevant publications. In addition, a paediatric endocrinologist, a content expert, played a crucial role in providing his expertise and insights for this research. This expert was contacted to gather additional information, validate findings, and ensure the accuracy and relevance of the study.

5.4.3 Study records

Study Selection

Two investigators (SF and JF) independently screened the titles and abstracts returned from the searches and removed ineligible records. The full texts of the remaining records, comprising those that appeared to meet the inclusion criteria and those where eligibility was uncertain after title and abstract review, were accessed and reviewed by the same two investigators to decide which records to include in the review. A third investigator (NS) resolved any discrepancies between the two investigators.

Data collection

Two investigators (SF and JF) independently extracted the relevant data using a standardised electronic data extraction form (see **Appendix 5**). Where possible, investigators were contacted to provide any missing information. Any disagreement between the SF and JF was resolved by further discussion with a third investigator (NS).

5.4.4 Quality Assessment

The risk of bias in the included studies was evaluated using the Robins I tool (Sterne et al. 2016). The risk of bias was graded as low, moderate, severe, or critical for the following domains based on their possible impact on the study's validity: recruitment strategies, sample size, data reporting, data coverage, statistical analysis, and confounding factors.

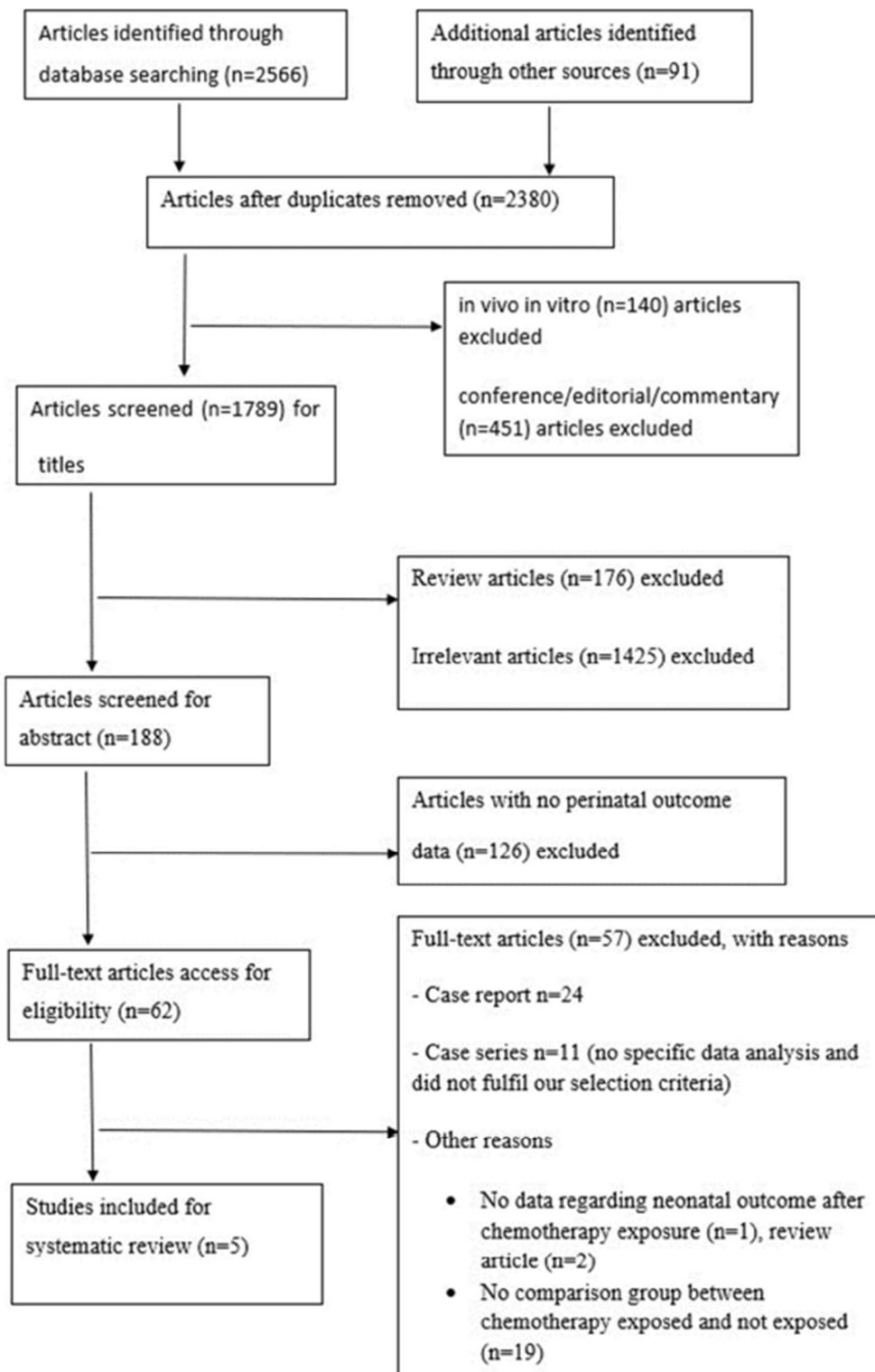
5.4.5 Data analysis

A random-effects model was used to calculate pooled odds ratios (pORs) and 95% confidence intervals (CIs) to measure the effects of exposure to systemic cancer treatment during gestation on spontaneous abortion, stillbirth, birthweight <10th percentile (small for gestational age or SGA), IUGR, and preterm birth (<37 weeks gestation). Statistical heterogeneity between studies was assessed using the χ^2 statistic. Sensitivity analyses were conducted by removing each study individually and recalculating the pooled results to evaluate whether a single study's overall findings could be markedly affected. A p-value of less than 0.05 ($p < 0.05$) was considered statistically significant. Statistical analyses were performed using Review Manager 5.4 software (*Review Manager (RevMan) [Computer software]. Version 5.4. The Cochrane Collaboration. 2020*).

5.5 Results

A total of 2,657 articles were identified: 2,566 through database searches and 91 through other sources (**Figure 5.1**). After removing duplicates, 2,380 articles remained. After excluding all conferences, reports, abstracts, editorials, commentaries, and animal studies, 1,789 articles remained. The titles of these articles were then screened; 1,425 articles were not relevant to the study questions, and 176 review articles were excluded. The abstracts of the remaining 188 articles were screened, and 126 articles were excluded because they did not report any perinatal outcomes. The full texts of the remaining 62 articles were reviewed, and five met the inclusion criteria for this systematic review.

Figure 5.1 Study flow diagram



5.5.1 Included studies

All five studies that met the inclusion criteria were cohort studies (Cardonick, Usmani & Ghaffar 2010; Cardonick et al. 2015; Loibl et al. 2012; Peres et al. 2001; Safi et al. 2019).

The characteristics of the included studies and perinatal outcomes reported are presented in **Table 5.1**.

5.5.2 Excluded studies

A total of 57 full-text articles were excluded after full-text review (see **Appendix 6**). We excluded 24 case reports and 11 case series that did not fulfil our selection criteria, contained no specific data analysis and did not examine neonatal outcomes. We excluded the remaining 22 articles because they reported outcome data only for babies of women with gestational cancer who had been exposed to chemotherapy in utero, and they did not include a comparison group (i.e. no babies of women with gestational cancer who were not exposed to chemotherapy in utero).

5.5.3 Settings

Three studies were conducted using data from national and international cancer in pregnancy registries (Cardonick, Usmani & Ghaffar 2010; Cardonick et al. 2015; Loibl et al. 2012), whereas two studies used data collected from hospital records (Peres et al. 2001; Safi et al. 2019), one from Brazil and one binational study from Australia and New Zealand. Of the three registry studies, one from the United States (US) (Cardonick, Usmani & Ghaffar 2010) drew upon data from the Cancer and Pregnancy Registry created in 1997. This registry collected data from various institutions in the US and included the type of cancer diagnosis, treatment categories, and maternal and neonatal outcomes for women who were diagnosed with cancer during pregnancy. A second US registry study (Cardonick et al. 2015) followed mother-infant pairs who had been enrolled in the Cancer and Pregnancy Registry to examine the developmental outcomes of children (18 months or more). In the third registry study (Loibl et al. 2012), women diagnosed with breast cancer were recruited, and data were collected from seven European countries through the Breast International Group and other international collaborations.

5.5.4 Characteristics of study cohorts

The five included studies compared the perinatal outcomes of 427 neonates born to mothers diagnosed with cancer who received systemic therapy during pregnancy with those of 283 neonates born to mothers who did not receive systemic therapy during pregnancy. The ages of the women included in these studies ranged from 18 to 45 years. The duration of follow-up for children differed among the five studies. In the studies conducted by (Safi et al. 2019) and (Loibl et al. 2012) the follow-up period was relatively short, extending to four weeks after delivery. In contrast, the studies by (Cardonick, Usmani & Ghaffar 2010; Cardonick et al. 2015; Peres et al. 2001) had a longer follow-up period,

spanning from 4 months to 14 years. Notably, in the (Cardonick et al. 2015) study, a Cancer and Pregnancy Registry was established in 1997, enrolling mother-infant pairs for an extended follow-up period of 18 months or longer.

Two studies have focused solely on breast cancer during pregnancy (Loibl et al. 2012; Safi et al. 2019) while the other three studies included women with breast cancer, Hodgkin's and Non-Hodgkin lymphoma, leukemia (ALL, AML, CML), ovarian cancer, and cervical cancer (Cardonick, Usmani & Ghaffar 2010; Cardonick et al. 2015; Peres et al. 2001).

5.5.5 Characteristics of treatments

Most women who participated in the included studies were treated with either single or combination therapy comprising taxane-based chemotherapy (paclitaxel, docetaxel), anthracycline (doxorubicin, epirubicin, bleomycin, idarubicin, daunorubicin), alkylating agents (cyclophosphamide, busulfan, dacarbazine), vinca alkaloids (vincristine and vinblastine), antimetabolites (5-Fluorouracil, cytarabine, methotrexate), and platinum agents (cisplatin and carboplatin). In one study (Safi et al. 2019), two women received hormonal therapy (tamoxifen), and one received monoclonal antibodies (trastuzumab) in addition to cytotoxic chemotherapy during pregnancy.

The most common chemotherapy agents used for women diagnosed with breast cancer during pregnancy were anthracyclines (doxorubicin, epirubicin), taxane-based chemotherapy (paclitaxel, docetaxel), cyclophosphamide, methotrexate, and five fluorouracil (Cardonick, Usmani & Ghaffar 2010; Cardonick et al. 2015). For women with haematological cancers (Hodgkin and Non-Hodgkin lymphoma and leukemia), the most common chemotherapy agents used during pregnancy were vincristine, idarubicin/doxorubicin, daunorubicin, cytarabine, cisplatin, etoposide, busulphan, L-asparaginase (Cardonick et al. 2015). Cisplatin/paclitaxel, etoposide, bleomycin, carboplatin, and paclitaxel were the standard chemotherapy drugs used for women diagnosed with ovarian cancer during pregnancy (Cardonick et al. 2015; Peres et al. 2001). None of the pregnant women included in these studies was exposed to non-cytotoxic chemotherapy or immunotherapy during pregnancy.

5.5.6 Perinatal outcomes

5.5.6.1 Spontaneous abortion and pregnancy termination

Two studies reported data on spontaneous abortion, with one study reporting pregnancy termination after cancer diagnosis. Loibl and colleagues (Loibl et al. 2012) reported a 1% (n=1) spontaneous abortion rate in the chemotherapy-exposed group compared to no spontaneous abortions in women not exposed to chemotherapy (not statistically significant, p=1.0). Similarly, Peres and colleagues (Peres et al. 2001) reported that 8% (n=1) of women exposed to chemotherapy during pregnancy had a spontaneous abortion compared to no women who were not exposed to chemotherapy (not statistically significant, p=0.60). Peres and colleagues also reported that 8% (n=1) of women

exposed to chemotherapy underwent a pregnancy termination compared to 33% (n=5) of women who were not exposed to chemotherapy. However, this difference was not statistically significant (p=0.12).

5.5.6.2 Intrauterine foetal death (IUFD), stillbirth, and neonatal mortality

Loibl and colleagues reported no significant differences in stillbirth (a baby is born without signs of life after the 20th week of pregnancy) rates for pregnant women exposed to chemotherapy compared with pregnant women not exposed to chemotherapy [1% (n=1) vs. 1% (n=2), p=0.60] (Loibl et al. 2012). Conversely, Peres and colleagues reported a stillbirth rate of 33% (n=4) for pregnant women exposed to chemotherapy (cytotoxic drugs) compared to 0% (n=0) for those not exposed to chemotherapy; nonetheless, the difference was not statistically significant (p=0.07) (Peres et al. 2001).

Cardonick and colleagues reported that there was no significant difference in the rate of intrauterine foetal death (a baby died in the mother's womb before birth) [0.7% (n=1) vs 0% (n=0)] and neonatal death [0.7% (n=1) vs 0% (n=0)] between pregnant women exposed to chemotherapy and pregnant women not exposed to chemotherapy (Cardonick, Usmani & Ghaffar 2010). The two remaining studies reported no stillbirths or neonatal deaths in the chemotherapy-exposed and non-exposed groups (Cardonick et al. 2015; Safi et al. 2019).

5.5.6.3 Intrauterine growth restriction (IUGR)

Two studies (Cardonick, Usmani & Ghaffar 2010) reported that infants exposed to chemotherapy (anthracyclines, cyclophosphamide, methotrexate, fluorouracil, taxane) and infants not exposed to chemotherapy experienced similar rates of IUGR [7.6% (n=12) vs 7.1% (n=5)] and [4% (n=7) vs 1% (n=1)], respectively, with no statistically significant differences.

5.5.6.4 Apgar score

Peres and colleagues compared Apgar scores between study groups and reported that 25% (n=2) of infants exposed to chemotherapy had Apgar scores of <7 at 5 minutes compared to 10% (n=1) of infants who were not exposed; however, the difference was not statistically significant (Peres et al. 2001). Safi and colleagues also reported no significant difference in Apgar scores at 5 minutes between infants exposed to chemotherapy and those not exposed (p=0.34) (Safi et al. 2019).

5.5.6.5 Birth weight and small for gestational age (SGA)

Three studies examined SGA as an outcome, but none reported a significant difference in the SGA rates between the chemotherapy-exposed and non-exposed groups. Safi and colleagues reported that 11.1% (n=2) of babies in the chemotherapy-exposed group were SGA, while 0% (n=0) in the non-exposed group, not statistically significant (p=1.00)

(Safi et al. 2019). Similarly, Loibl and colleagues reported no significant difference in SGA between chemotherapy-exposed and non-exposed infants [9% (n=15) vs. 4% (n=5), p=0.10]. Cardonick and colleagues reported 7.6% (n=12) SGA in the chemotherapy-exposed group compared to 7.1% (n=5) in the non-exposed group, but they did not mention the statistical significance (Cardonick, Usmani & Ghaffar 2010).

All studies reported no statistically significant differences in birth weight between infants exposed to chemotherapy in utero and those not exposed (Cardonick, Usmani & Ghaffar 2010; Cardonick et al. 2015; Loibl et al. 2012; Peres et al. 2001; Safi et al. 2019). However, Safi and colleagues (Safi et al. 2019) observed a noteworthy contrast between infants born with low birth weight (<2500 g) in the exposed group (50%, n=9) compared to none in the non-exposed group. This difference was not statistically significant (p=0.052).

5.5.6.6 Preterm birth

Peres and colleagues reported that preterm birth was significantly higher for women exposed to chemotherapy during pregnancy (75%, n=6) than for women not exposed to chemotherapy (20%, n=2), (p=0.03) (Peres et al. 2001). Safi and colleagues (2019) also reported a significantly higher rate of preterm birth for women exposed to chemotherapy during pregnancy (66.7%, n=12) compared to those not exposed (0%, n=0), (p=0.014) and stated that this difference was primarily due to induced labour or planned caesarean section in the exposed group (Safi et al. 2019). In contrast, two studies reported that the risk of preterm birth for women exposed to chemotherapy was not significantly different to women who were not exposed to chemotherapy (Cardonick et al. 2015; Loibl et al. 2012) Cardonick, Usmani & Ghaffar (2010) reported that the rate of preterm birth in women exposed to chemotherapy in the first trimester (5.8%) was similar to the rate seen in the general population; they did not report the preterm birth rate for the non-exposed group in this study (Cardonick, Usmani & Ghaffar 2010).

5.5.6.7 Congenital anomalies/congenital disabilities

Three studies reported no specific neonatal congenital anomalies or disabilities in babies born to mothers with gestational cancer who were exposed or not exposed to chemotherapy during pregnancy (Loibl et al. 2012; Peres et al. 2001; Safi et al. 2019). In one study (Cardonick et al. 2015), congenital anomalies were reported in two (5.7%) cases in the chemotherapy-exposed group, while none were reported in the non-exposed group, and no statistical testing was undertaken. In another study (Cardonick, Usmani & Ghaffar 2010), six (3.8%) cases of congenital anomalies were reported after chemotherapy exposure during all trimesters of pregnancy, and no congenital anomalies were reported for the non-exposed group. However, the authors noted that the rate of congenital anomalies observed in the exposed group was equivalent to that in the general population (Cardonick, Usmani & Ghaffar 2010), and no statistical testing was carried out to determine this significance.

5.5.6.8 Neonatal intensive care unit admission

Only one study investigated neonatal admission to the Neonatal Intensive Care Unit (NICU). Safi and colleagues (2019) reported that 50.0% (n=9) of neonates exposed to chemotherapy were admitted to NICU compared to 16.7% (n=1) of neonates who were not exposed to chemotherapy during pregnancy (Safi et al. 2019). However, this difference was not statistically significant (p=0.34).

5.5.6.9 Long-term outcomes

Two studies reported an association between cyclophosphamide exposure during the first trimester of pregnancy and increased long-term risk in offspring of being diagnosed with cancer. Peres and colleagues (2001) reported that one of the children in their cohort who had been exposed to cyclophosphamide in utero had a developmental disability and papillary carcinoma of the thyroid and neuroblastoma during adolescence (Peres et al. 2001). Cardonick and colleagues (2010) reported a single instance of poor long-term outcomes in one child from their cohort who had been exposed to chemotherapy in utero (Cardonick, Usmani & Ghaffar 2010). This child was diagnosed with thyroid malignancy and neuroblastoma during adolescence. Interestingly, the child had a twin who was unaffected. However, no information was provided about inherited cancer predisposition syndromes.

Two studies reported no significant differences in developmental delay, speech delay, cognitive skills, and academic achievement in early childhood (between 12 and 42 months of age) between children who had been exposed to chemotherapy in utero and those who had not (Cardonick, Usmani & Ghaffar 2010; Cardonick et al. 2015).

5.6 Risk of bias in individual studies

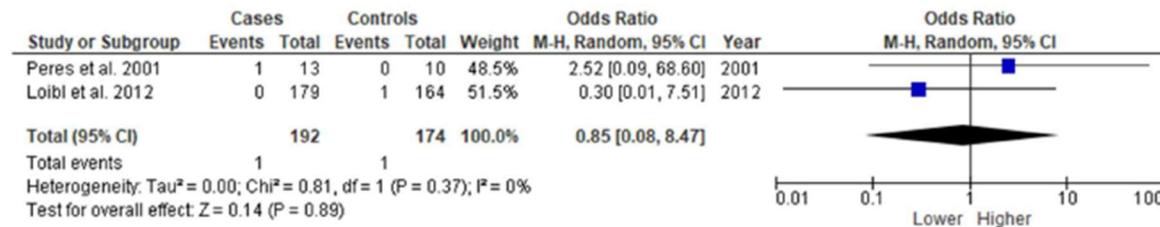
The results of the evaluation of the risk of bias in the included studies are presented in **Table 5.2**. Three studies (Cardonick et al. 2015; Peres et al. 2001; Safi et al. 2019) as being at low risk for bias, and two studies as being at moderate risk of bias. One of the studies assessed to be at moderate risk of bias was conducted by Loibl and colleagues (Loibl et al. 2012); it exhibited reporting bias as there was much closer monitoring of the systemic therapy-exposed group compared to the unexposed group. In the other study at moderate risk of bias, Cardonick and colleagues reported inherent bias due to most participants enrolled before knowing the birth outcomes, which mitigates concerns that only women with adverse pregnancy outcomes were likely to report information about chemotherapy during pregnancy (Cardonick, Usmani & Ghaffar 2010).

5.7 Meta-analysis

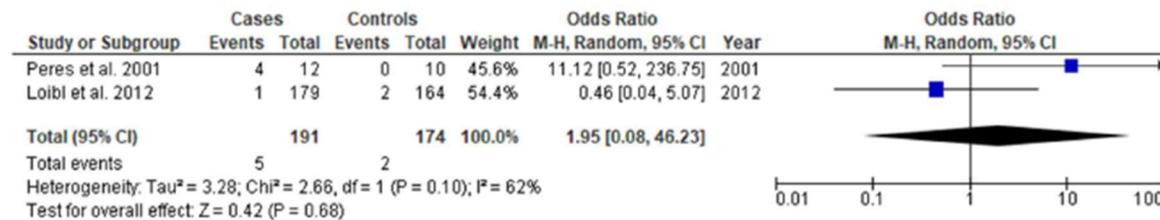
Forest plots displaying the results of the meta-analysis are presented in **Figure 5.2**. Four of the five studies reporting preterm birth reported results for both cases (exposed to systemic therapy during pregnancy) and controls (not exposed). When these data were pooled and tested, a statistically significant increase in the odds of preterm birth was observed (pOR 3.76, 95% CI: 1.44 – 9.83) in cases. Three studies reported data on SGA for both cases and controls. The pooled analysis did not indicate a statistically significant increase in the odds of SGA (pOR 1.69, 95% CI: 0.81-3.50) in cases. Similarly, two studies reported spontaneous abortion and stillbirth rates for both cases and controls; pooled analysis did not reveal a significant increase in the odds of either outcome in the exposed group (pOR 0.85, 95% CI: 0.08-8.47) and (pOR 1.95, 95% CI: 0.08-46.23), respectively. Two studies provided data on IUGR for both cases and controls; pooled analysis did not reveal a significant increase in the odds of IUGR in the exposed group (pOR 2.14, 95% CI: 0.37-12.45).

Figure 5.2 Forest plot of random-effects meta-analysis of in utero exposure to systemic cancer treatment and its association with spontaneous abortion, stillbirth, SGA, IUGR and preterm birth

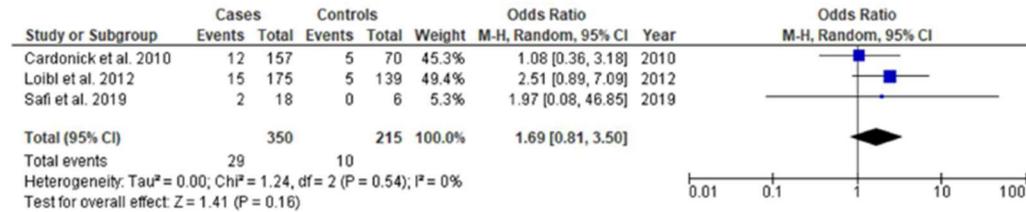
Forest plot of random effect meta-analysis of the association between in-utero exposure to systemic cancer treatment and spontaneous abortion



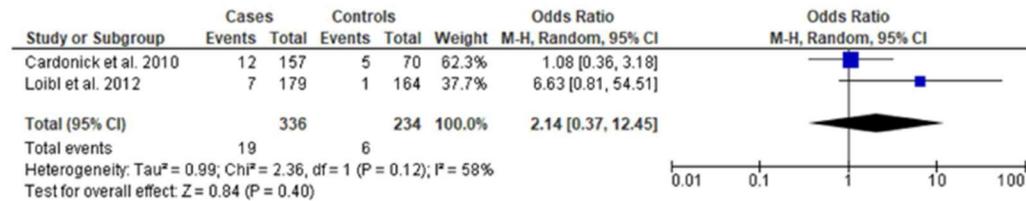
Forest plot of random effect meta-analysis of the association between in-utero exposure to systemic cancer treatment and stillbirth



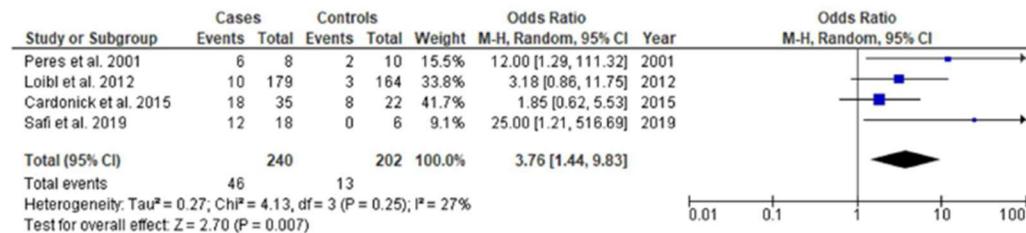
Forest plot of random effect meta-analysis of the association between in-utero exposure to systemic cancer treatment and birthweight < 10th percentile (SGA)



Forest plot of random effect meta-analysis of the association between in-utero exposure to systemic cancer treatment and IUGR



Forest plot of random effect meta-analysis of the association between in-utero exposure to systemic cancer treatment and Preterm birth



5.8 Discussion

Systemic cancer treatment during pregnancy is challenging, as it seeks to balance the most effective treatment for mothers with foetal safety. Many competing factors must be considered, including the choice of therapy in each pregnancy trimester, dose and duration of treatment, and transplacental transfer of medication to the foetus, all of which may have an impact on perinatal and neonatal outcomes following systemic therapy (Bell & Kerr 2015; Miyamoto et al. 2016).

Reassuringly, the findings from this systematic review and meta-analysis suggest no significant differences in spontaneous abortion or stillbirth rates for women with gestational cancer who are exposed or not exposed to systemic therapy during pregnancy, nor any difference in the rates of SGA or congenital malformations in their infants. Nonetheless, one study included in this review (Peres et al. 2001) reported a higher stillbirth rate in women with gestational cancer who received chemotherapy. It is important to note that this increase was observed in women who received treatment for aggressive tumours in the first trimester (Peres et al. 2001).

In contrast, the other studies included in this review reported no differences in the rates of stillbirth in women who were exposed to chemotherapy during the second and third trimesters, which is known to be comparatively safer for the developing foetus than exposure during the first trimester (Cardonick, Usmani & Ghaffar 2010; Peres et al. 2001). These findings align with previous research that suggests that approximately 15% of pregnant women exposed to chemotherapy during the first trimester will experience spontaneous abortion, and 20% of their live-born infants will have congenital malformations, mainly due to the impact of early treatment on organogenesis and foetal development (Garofalo et al. 2017; Maggen et al. 2019; Miyamoto et al. 2016). Other factors, apart from the timing of exposure to chemotherapy during pregnancy, are essential in this context, including cancer type, disease severity, and cancer progression.

Previous research has suggested that a higher rate of preterm birth is expected in women with gestational cancer who are exposed to systemic therapy during pregnancy (Esposito et al. 2021; Maggen et al. 2019; Momen et al. 2018). The studies included in this review supported this suggestion. However, it is worth noting that two studies (Peres et al. 2001; Safi et al. 2019) reported a statistically significant increase in preterm birth rates for infants exposed to systemic therapy in utero. Notably, one of these studies was conducted nearly two decades ago, whereas the other was more recent, highlighting the persistent concern surrounding preterm birth in this context. Safi and Peres, along with their colleagues, contend that the increased incidence of preterm birth can be attributed primarily to factors such as exposure to systemic therapy, iatrogenic-induced delivery, and, in some instances, the exacerbation of the maternal condition resulting from gestational cancer or the severity of the cancer diagnosis (Peres et al. 2001; Safi et al. 2019). Other studies have also suggested that a higher rate of preterm birth may be due to iatrogenic factors, such as induced

labour following a cancer diagnosis to start systemic therapy (Lataifeh et al. 2011; Momen et al. 2018; Murthy et al. 2014).

In the context of gestational cancer, prematurity is the most common cause of neonatal mortality and morbidity, developmental delay, and neurodevelopmental impairment, particularly in late preterm (34-37 weeks) infants (Amant et al. 2015; Lataifeh et al. 2011; Murthy et al. 2014). Therefore, it is of the utmost importance to address the issue of iatrogenically induced preterm birth and explore ways to mitigate it. Interestingly, recent data over the past decade suggest a reduction in the rates of iatrogenic preterm delivery in women with gestational cancer.

A 20-year international cohort study conducted by De Haan et al. revealed that, while the rate of chemotherapy treatment during pregnancy has increased among women with gestational cancer, the rate of iatrogenic preterm deliveries has declined (De Haan et al. 2018). One possible explanation for the observed decline in premature birth rates among infants exposed to systemic treatment during gestation is the practice of extending systemic therapy courses during pregnancy. This approach may enable the postponement of delivery until the foetus is more developed and better equipped to withstand delivery stresses, potentially leading to improved neonatal and long-term developmental outcomes in children. To further advance the trend of increasing the proportion of women with gestational cancer who can carry their babies to term, it is imperative to foster multidisciplinary collaboration, thoughtful planning, and vigilant monitoring of mothers and babies (Maggen et al. 2019; Silverstein et al. 2020).

Several extensive cohort studies have demonstrated that NICU admission is associated with preterm birth (De Haan et al. 2018; Garofalo et al. 2017). In this review, only one study examined NICU admission and reported a non-significant increased rate of NICU admissions for infants exposed to systemic cancer therapy in utero (Safi et al. 2019). Regrettably, the remaining four studies did not include data on NICU admissions, which prevented us from conducting a meta-analysis to determine whether there is good evidence to support the argument that there is a conclusive link between preterm birth and NICU admissions (Cardonick, Usmani & Ghaffar 2010; Cardonick et al. 2015; Loibl et al. 2012; Peres et al. 2001). NICU admission is an expensive intervention. Regular perinatal care during pregnancy, effective interventions during delivery (such as prophylactic maternal steroids in preterm labour, antibiotics, vitamin K supplementation at delivery, etc.), and monitoring and resuscitation of newborn babies with better therapy (surfactant replacement therapy) can minimise NICU length of stay and thereby reduce associated costs (Cheah 2019). However, the association between preterm birth, SGA, NICU admissions, and the long-term effect of chemotherapy remains inconclusive; therefore, caution is warranted in relation to any recommendation for systemic therapy (De Haan et al. 2018; Hepner et al. 2019; Silverstein et al. 2020).

There is a lack of published long-term follow-up data on infants and children exposed to chemotherapy while in utero. The limited findings from our review suggest that children born to women with gestational cancer who received chemotherapy during pregnancy have no significant differences in developmental delay, speech delay, or cognitive skills compared to children born to women with gestational cancer who did not receive chemotherapy during

pregnancy. A multicentre case-controlled study of 129 children conducted between 2005 and 2015 that used health questionnaires and medical files to collect data reported no significant differences in general health development, cognitive skills, and cardiac function development between children exposed to chemotherapy in utero and the children of women without cancer (Amant et al. 2015).

In addition to developmental outcomes, two studies in this systematic review reported that exposure to cyclophosphamide in utero may be associated with long-term carcinogenicity. However, given the small number of cases, this finding should be treated cautiously. This review highlights that very little research has been published on the long-term outcomes in children or adults exposed to chemotherapy in utero. Longitudinal studies with extended follow-up periods are required to examine the relationship between cyclophosphamide (or other chemotherapeutic drugs) and carcinogenicity. Knowledge of the long-term outcomes for babies exposed to cancer treatment during pregnancy is essential for clinicians and patients to make better-informed decisions about managing gestational cancer.

Improved safety concerning the use of systemic therapy during pregnancy is one of the most significant accomplishments in cancer treatment during pregnancy in the last 20 years (De Haan et al. 2018; Silverstein et al. 2020). Women diagnosed with cancer during pregnancy may wish to continue their pregnancy even after exposure to targeted agents, noncytotoxic therapy, or immunotherapy. However, uncertainty regarding maternal and neonatal outcomes due to a lack of data makes treatment and pregnancy decisions difficult. Additional research is required to better understand the impact of systemic cancer treatment during pregnancy on infant and maternal outcomes.

5.9 Strengths and limitation

To our knowledge, no prior studies have compared perinatal outcomes between women who were exposed to systemic therapy after a cancer diagnosis during pregnancy and those who were not exposed.

This study had several limitations. We conducted this systematic review over a relatively concise timeframe, encompassing the period from 2001 to 2023. Most included studies had small sample sizes and lacked long-term follow-up data on infants and children exposed to systemic therapy during gestation. Most drugs investigated in the included studies were cytotoxic; did not identify any studies reporting specific neonatal outcomes after exposure to new targeted agents or non-cytotoxic medications during pregnancy. Lastly, the included studies may have been subject to biases (reporting bias or inheritance bias), as some studies collected data via questionnaires, whereas others analysed data collected via cancer and pregnancy registries. However, these data collection techniques are unsurprising, as the involvement of pregnant women in clinical research trials is a complex issue, particularly when evaluating the safety and efficacy of medical treatments. Given that this systematic review only included cohort studies with small sample sizes, it might be considered a level 2 or 3 evidence-guided review (Burns, Rohrich & Chung 2011).

5.10 Conclusion

Mothers with gestational cancer and their foetuses can tolerate most chemotherapy agents after the first trimester. However, the findings from this review suggest that such treatment may be associated with increased rates of preterm birth. However, the validity and strength of any such association are unclear, as few studies have compared the outcomes of systemic therapy in the exposed and non-exposed babies of women with gestational cancer. There is very little data regarding the impact of new cancer therapies during pregnancy, including non-cytotoxic chemotherapy and immunotherapy, and this area requires further research. The incidence of gestational cancer is increasing, and oncological and obstetric management in this context is challenging. Collaborating with multidisciplinary healthcare professionals can provide evidence-based best-practice care to ensure the safest treatment with the lowest risk for the mother and her unborn baby. This systemic review synthesises the current data and may help inform clinical practice and treatment guidelines regarding the admission of systemic therapy for pregnant women diagnosed with cancer.

5.11 Chapter summary

This systematic review synthesised evidence regarding perinatal outcomes following systemic cancer treatment during pregnancy. While it contributed important knowledge about clinical safety of systemic therapies and outcomes, it also highlighted significant limitations in the available literature, including a lack of data on women's emotional experiences, decision-making processes, and the support structures available to them during treatment. These limitations underscore the importance of complementing clinical evidence with qualitative research that captures the lived realities of women navigating cancer during pregnancy, as explored in Chapters 6 and 7.

Table 5.1 Perinatal outcomes of included studies

Authors	Study population		No of births		Spontaneous abortion % (n)		Stillbirth % (n)		Birthweight ≤10 th percentile (SGA) % (n)		Intrauterine growth restriction (IUGR) % (n)		Preterm birth (<38 weeks) % (n)		Congenital disabilities % (n)		Long-term outcomes % (n)	
			Cases	Controls	Cases	Controls	Cases	Controls	Cases	Controls	Cases	Controls	Cases	Controls	Cases	Controls	Cases	Controls
Peres et al. 2001	Perinatal outcome of neonates born to mothers who received chemotherapy during pregnancy	Perinatal outcome of neonates born to mothers who didn't receive chemotherapy during pregnancy	14	15	8% (n=1)	0% (n=0)	33% (n=4)	0% (n=0)	NA	NA	NA	NA	75% (n=6)	20% (n=2)	0% (n=0)	0% (n=0)	1% (n=1) Carcinogenic and mental retardation	NA
Cardonick et al. 2010	Perinatal outcome of neonates born to mothers who received chemotherapy during pregnancy	Perinatal outcome of neonates born to mothers who did not receive chemotherapy during pregnancy	157	70	NA	NA	0.7% (n=1)	0% (n=0)	7.6% (n=12)	7.1% (n=5)	7.6% (n=12)	7.1% (n=5)	5.8% (n=?)	NA	3.8%(n=6)	0% (n=0)	1% (n=1) carcinogenic	NA
Loibl et al. 2012	Perinatal outcome of neonates born to women who received chemotherapy during pregnancy	Perinatal outcome of neonates born to mothers who did not receive chemotherapy during pregnancy	203	170	1% (n=1)	0% (n=0)	1% (n=1)	1% (n=2)	9% (n=15)	4% (n=5)	4% (n=7)	1% (n=1)	6% (n=10)	2% (n=3)	0% (n=0)	0% (n=0)	NA	NA
Cardo nick et al. 2015	Neonates whose mothers had cancer and were treated with chemotherapy	Neonates whose mothers had cancer and were not treated with chemotherapy	35	22	NA	NA	NA	NA	2.8% (n=1)	NA	NA	NA	51.4% (n=18)	n=8	5.7%(n=2)	NA	BP-23% (n=8) ADM-25% (n=2) ADR-25% (n=2)	BP-18% (n=4) ADM-33% (n=2)

																			ADR-17% (n=1)
Safi et al. 2019	Neonates whose mothers had cancer and were treated with chemotherapy	Neonates whose mothers had cancer and did not expose to chemotherapy	18	6	NA	NA	0% (n=0)	0% (n=0)	11.1% (n=2)	0% (n=0)	NA	NA	66.7% (n=12)	0% (n=0)	0% (n=0)	0%(n=0)	NA	NA	NA

BP-Behavioural problem, ADM-Academic deficit math, ADR- academic deficit reading, CD-cardiac function, RBV- Regional brain volumes, NDO- neurodevelopmental outcome, ASQ- ages and stages questionnaire

Loibl 2012: The study used the number of women (179 received chemotherapy and 164 did not receive chemotherapy during pregnancy) as a denominator for outcomes such as preterm birth, IUGR, and stillbirth (Table 4). However, for Birthweight< 10th percentile, they used the number of babies (203 neonates exposed to chemotherapy and 170 not exposed) as the denominator (supplementary table 1)

Table 5.2 Robins I tool - Risk of bias for individual study

Study	Year	Preintervention		At intervention		Post-interventions			The overall risk of bias
		Bias due to confounding	Bias in the selection of participants into the study	Bias in the classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in the measurement of outcomes	Bias in the selection of the reported result	
Peres, R.M., Sanseverino, M.T., Guimaraes, J.L., Coser, V., Giuliani, L., Moreira, R.K., Ornsten, T. & Schuler-Faccini, L., 'Assessment of fetal risk associated with exposure to cancer chemotherapy during pregnancy: a multi-center study', Brazilian Journal of Medical & Biological Research, vol. 34, no. 12, pp. 1551-9.	2001	Low	Low	Low	Low	Low	Low	Low	Low
Cardonick, E., Usmani, A. & Ghaffar, S. 2010, 'Perinatal outcomes of a pregnancy complicated by cancer, including neonatal follow-up after in utero exposure to chemotherapy: Results of an international registry', American Journal of Clinical Oncology: Cancer Clinical Trials, vol. 33, no. 3, pp. 221-8.	2010	Low	Moderate	Low	Low	Low	Moderate	Moderate	Moderate
Loibl, S., Han, S.N., von Minckwitz, G., Bontenbal, M., Ring, A., Giermek, J., Fehm, T., Van Calsteren, K., Linn, S.C., Schlehe, B., Gziri, M.M., Westenend, P.J., Müller, V., Heyns, L., Rack, B., Van Calster, B., Harbeck, N., Lenhard, M., Halaska, M.J. & Kaufmann, M. 2012, 'Treatment of breast cancer during pregnancy: an observational	2012	Low	Low	Low	Low	Low	Moderate	Moderate	Moderate

study', Lancet Oncology, vol. 13, no. 9, pp. 887-96.									
Cardonick, E.H., Gringlas, M.B., Hunter, K. & Greenspan, J. 2015, 'Development of children born to mothers with cancer during pregnancy: comparing in utero chemotherapy-exposed children with non-exposed controls', American Journal of Obstetrics and Gynecology, vol. 212, no. 5, pp. 658.e1-.e8.	2015	Low							
Safi, N., Anazodo, A., Dickinson, J.E., Lui, K., Wang, A.Y., Li, Z. & Sullivan, E.A. 2019, 'In utero exposure to breast cancer treatment: a population-based perinatal outcome study', British Journal of Cancer, vol. 121, no. 8, pp. 719-21.	2019	Low							

Chapter 6: Women's perspectives on communication following the diagnosis of gestational or postpartum Cancer: A qualitative study

6.1 Publication

The results contained within this chapter have been published in the *Midwifery* journal as follows: Sultana Farhana, Jane Frawley, Antoinette Anazodo, Elizabeth A. Sullivan. 2024. Women's perspectives on communication following the diagnosis of gestational or postpartum Cancer: A qualitative study. *Midwifery*, 2025-06, Vol. 145, p.104374.

6.2 Chapter introduction

Chapter 6 focuses on women's experiences of communication with healthcare providers (HCPs) following a diagnosis of pregnancy-associated cancer, highlighting the critical role of effective services in enhancing women's care. Chapter 1 established the significance of this research and introduced the research question: *What are women's experiences of communication with their healthcare providers following a diagnosis of pregnancy-associated cancer?* Chapter 2 reviewed national and international literature, emphasising the importance of effective communication between HCPs and women when they are diagnosed with pregnancy-associated cancer. Ineffective communication can lead to safety risks, inefficient resource use, and confusion due to conflicting advice, especially in pregnancy-associated cancer care (Maggen et al. 2019; Stafford et al. 2022). Despite its importance, research on communication experiences still requires further development. Chapter 6 explicitly explores these issues within Australian healthcare and the challenges and potential strategies for improving communication to enhance women's outcomes.

6.3 Background

Pregnancy-associated cancer is relatively rare, but its incidence has increased over time (Cottreau et al. 2019; Safi et al. 2023). It is anticipated that the incidence may continue to rise in the next decade, especially among women who delay pregnancy until their late thirties and early forties (Eastwood-Wilshire et al. 2019). Cancer diagnosed during pregnancy or postpartum presents a complex and multifaceted challenge for healthcare providers (HCPs) regarding care delivery and management (Hurren et al. 2023; Silverstein et al. 2020). Less evidence-based approaches and logistical difficulties due to the rare nature of these cases and dispersed patient populations hinder optimal care (Hunter

et al. 2019; Hurren et al. 2023). These challenges highlight significant gaps in existing healthcare systems, particularly in addressing the unique needs of women with pregnancy-associated cancer.

Improved access to medical specialists and effective communication is crucial to enhancing knowledge and providing quality care (Hurren et al. 2023; Stafford et al. 2022). The Royal College of Obstetricians and Gynaecologists (2023) reinforces the fundamental importance of women and their partners or families with a clear understanding of all available options for cancer treatment as a cornerstone of person-centred care (Giusti et al. 2020; Loonen et al. 2018; Royal College of Obstetricians and Gynaecologists 2023). This approach empowers women to make informed decisions, promotes shared decision-making, and aligns treatment plans with individual values and preferences, ultimately enhancing the overall quality of care (Attanasio et al. 2022; Loonen et al. 2018; McCormack & McCance 2006; Royal College of Obstetricians and Gynaecologists 2023). By prioritising transparent communication and comprehensive education, healthcare providers can better address women's psychological and emotional needs while navigating complex treatment pathways (Hammarberg et al. 2018; Stafford, Sinclair, Gerber, Collins, et al. 2021; Stafford et al. 2022).

Advancements in cancer treatments have increased the use of intensive therapies. However, managing cancer in this population presents additional challenges, especially with the increasing use of novel therapies and the limited data on pregnancy. The involvement of multiple healthcare teams during the diagnosis and treatment of pregnancy-associated cancer presents challenges in coordination and communication. These challenges may lead to conflicting advice and delays in decision-making, which can cause confusion for patients and potentially compromise trust in their care team. Clear, coordinated communication among healthcare providers is essential to ensure consistent advice and timely decisions, which are critical for improving patient understanding, fostering trust, and enhancing overall care quality (Hammarberg et al. 2018; Maggen et al. 2019; Stafford, Sinclair, Gerber, Collins, et al. 2021).

Additionally, poor communication between women and HCPs within and across medical teams can result in negative consequences, including compromised patient safety and inefficient use of valuable resources (Hammarberg et al. 2018). The need for effective team communication is further underscored by the importance of identifying and addressing the gap experienced by women with cancer during pregnancy or postpartum. The women-centred approach is essential to recognise individuals' unique needs and challenges during this highly challenging period (Kozu, Masujima & Majima 2020).

Despite the significance of this topic, there is a paucity of research addressing the importance of communication between HCPs and women with cancer during pregnancy and the postpartum period, and identifying services that enhance their overall experience (Hammarberg et al. 2018; Stafford et al. 2022). We aimed to offer valuable insights into the development of patient-centred care approaches to enhance support and achieve improved outcomes for those facing these unique challenges.

6.4 Methods

6.4.1 Study design

A qualitative study was designed to investigate the effective communication practices and gaps between HCPs and women with cancer during pregnancy and the available services that could enhance women's experiences. An individual semi-structured interview approach was utilised, a well-established qualitative research method particularly suited for exploring topics that need to be better understood (Cohen & Crabtree 2008). The primary goal of qualitative research is to understand how individuals interpret and give meaning to their experiences and the social and cultural contexts in which these experiences occur. This approach focuses on exploring the complexities of human behaviour and its underlying reasons rather than simply quantifying them (Creswell 2013). The Human Research Ethics Committee of the University of Technology, Sydney (UTS HREC, REF No. ETH19-4526) reviewed and approved the study protocol before participant recruitment.

6.4.2 Participants and procedure

The eligibility criteria for participants in this study comprised all women in Australia diagnosed with cancer during pregnancy or within one year postpartum. Other eligibility criteria required that participants be at least 18 years of age or above at the time of recruitment, be able to speak and read English, possess psychological and cognitive capacity to provide informed consent, and actively participate in the interviews.

After obtaining ethical approval (UTS; HREC REF NO. ETH19-4526) for the project, participants were recruited via national advertisements on popular social media platforms (Facebook, Twitter, and Instagram) and established community networks (such as Cancer Council NSW, Cancer Council Victoria, Breast Cancer Network Australia, Mummy's Wish group, and Bub Hub). These community entities

shared this promotional content on their websites, allowing potential participants to access the study details, eligibility criteria, and the researcher's contact information.

Interested women were encouraged to reach the study team via email. Subsequently, potential participants were provided with a participant information sheet and a consent form. Once informed consent was obtained, the study team scheduled interview appointments. Over time, 17 women who met the inclusion criteria were successfully interviewed. Among the participants, 11 resided in metropolitan areas, while six lived in regional areas. Sixteen women had attained a tertiary-level education, and one had completed high school education. Most women (58.8%) were diagnosed during the postpartum period, aged 35-44 years. The remaining participants (41.1%) were diagnosed during pregnancy, aged 25-34 years. Further details regarding participant characteristics are presented in **Table 6.1**.

6.4.3 Data collection

Semi-structured interviews were conducted with individuals, allowing us to concentrate on essential issues for participants and gain insight into their experiences (DeJonckheere & Vaughn 2019). The research team developed an interview guide designed to explore women's experiences of care during pregnancy and postpartum, communication practices of healthcare professionals, and potential services that enhanced women's experiences.

Two experienced qualitative researchers conducted the interviews, which were administered via phone. The average duration of the interviews was 50 minutes. Audio recordings of the interviews were made with permission from the participants, and noteworthy nonverbal responses such as crying or laughing were also captured. The confidentiality and anonymity of the participants were maintained, and the information was identifiable only to the interviewer.

6.4.4 Data analysis

All interviews were transcribed verbatim and subjected to inductive reflexive thematic analysis following Braun and Clarke's methodological guidelines (Braun & Clarke 2021). The six stages outlined by Braun and Clarke were meticulously followed during the thematic analysis process to ensure

methodological accuracy, including familiarisation, code generation, theme development, reviewing and refining themes, defining themes, and report writing (Braun & Clarke 2021; Byrne 2022).

As a research team member, researcher SF listened to the interviews repeatedly, transcribed them, and took field notes during the listening process to capture contextual and observational insights that complemented the transcripts. These field notes were instrumental in supporting the data analysis by providing additional layers of understanding and identifying key themes. The interview transcripts were imported into NVivo 12 Pro, and the initial coding of the data was conducted. Themes and relevant quotes emerged from the coded data. Discussions and consultations between two researchers (SF and JF) were undertaken to review and finalise the identified themes and associated quotes. Through this repetitive process, the researchers explored individual and shared perspectives and uncovered patterns within and across women's narratives.

In this qualitative study employed a phenomenological approach to understand the lived experiences of women diagnosed with pregnancy-associated cancer (Emiliussen et al. 2021; Neubauer, Witkop & Varpio 2019). Thematic analysis focuses on identifying semantic themes that reflect the explicit content of the data (Braun & Clarke 2006, 2021; Byrne 2022). By adhering to these rigorous guidelines, this study ensured the trustworthiness and credibility of its findings.

6.5 Results

The study included a diverse range of participants in terms of age, cancer diagnosis, and the timing of diagnosis. Seven women had breast cancer, while the remaining participants had various other types of cancer (melanoma, lymphoma, thyroid cancer, ovarian cancer, uterine cancer, bowel cancer, and oropharyngeal cancer). Ten of the participants were diagnosed postpartum, and seven were diagnosed during pregnancy.

Thematic analysis of the collected data revealed three overarching themes: "Scarcity of information," "Not involved in treatment decisions," and "Lack of resources and advocates". The theme "Scarcity of information" was further divided into three subthemes: "I was an enigma: Identifying training gaps and education needs", "Short on information", and "Overwhelmed and unable to ask questions". The theme "Not involved in treatment decision" consisted of two subthemes: "Rushed and abrupt" and "Options not communicated." Lastly, the theme "Lack of resources and advocates" encompassed two subthemes: "Central resource of information," "Someone to advocate for me". These themes with quotes are presented below, along with the additional quotes in **Table 6.2**.

6.5.1 Scarcity of information

6.5.1.1 "I was an enigma": Identifying training gaps and education needs

Many women regarded a cancer diagnosis during pregnancy or postpartum as a rare and unfamiliar event. They were ill-prepared to confront the entire situation. They also perceived that some HCPs lacked adequate knowledge and shared instances of delayed diagnoses due to suboptimal care or a lack of expertise in the diagnosis and management of cancer during pregnancy or postpartum.

"I would say particularly in identifying this sort of thing in pregnancy and just after, there is a massive gap there. It's an education gap. Because you know, if I had listened to all the HCPs, I may have dismissed this, and it would have been a few months' time, a very different story for me. So, I feel that there is a massive gap there". (W15, breast cancer)

Women reported feeling like an 'enigma' due to their diagnosis during pregnancy or postpartum, which includes common cancers, such as breast cancer, or rare types, such as choriocarcinoma. Women felt that there were gaps in training, as their HCPs sometimes reported not knowing much about their condition when they were diagnosed, either during pregnancy or postpartum.

"Obviously, communication between the obstetrician and the cancer team was not great because it was something they had not dealt with before. I could tell who got well taken care of, but I was an enigma". (W5, breast cancer)

Some women commented that HCPs seemed easier to treat in non-pregnant patients with cancer than in women with cancer during pregnancy or postpartum. Women felt a lack of communication, knowledge, and experience in HCPs regarding cancer management during pregnancy or postpartum.

"The challenging part was that they genuinely did not know how to handle my situation regarding the maternity or obstetric aspect. I felt that they were drawing a blank". (W5, breast cancer)

However, despite the efforts of certain women to ask numerous questions and consider various options, they expressed a need for more support from their HCPs. This lack of communication underscores the complex, multidisciplinary, and potentially fragmented nature of care for cancer in pregnancy or postpartum that impacts the experiences of women with HCPs.

"So, I think it's hard, though, because how are you going to tell those people [HCPs] that they need to upskill? How do you tell those people that you need them to be more empathic, and I am not in that frame of mind to provide that feedback?". (W12, thyroid cancer)

6.5.1.2 Short on information

Some women reported that HCPs did not adequately inform them about their cancer diagnosis, the risks and benefits of treatment options, or the potential treatment outcomes. If the cancer was rare, it was more challenging to get information. Without adequate information, women felt overwhelmed by the decisions they had to make regarding treatment and felt unsure about the potential side effects of treatment on their pregnancy, postpartum health, and infant development. This lack of communication and information from their HCPs left them anxious and uncertain about their situations.

"They [HCPs] were not very clear that chemo might affect the baby; well at the same time, they were very confident that it won't. I mean, I was short of information. I guess, again, it's probably because I know I am an unusual type of patient; the whole picture was not probably presented in a great way". (W5, breast cancer)

Women who felt that communication needed to be improved felt frustrated and confused, especially when receiving conflicting information from HCPs with different areas of specialist expertise and opinions.

"That was so overwhelming, and getting different things from different doctors felt frustrating.... It was like, come on guys, are you talking to each other?". (W14, breast cancer)

Furthermore, many women explained that they did not know about the available services and resources for cancer patients during pregnancy or postpartum and felt that their HCPs could have communicated this information. Some women reported that their HCPs did not holistically discuss the support available to them; instead, they focused solely on the physical aspects of their cancer treatment.

"The other thing, in retrospect, was that I did not know about all the support that existed, for example, the Cancer Council. No health professional said, 'Look, there are support services available through the Cancer Council'." (W3, non-Hodgkin lymphoma)

In addition to a lack of communication with HCPs, some women reported a lack of communication between HCPs and their families. Women felt that their families lacked access to comprehensive information about their cancer diagnosis, treatment options, and potential outcomes unless they were HCPs themselves, which was a minimal number.

"I had chemo, and it was good. However, when my family asked about my situation, the doctors used to say, 'She is having chemo' and never explained the outcomes. You can explain more about the outcomes; that's not right. That's still sad". (W5, breast cancer)

Despite the concerns expressed by women diagnosed with cancer during pregnancy and the postpartum period regarding the lack of information provided by HCPs, the experience was not uniform. Some women were satisfied with receiving complete and precise information that they deemed crucial and appreciated how HCPs communicated with each other during their illness diagnostic and management phases.

"I think the specialist actually gave me this formal diagnosis. She did really well and said, 'I will start with the good news; it hasn't spread anywhere'. So, that was what I wanted to know, and that was the first thing she said to me. And then she said, 'But you know, it is cancer, and it is local. It has not been spread anywhere. That is a good thing; we can treat it'. She really gave good information there". (W15, breast cancer)

6.5.1.3 Overwhelmed and unable to ask questions.

Women diagnosed with cancer during pregnancy, or the postpartum period often reported feeling overwhelmed after their diagnosis and did not ask many questions. Some women felt reluctant to ask questions, which may have offended their HCPs. As time passed, they felt they had to ask more questions and seek more information from their HCPs.

"Probably at the time, I didn't feel it, and in hindsight, I realise I was naive about it [cancer] and wasn't told much. So, at that time, I felt comfortable, but now, knowing everything that's transpired, I thought maybe I could have been given more information". (W13, breast cancer)

6.5.2 Not involved in treatment decisions

6.5.2.1 Rushed and abrupt

Many women felt a sense of urgency or pressure immediately after diagnosis. This feeling was primarily attributed to the need for quick treatment to reduce poor outcomes, especially when the diagnosis was made late in pregnancy or when the cancer was in an advanced stage. Some women did not understand the urgency and felt their (HCPs) communication could have improved.

"So, it was hard to sort of comprehend that everything had to happen so quickly... I said, "Couldn't we wait a little bit because surely it would be better for the baby to stay inside a bit longer?" and the oncologist said, "The best thing for the baby is not to have a dead mom". (W9, oropharyngeal cancer)

6.5.2.2 Options not communicated

Women reported that their HCPs did not provide sufficient information about the options to help them make informed decisions about their care. In rare and challenging cancer cases, HCPs appeared reluctant to proceed with pregnancy due to perceived risks for the mother and baby. This situation added to the difficulty these women experienced when confronted with an entirely new and unfamiliar scenario.

"I think it should be standard that every haematologist and oncologist in Australia offers a pregnant woman options when they are diagnosed with cancer. They should not make a decision for the woman but rather provide information and support for her to make the decision herself. Terminating the pregnancy may be an option, but continuing with chemotherapy or treatment during pregnancy may also be an option". (W2, Hodgkin's lymphoma)

Some women felt that HCPs did not engage in sufficient discussion regarding available treatment and birth options during pregnancy or after birth. Instead, they felt that HCPs followed a predetermined plan.

"My surgeon told me, 'Well, this is what we are doing for post-delivery treatment', and that made me think. I wanted to know who had made these decisions. I did not want it to be a matter of simply following a standard procedure; I preferred it to be more of a collaborative decision-making process. It felt like a local hospital policy, where everything is done step by step without considering the bigger picture". (W12, thyroid cancer)

Most women indicated that there was limited discussion regarding their desire for future pregnancy or fertility preservation. However, women sometimes found this conversation distressing when HCPs were straightforward about potential future pregnancy challenges rather than offering a more optimistic and empathetic approach. Many women also added that they were not overly concerned about future pregnancies; most were uncertain and focused primarily on their current pregnancy and health improvement.

"He [the oncologist] made it very clear that for me to become pregnant would just not happen by the time you have had chemo and radio. It is pretty impossible. So, he was very upfront about that, which was upsetting, but I did not want to think about that too much because I just needed to save my own life first. I needed to be well to look after this baby already here". (W14, breast cancer)

Even if some women became pregnant soon after their diagnosis, HCPs were not always pleased as they perceived it as a risk factor for both cancer recurrence and the baby's well-being.

"So, my next son was born two years later, and I got into a bit of trouble with my oncologist for that. She said it was too close to my diagnosis and things like that. However, there had been nothing said to me since the initial conversation after the diagnosis. I did not realise; it is not like we were trying to have another child; it just happened naturally". (W13, breast cancer)

Although getting pregnant and having a baby in the future is challenging, some women desired future pregnancies and wanted to discuss treatment options that would be compatible with future pregnancies. They found it valuable when HCPs offered them hope and engaged in thorough discussions about the advantages and disadvantages of treatment that could affect their chances of having a baby later.

"So, it is [future pregnancy] still to be decided. He [the oncologist] gave me a bit of hope, and I think, even if I decide that it is best if we do not try to have another baby, I still kind of like having that little bit of hope that there is a possibility". (W16, breast cancer)

6.5.3 Lack of resources and advocates

Owing to their experiences of communication during cancer diagnosis and treatment, many women have suggested resources that would have been helpful.

6.5.3.1 Central resource of information

A central hub or repository of practical information is suggested by women to prevent them from gathering information from multiple sources, acknowledging that HCPs cannot be expected to hold all the information. This centralised approach provides women with a clear understanding of where to access comprehensive and reliable information. Women also stressed the importance of receiving information that was easy to understand, written in plain language and reassuring.

"A lot of the time, you have to be the one who's leading your own journey, and that's quite frightening in the beginning because you're not armed with the information. That's why I think it's so important that you are given the information straight up first of all". (W3, non-Hodgkin lymphoma)

6.5.3.2 Someone to advocate for me

Women felt that making critical healthcare decisions while managing their pregnancy's physical and emotional demands was daunting: they felt helpless and alone. As a result, many women felt that a dedicated person who could liaise with them with HCPs and other services would alleviate some of their stress. A dedicated liaison would allow women to focus on health while ensuring that all aspects of their care were well coordinated and managed effectively.

"I just wanted someone to tell me what I needed to do. I didn't want to make decisions at that point in time because it felt so overwhelming". (W14, breast cancer)

6.6 Discussion

This study investigates the communication between women and their HCPs following cancer diagnosis during pregnancy or postpartum. Unfortunately, these findings reveal an unmet need for effective communication. Women require more information about their diagnosis, treatment options, prognosis, and tailored resources, emphasising the critical role of information, communication with HCPs, and advocacy in their healthcare journey. This study identified three overarching themes that summarised the challenges faced by women: "Scarcity of information," "Not involved in treatment decisions," and "Lack of resources and advocates." These themes reflect the vulnerability that many women described in this study after being diagnosed with cancer during pregnancy or postpartum (Stafford, Sinclair, Gerber, Collins, et al. 2021; Vanstone et al. 2021).

From the perspective of the women in our study, HCPs encountered unique challenges when treating women diagnosed with cancer during pregnancy or postpartum. Women often felt that HCPs were unprepared and lacked confidence in managing these cases, which may be due to rare diagnoses, complexity of information, lack of communication skills, and time constraints. Consequently, some women experienced frustrating delays in their diagnosis. Women stressed the urgent need for HCPs to enhance their skills and be better equipped to handle the complexities of cancer diagnosis during pregnancy or postpartum. Poor communication with HCPs poses significant challenges for women diagnosed with pregnancy-associated cancer, leading to heightened uncertainty, potential misunderstandings, feelings of powerlessness, and dissatisfaction with the healthcare system.

A recent study reported that HCPs experienced a more significant emotional impact when caring for women with gynaecological cancer and invested more time in their care than other patient groups (Stafford et al. 2022). Two other studies also highlighted the importance of HCPs well-being in managing cancer patients (Eelen et al. 2014; Russo et al. 2014). Recommendations for supporting HCPs treating women with pregnancy-associated cancer include communication training, access to cancer care coordinators, increased availability of experienced clinicians/mentors, and centralised resources (Stafford et al. 2022). The women in our study echoed these suggestions. Rajagopal et al. (2019) also suggest mandatory communication training programs for HCPs in oncology settings to ensure they provide necessary information to patients and families, offer consistent support during diagnosis and treatment, and initiate timely ongoing discussions to alleviate these challenges (Rajagopal, Liamputtong & McBride 2019).

Prompt, consistent, and transparent communication between patients, treatment teams, and hospitals fosters trust in treating clinicians and enhances care coordination, contributing to a positive healthcare experience for women (Panagiotopoulou et al. 2018; Stafford et al. 2022). This study's findings resonate with previous studies highlighting that efficient communication is crucial in enabling clinicians to connect with women who struggle with fear and uncertainty, ensuring that they receive thorough explanations with empathy and transparency (Hammarberg et al. 2018; Rajagopal, Liamputtong & McBride 2019).

Previous studies (Hammarberg et al. 2018; Ives, Musiello & Saunders 2012; Kozu, Masujima & Majima 2020; Leung, Bryant & Stafford 2020; Zanetti-Dällenbach et al. 2006) highlight that women diagnosed with pregnancy-associated cancer often experience psychological distress related to concerns about their babies' health. The divergence in different specialist opinions further compounded the challenges these women and their partners faced during an already stressful period, echoing our study findings. Moreover, the women in this study also expressed that families struggled to initiate discussions or raise questions regarding cancer-related matters during pregnancy or postpartum, which might contribute to the perception of inadequate communication and understanding. Experts argue that it is crucial for clinicians to proactively connect with women and their families who are grappling with fear and uncertainty, offer comprehensive explanations regarding the safety of prescribed drugs, and emphasise the compelling advantages of not delaying treatment (Hammarberg et al. 2018; Lambertini et al. 2015). Future research could benefit from examining partners' or family members' perspectives and their information needs when involved in HCPs decisions.

As indicated by Mika et al. (2020) and Leung et al. (2020), women with pregnancy-associated cancer encounter challenges because they navigate the complexities of diagnosis and consider options such as abortion, birth plans, breastfeeding, and fertility preservation (Kozu, Masujima & Majima 2020; Leung, Bryant & Stafford 2020). Our study also observed instances where some women regretted not asking more questions and seeking greater clarity about their circumstances. Women felt rushed and pressured when making critical decisions because of insufficient information and poor communication with HCPs regarding cancer treatment and birth options. This challenging situation compelled women and their partners to make decisions under time constraints, as they had to balance the imperative need for the mother's treatment with the potential impact of such treatment on the foetus or the well-being of the newborn. This underscores the importance of fostering an environment where women feel empowered to engage in open dialogue with their HCPs, ensuring they receive the support and information they need during this challenging time. This study's findings align with those of other studies (Kozu, Masujima & Majima 2020; Stafford, Sinclair, Gerber, Collins, et al. 2021), indicating that

adequate communication is essential in every aspect of cancer care, including decision-making in pregnant women and postnatal care.

Prior studies have underscored the significance of healthcare professionals in respecting patients' autonomy and offering treatment alternatives that align with their values and beliefs (Amant et al. 2013; Hammarberg et al. 2018). Frequent and open communication between women and their HCPs is pivotal in helping women navigate the multifaceted challenges of pregnancy and postpartum (Vanstone et al. 2021). However, cancer care is complex, and providing well-coordinated cancer care with open communication remains challenging due to the absence of an integrated, multidisciplinary, and holistic model of care to support cancer patients in Australia (Hunter et al. 2019; Robson et al. 2020; Stafford et al. 2022).

Women of childbearing age who have been diagnosed with reproductive cancers, such as cervical, ovarian, or uterine cancer, often experience significant concern about their future fertility (Ferrari et al. 2018; Vanstone et al. 2021). This concern hinders the potential impact of the cancer itself and its treatments, such as surgery, chemotherapy, or radiation, on their ability to conceive (Vanstone et al. 2021). A U.S. study of female patients aged 18-40 revealed that many participants did not recall any discussions regarding fertility options before the commencement of treatment, with only 5% being referred to a fertility specialist (Gonçalves & Quinn 2016). Lack of attention to fertility options leaves women feeling uncertain about their ability to have children in the future, leading to heightened anxiety and uncertainty (Vanstone et al. 2021). Despite ongoing research on fertility options and preservation, women continue to report scarce information (Speller et al. 2019; Vanstone et al. 2021). Experts have suggested that HCPs should undergo training and enhance their communication skills within clinical settings, utilising available oncofertility resources to cater to the unique requirements of their patients (Speller et al. 2019). Although this study did not capture explicit references to interprofessional communication challenges within the multidisciplinary team, this remains an area warranting further investigation, given its importance in managing complex conditions such as pregnancy-associated cancer.

In this study, women also voiced their desire for a centralised information source, which could provide a clear and reliable channel for accessing comprehensive and trustworthy information. HCPs also often face uncertainties in treating gestational cancer because of limited exposure, resource access, and the need to collaborate with unfamiliar services (Stafford et al. 2022). Potential solutions include centralising resources, creating clinical liaison roles, and connecting women with gestational cancer to peer support (Stafford et al. 2022). This study also supports this need. Improved access to resources

could alleviate the stress and anxiety experienced by women, enabling them to play an engaged role in their healthcare (Hammarberg et al. 2018; Kozu, Masujima & Majima 2020; Stafford et al. 2022). There is a pronounced need for cancer information resources tailored specifically to address the nuances of gestational cancer, ideally tailored to different types of cancer, including the rarer forms, and for women who live in regional areas where there is still a lack of information and all health facilities.

This study highlighted women's desire for advocacy support throughout their journey, including diagnosis, treatment, and postpartum care, to an extent not previously emphasised in other studies. This support could be facilitated by a dedicated midwife or nurse who attended all multidisciplinary team meetings related to the woman's case, assessed all information and treatment decisions, and tailored the support to the needs of individual women (Luck et al. 2017). Emphasising clinical care, offering professional guidance, and fostering resource development are essential for improving the quality of care (Hammarberg et al. 2018). This study extends this focus to include patient challenges, enhanced support for women by providing adequate communication between women and HCPs, and the pivotal role of advocacy. Despite the efforts of foundations such as McGrath and Mark Hughes in Australia, there is still a scarcity of dedicated care nurses or midwives, especially for rare cancers (oropharyngeal cancer or uterine choriocarcinoma) and in rural areas (Ahern & Gardner 2015; Anna et al. 2019; Paynter et al. 2013). According to Hunter et al. (2019), a noticeable service gap exists in cancer support and survivorship care across various service providers, underscoring the pressing need for a more integrated, holistic, and multidisciplinary approach to care (Hunter et al. 2019).

Overall, this study identified a gap in HCP's communication with women diagnosed with cancer during pregnancy or postpartum. The implications of these findings are substantial. Women express a sense of inadequate communication regardless of the type of cancer, providing further insight into the importance of open communication between HCPs and women with gestational cancer. Furthermore, these insights can guide the creation of resources and advocacy to support women and their families during this challenging time, ultimately enhancing the outcomes for this vulnerable population.

6.7 Strengths and limitations

The strength of this study lies in its exploration of the communication experiences between HCPs and women diagnosed with cancer during pregnancy or postpartum, shedding light on the challenges that these women encounter while seeking comprehensive care. This serves as a fundamental cornerstone for comprehending the specific challenges and demands of this distinctive group of patients. Notably,

such research in this specific context is scarce, making the data generated by our study novel and valuable.

The limitation of this study is the need for more diversity within our sample. All participating women were English speakers, so we did not capture their experiences from diverse ethnic and cultural backgrounds. A more varied sample could have yielded additional themes and insights. Furthermore, the generalisability of our findings may be constrained by the relatively modest sample size and inherent diversity in patient information needs arising from their distinct circumstances and personal experiences. Despite these limitations, our study offers valuable insights into the importance of insightful communication between women, HCPs, and cancer care nurses or midwives.

6.8 Conclusions

This study comprehensively explored the challenges faced by women diagnosed with pregnancy-associated cancer, focusing on their interactions with healthcare professionals (HCPs). It found that communication experiences were notably similar between pregnant and postpartum women, regardless of the type of cancer diagnosed. The findings underscore the urgent need for adequate communication between HCPs and women, targeted education and support for HCPs, as well as the development of tailored resources for women diagnosed with pregnancy-associated cancer. Furthermore, coordinated multidisciplinary care and dedicated advocacy, particularly from nurses or midwives, are pivotal in addressing these challenges and fostering positive healthcare outcomes for women and their families.

6.9 Chapter summary

This study explored women's experiences of communication and care coordination following a diagnosis of pregnancy-associated cancer. The findings highlighted key areas of unmet need, including inconsistent information, fragmented care pathways, and emotional strain caused by uncertainty and rushed decision-making. While communication and clinician relationships were central to women's experiences, their narratives also revealed mental health challenges and distress related to the diagnosis, treatment, and women's overall journey. These emerging insights pointed to a broader impact on women's mental health and emotional well-being, warranting further investigation. Chapter 7 addresses this gap by exploring women's mental health needs and coping experiences through in-depth qualitative interviews.

Table 6.1 Participant characteristics

No of women	Cancer diagnosis (pregnancy or postpartum)	Age at diagnosis (Y)	Type of cancer	Hospital services (Public or private)	Delivery (vaginal delivery or CS)	Preterm or Term delivery	Residence
W1	Pregnancy	33	Breast cancer	Public and private	vaginal delivery	Preterm	Regional
W2	Pregnancy	34	Hodgkin Lymphoma	Private	CS	Preterm	Metropolitan
W3	Postpartum	43	Non-Hodgkin Lymphoma	Public	CS	Term	Regional
W4	Postpartum	40	Melanoma	Private	CS	Preterm	Metropolitan
W5	Pregnancy	38	Breast cancer	Public	vaginal delivery	Preterm	Metropolitan
W6	Postpartum	32	Uterine choriocarcinoma	Public and private	CS	Term	Metropolitan
W7	Postpartum	41	Ovarian cancer	Private	CS	Term	Regional
W8	Postpartum	35	Bowel cancer	Private	Vaginal delivery	Term	Metropolitan
W9	Pregnancy	32	Oropharyngeal cancer	Public	CS	Preterm	Metropolitan
W10	Pregnancy	35	Melanoma	Public and private	Vaginal delivery	Term	Metropolitan
W11	Postpartum	39	Breast cancer	Public	CS	Term	Regional
W12	Pregnancy	29	Thyroid cancer	Public and private	Vaginal delivery	Term	Regional
W13	Postpartum	33	Breast cancer	Private	CS	Term	Metropolitan
W14	Postpartum	35	Breast cancer	Public and private	Vaginal delivery	Term	Regional
W15	Postpartum	36	Breast cancer	Public	CS	Term	Metropolitan
W16	Pregnancy	40	Breast cancer	Private	CS	Term	Metropolitan
W17	Postpartum	25	Melanoma	Public	Vaginal delivery	Term	Metropolitan

Table 6.2 Additional quotes

Themes	Quotes
1. Scarcity of information	
1.1 "I was an enigma": Identifying training gaps and education needs	<i>"I think there's a huge gap in knowledge and comfort among health professionals when working with women diagnosed with cancer, especially breastfeeding women." (W12, thyroid cancer)</i>
1.2 Short on information	<i>"I would not say it [information regarding diagnosis and treatment] was adequate. I was probably told what I needed to know, but I think a lot was left out". (W13, breast cancer)</i>
1.3 Overwhelmed and unable to ask questions.	<i>"It would be wonderful if there was someone, whether it be a nurse or doctor, someone with medical expertise, to explain that this is an informed decision we can make. We will provide you with all the information so that you can make it. Because people often do not ask questions, it's scary to go up against a doctor." (W2, Hodgkin's lymphoma)</i>
2. Not involved in treatment decisions	
2.1 Rushed and abrupt	<i>"It all happened very quickly, for a reason, of course. However, it felt very rushed. There was a pregnancy diagnosis, and they [HCPs] had to schedule surgery and everything quite fast. Then chemo started right away, and it all felt like I was in fast forward." (W1, Breast cancer)</i>
2.2 Options not communicated	<i>"So, I didn't feel like there was a lot of discussion about how the baby was going to be born. I think the medical team's preference was definitely just to have a caesarean. I probably didn't explore that a lot because I was anxious about having a baby a bit early. I didn't want her [baby] to be distressed in anyway." (W9, oropharyngeal cancer)</i>
3. Lack of resources and advocates	
3.1 Central resource of information	<i>"I think that if there could be a care pack for mums during pregnancy, with all the information in one place and a few tips on what they could do to go through this, and get the help they need, that would be really helpful." (W10, melanoma)</i>
3.2 Someone to advocate for me	<i>"If you just had one person to liaise with and support you throughout your journey, attending appointments with you, I think that would be an amazing service." (W6, uterine choriocarcinoma)</i>

Chapter 7: Cancer diagnosis during pregnancy and the postpartum period: Impact on well-being and mental health

7.1 Publication

The results contained within this chapter have been published in the *Women's Reproductive Health* journal as follows:

Sultana Farhana, Jane Frawley, Antoinette Anazodo, Elizabeth A. Sullivan. 2024. Cancer diagnosis during pregnancy and the postpartum period: Impact on well-being and mental health. *Women's Reproductive Health*, 2025-06, p.1-16

7.2 Chapter introduction

This chapter explores the mental health impacts of pregnancy-associated cancer on women, addressing the research question: "*What are the mental health impacts for women diagnosed with pregnancy-associated cancer?*" Chapter 2 reviewed the diagnosis of pregnancy-associated cancer affects the mental health and well-being of women with common issues including stress, anxiety, and depression, particularly concerning the health of their unborn children exposed to treatment (Ferrari et al. 2018; Roberts & Andrewes 2022). Despite the importance of mental healthcare, research on this topic remains limited. This chapter examines the mental health impacts and challenges faced by women within the Australian healthcare system and identifies potential strategies for improving mental health outcomes.

7.3 Background

Pregnancy-associated cancer is rare but is becoming more common due to the growing trend of delayed childbearing (Eastwood-Wilshere et al. 2019; Maggen et al. 2019). Although it affects a small percentage of women, it profoundly impacts their mental health and well-being as they navigate the emotional vulnerabilities of both life events (Ferrari et al. 2018; Leung, Bryant & Stafford 2020; Roberts & Andrewes 2022). Following cancer treatment, women may experience anxiety about their unborn child's health, future fertility, and the safety of future pregnancies (Gorman et al. 2015). When cancer occurs during pregnancy or the postpartum period, additional psychological challenges arise as

women transition to motherhood while facing a survival threat. Unfortunately, research on cancer experiences during pregnancy and motherhood is limited (Faccio et al. 2020).

Each woman's experience of motherhood while dealing with cancer is unique and presents mental health challenges. Beyond stress and anxiety, it may also impact a mother's ability to bond with her newborn and other children (Faccio et al. 2020; Ferrari et al. 2018). Studies have shown that pregnancy-associated cancer can be an isolating experience, leading to significant anxiety and distress throughout pregnancy and even years afterwards (Faccio et al. 2020; Ferrari et al. 2018; Stafford, Sinclair, Gerber, Collins, et al. 2021). Perinatal anxiety affects maternal and child health, contributing to adverse outcomes like preterm birth, low birth weight, and postpartum depression (Fairbrother et al. 2017; Leung, Bryant & Stafford 2020).

Despite these challenges faced by women with pregnancy-associated cancer, empirical research on the psycho-oncological aspects of this population remains scarce (Roberts & Andrewes 2022; Stafford, Sinclair, Gerber, Collins, et al. 2021). Most of the studies have predominantly focused on medical treatment, with limited attention given to the mental health support required by these women (Faccio et al. 2020; Ferrari et al. 2018; Leung, Bryant & Stafford 2020). Consequently, recommendations for psycho-oncological management and interventions for perinatal mental health are lacking.

This study aims to explore the well-being and mental health impact of a cancer diagnosis during pregnancy and the postpartum period, enhancing understanding of ongoing challenges and informing psycho-oncological care for this vulnerable population.

7.4 Methods

7.4.1 Study design

A qualitative study explored the ongoing mental health effects following cancer diagnosis during pregnancy or the postpartum period. An individual semi-structured interview approach was employed, a well-established qualitative research method known for its suitability in exploring subjects that require a deeper understanding (DeJonckheere & Vaughn 2019). The primary objective of qualitative research is to explore the depth of human experiences, seeking to understand how individuals interpret and attribute meaning to their lived experiences. This approach acknowledges that broader social and cultural settings shape people's perceptions, beliefs, and interpretations (Braun & Clarke

2021). The study protocol was reviewed and approved by the University of Technology Sydney's Human Research Ethics Committee (UTS HREC REF NO. ETH19-4526).

7.4.2 Participant selection and recruitment process

Australian women (residents or citizens) diagnosed with cancer during pregnancy or within one year postpartum were eligible to participate. Participants also needed to be 18 years or older, proficient in English, and possess the psychological and cognitive capacity to provide informed consent and actively engage in interviews.

Following ethical approval, a nationwide recruitment strategy was implemented using popular social media platforms (Facebook, Twitter, and Instagram) and established community networks (Cancer Council NSW, Cancer Council Victoria, Breast Cancer Network Australia, Mummy's Wish Group, and Bub Hub). Advertisements and promotional content were disseminated through these channels, providing women of interest with study details, eligibility criteria, and contact information for the research team. Interested individuals were encouraged to contact the study team by email. Upon expressing interest, potential participants were provided with a participant information sheet (PIS) and a consent form. After obtaining informed consent, the study team scheduled interview appointments.

7.4.3 Data collection

Semi-structured interviews were employed because of their established effectiveness in qualitative health service research, particularly in exploring topics with limited knowledge. This approach allows for a focused exploration of participants' critical issues and provides valuable insights into their experiences and emotions (DeJonckheere & Vaughn 2019). To guide the interviews, the research team developed an interview guide specifically tailored to explore women's mental health experiences and their effects on ongoing mental health during pregnancy and postpartum, effective practices of healthcare professionals, identified gaps in mental health care, and potential services that could enhance women's mental healthcare experiences.

An experienced qualitative researcher conducted the interviews via phone. The average duration of the interviews was 50 minutes, depending on the depth of discussion and participant engagement. With permission from the participants, audio recordings of the interviews were made, capturing not only verbal responses but also noteworthy nonverbal cues, such as crying or laughter. The confidentiality and anonymity of the participants were strictly maintained, with the information identifiable only to the interviewer.

Seventeen women were interviewed for the study; eleven resided in metropolitan areas, while six lived in regional areas. Most participants attained tertiary-level education, with one having completed high school. The age range of the participants varied, with 58.8% being diagnosed during the postpartum period and between 35 and 44 years of age, while 41.1% were diagnosed during pregnancy and between 25 and 34 years of age. Additional details regarding the participant characteristics are presented in **Table 7.1**.

7.4.4 Data analysis

The interviews were transcribed verbatim and underwent inductive reflexive thematic analysis using NVivo 12, following the methodological framework proposed by Braun and Clarke (Braun & Clarke 2006, 2021). The thematic analysis process encompasses the six stages outlined by Braun and Clarke: familiarisation, code generation, theme development, reviewing and refining themes, defining themes, and reporting writing (Braun & Clarke 2006, 2021).

Researcher SF initially listened to the interviews repeatedly, transcribed them, and took field notes during the listening process to capture contextual and observational insights that complemented the transcripts. These field notes were instrumental in supporting the data analysis by providing additional layers of understanding and identifying key themes. Using NVivo 12 Pro, the interview transcripts were imported for data analysis, and initial data coding was conducted. Themes and relevant quotes emerged from the coded data. Ongoing discussions and consultations between two researchers (SF and JF) took place to review and finalise the identified themes and associated quotes. This process allowed researchers to explore individual and shared perspectives and uncover patterns within and across women's narratives.

A phenomenological approach was employed, aiming to understand the lived experiences of women diagnosed with pregnancy-associated cancer (Emiliussen et al. 2021; Neubauer, Witkop & Varpio 2019). This systematic process ensured that the semantic themes accurately reflected the explicit content of the data. Strategies were employed to enhance reliability and trustworthiness, such as double coding by multiple researchers to ensure consistency and cross-check interpretations with the data to prevent bias. These steps ensured adherence to Braun and Clarke's guidelines and strengthened the credibility of the findings (Braun & Clarke 2006, 2021).

7.5 Results

This study included diverse participants, reflecting various ages and cancer diagnoses. Among the participants, seven women had breast cancer; the remaining individuals were diagnosed with other types of cancer, including melanoma, lymphoma, thyroid, ovarian, uterine, bowel, and oropharyngeal cancer. The timing of diagnosis also varied, with ten participants diagnosed postpartum and seven during pregnancy. Two-thirds of women were married and had multiple children.

After a thorough thematic analysis of the data, three overarching themes emerged: 1. "Alone on the road", 2. "It was absolutely devastating; emotional turmoil and a deep fear of the unknown," and 3. "Autopilot; you have no choice". The themes and quotes are presented below, with additional quotes in **Table 7.2**.

7.5.1 Alone on the road

Women reported that experiencing cancer during pregnancy or the postpartum period was incredibly challenging, terrifying, and traumatic. This sentiment arose from the simultaneous navigation of the intricate challenges associated with managing cancer while pregnant or coping with a newborn after being diagnosed with cancer. Women often experience a profound sense of isolation. This unique and rare nature led to feeling alone on their journey.

"So, it felt like a really bumpy road to get this diagnosis and get started. It was so draining, confusing, and isolating, and I just remember not sleeping much those first few weeks. And if I did fall asleep, the second I woke up, my first thought was, 'Oh my God, I have cancer'."
(W14, Breast cancer)

Many women felt restless, isolated, and overwhelmed as they endured prolonged waiting periods for essential medical assessments such as scans and mammograms. During this distressing process, the burden of waiting for crucial medical evaluations was added to their anxiety levels. Feeling alone in their journey, women endured extended periods of uncertainty, with some doctors hesitating to conduct necessary tests during pregnancy or even after childbirth. The waiting period became a source of frustration, as pregnancy is a difficult journey, and the fear of a cancer diagnosis shattered their emotional well-being.

"I think they wasted so much time on the diagnosis because I was pregnant, and that was a big frustration." (W10, Melanoma)

Women reported that mental health assistance was lacking, with a predominant focus on addressing the physical aspects of the disease. Their journey's emotional and mental health aspects were frequently overlooked, leaving them to grapple with their feelings without adequate support.

"It's just really coming back to no one gets it. It's just such a harder stage of life to be in, and it was really unique. I genuinely think I wish I had this five years earlier, or I wish I had this five years later." (W12, Thyroid cancer)

Additionally, being diagnosed with a rare form of cancer further compounded the sense of isolation for women, even within the broader cancer community. While medical treatment naturally took precedence in managing cancer, women facing this unique situation emphasised the need for more comprehensive mental health support.

"There were many women's cancer support groups, such as breast and ovarian cancer, and they all seemed to have quite strong support networks. However, I could not access any of these kinds of support; there were no support groups for head and neck cancer." (W9, Oropharyngeal cancer)

Women reported that a delayed cancer diagnosis triggered anxiety, but positive words and reassurance from healthcare professionals helped them feel less alone and brought comfort and relief. Despite difficulties and isolation, compassionate healthcare providers have become a crucial source of emotional solace, enhancing women's overall well-being as they navigate this phase.

"He (obstetrician) had been in constant contact with me during that time (diagnosis period), providing straightforward information while incredibly kind and understanding. He was transparent about the situation and explained everything that had happened." (W6, Uterine choriocarcinoma)

7.5.2 It was absolutely devastating; emotional turmoil and a deep fear of the unknown

The news of a cancer diagnosis alone was overwhelming, but the additional layer of pregnancy added immense complexity and emotional weight to women. Fear of unknown outcomes and uncertainty about the future have created constant anxiety and worry.

"When you're faced with the idea that you probably won't survive, and you are not spending time with your baby to bond, the emotional distress far outweighs the physical side." (W2, Hodgkin-lymphoma)

Treatment considerations were complex for some women diagnosed during pregnancy, adding another layer of fear and uncertainty.

"At that point, all I knew was I had cancer; I didn't know anything else. I didn't know what they were going to tell me. I didn't know if the right time [to have treatment] was six months later because everything spiked out of control. I thought that was it!" (W7, Ovarian cancer).

Women who were diagnosed following pregnancy also struggled with the thought that they may not survive, especially now they had given birth and had a child to care for.

"We were really enjoying parenthood, and we thought, you know, our baby was a pretty active newborn, so we felt lucky. But then it just felt like our world turned upside down. It was absolutely devastating! They started talking about life expectancy, and the idea of leaving my husband as a widow with this tiny baby was so terrifying!" (W14, Breast cancer)

All women, regardless of their diagnosis, experienced a deep-seated fear of cancer recurrence, which became a constant concern. Women found it challenging to fully enjoy motherhood because of this lingering fear. The uncertainty of how a cancer recurrence would affect their health, their ability to care for their child, and their future added to their emotional distress.

"It's still a bit daunting. Every time there's something wrong with me, I find myself hoping it's [cancer], not coming back. It's like you always have this Damocles' sword hanging above your head that could drop anytime." (W10, Melanoma)

7.5.3 Autopilot; you have no choice

After the initial emotional turmoil, many women found strength in motherhood. They saw this life stage as pivotal in keeping them motivated and robust despite the physical and emotional toll of being diagnosed with cancer and undergoing treatment. The presence of an unborn child brought a profound sense of purpose and responsibility.

"I remember when my dad passed away from cancer five years ago; it knocked him around quite a fair bit. But I don't know, maybe being pregnant helped me a lot, and I don't know if it's just because I had something else to focus on, maybe rather than cancer." (W1, Breast cancer)

Several mothers also candidly expressed that their parental duties were essential to sustaining their perseverance throughout the challenges of cancer treatment, as the responsibilities of caring for their young infants or multiple children left them with little opportunity to focus on cancer.

"I think it would have been much more difficult if I didn't have kids and was going through the same thing. But because I had to care for them, I had to be there for them; I found a big strength to fight and see the outcome." (W10, Melanoma)

Some women felt extraordinarily unwell and struggled to cope during and after the treatment. However, their profound sense of motherhood left them with no alternative but to find ways to cope for the sake of their baby. The overwhelming desire to provide the best for their child served as a powerful driving force, helping them navigate challenges and maintain a positive outlook.

"I think I just went on autopilot and functioned because I had to wake up and care for a tiny human who was dependent on me to stay alive." (W17, Corneal, ocular, and uvular melanoma)

In the face of uncertainty and the inherent risk of recurrence, the women in this study exhibited remarkable positivity throughout cancer treatment. Their unwavering determination to witness their children grow up was a driving force, compelling them to maintain a calm and positive outlook. Despite the challenges posed by the disease, these women prioritised their own lives, prioritising living longer to be present for their children's milestones and growth.

"So, it's very important to take each day as a new day, and that's what I do. I just take one step at a time; I try not to overwhelm myself with anything. My primary focus is myself, my little boy, and my partner, and everything else can come second. Everything else is not important." (W6, Uterine choriocarcinoma)

Some women underscored the importance of specialised newborns and childcare support to help them cope with their treatment and recovery. After treatment, they experienced emotional exhaustion and required mental and physical recovery. While some women had the advantage of family support, others felt helpless, overwhelmed, and exhausted, notably if they lacked adequate newborn or childcare assistance. Many of these women believed that additional help with childcare, such as in-home childcare or assistance with transportation to medical appointments, would significantly alleviate their mental and emotional challenges.

"So, usually, I would have my husband come with me for chemo because, you know, it is emotionally draining... However, we had no one to care for the kids. So, that was a challenge." (W15, Breast cancer)

7.6 Discussion

A rare diagnosis of pregnancy-associated cancer profoundly affects the mental health and well-being of affected women, presenting a challenging paradox as they nurture a new life while facing mortality (Faccio et al. 2020; Ferrari et al. 2018; Roberts & Andrewes 2022). Three dominant themes were identified related to the effect of pregnancy-associated cancer on well-being and mental health.

Women described the immense challenges and fears associated with pregnancy-associated cancer diagnosis, navigating a complex and daunting journey. They often felt a profound sense of isolation, particularly when dealing with rare cancers. The simultaneous experience of pregnancy and cancer created overwhelming stress as they adapted to two significant life events. Unfortunately, many women reported a lack of sufficient mental health support, leaving them isolated.

Each woman's experience of motherhood while dealing with cancer is personal and presents unique emotional hurdles (Faccio et al. 2020; Ferrari et al. 2018; Ives, Musiello & Saunders 2016). Healthcare professionals must consider these psycho-oncological aspects and integrate appropriate support into their practices. The women in this study emphasised the need for more mental health and emotional support, particularly for rare pregnancy-associated cancers. Feeling understood and supported by

medical providers empowers them to overcome these challenges. Hurren et al. (2023) also emphasised the importance of educating healthcare professionals to facilitate early identification of mental health and psycho-oncological support needs (Hurren et al. 2023). There is a compelling need for mental health care that prioritises individuals and enhances collaboration between service providers, particularly between oncology and obstetric teams.

Women with pregnancy-associated cancer often feel isolated in general cancer groups, as they may be the only pregnant patient or new mother, leading to a sense of not belonging to either oncology or maternity groups (Hammarberg et al. 2018). Peer support programs have significant psychological benefits (Gould et al. 2006; Hoey et al. 2008), but there are limitations to the available groups for women with gestational cancer (Leung, Bryant & Stafford 2020). Women in this study advocated for more social support groups, particularly for rare haematological or head and neck cancers during pregnancy or postpartum.

This study revealed a range of emotions among women diagnosed with pregnancy-associated cancer, from initial shock and anxiety to fear of the unknown. They faced the dual challenge of protecting their health and receiving the best treatment while ensuring their unborn child's well-being. Approximately one-third of cancer patients experience mental health conditions such as anxiety or depression, a rate likely higher for those with pregnancy-associated cancer (Mental Health Foundation 2018). The unique challenges of pregnancy-associated cancer, compounded by its rarity, intensify the emotional toll, leading to increased rates of mental health conditions during diagnosis and treatment.

Previous studies have shown that women diagnosed with pregnancy-associated cancer experience significant distress regarding their diagnosis, treatment, and ability to parent, thereby impacting their families (Leung, Bryant & Stafford 2020; Roberts & Andrewes 2022). Both cancer and pregnancy make individuals emotionally vulnerable, posing unique challenges for women diagnosed during pregnancy or in the postpartum period. Even after completing treatment, women may continue to worry about their children's exposure to chemotherapy in utero and concerns about future fertility (Leung, Bryant & Stafford 2020). Anxiety during pregnancy and the postnatal period can affect the well-being of both mothers and children, leading to complications such as miscarriage, preeclampsia, premature birth, NICU admissions, foetal distress, low birth weight, and an increased risk of postpartum depression (Fairbrother et al. 2017; Kozu, Masujima & Majima 2020; Van Assche et al. 2022).

Furthermore, women expressed ongoing concerns regarding the possibility of cancer recurrence. *Fear of cancer recurrence (FCR)* is defined as "the fear or worry that cancer will return or

progress in the same organ or another part of the body" (Vanstone et al. 2021). This constant stress and worry are pervasive in their stories. One study identified variations in several psychological aspects, including differences in quality of life, post-traumatic symptoms, the importance of pregnancy to one's sense of self, and life narratives between pregnant cancer survivors and individuals who have not encountered cancer (Faccio et al. 2020). Tailored programs are needed to address the ongoing mental health challenges for women diagnosed with pregnancy-associated cancer to improve their health and the health of their families.

Many women in this study found that motherhood served as a profound coping mechanism amid challenging cancer diagnoses. Some women stated that the act of being pregnant served as a source of resilience, aiding them in dealing with the treatment of their cancer. Other participants highlighted that the demands of newborns and, for some, the responsibilities of caring for their other children played a pivotal role in facilitating the battle against cancer during the postpartum period. These maternal duties gave them renewed energy, hope, and a heightened desire for a prolonged life. In contrast to previous studies that highlighted women's fears regarding their ability to care for their children and concerns about their children's well-being after chemotherapy exposure (Faccio et al. 2020; Ferrari et al. 2018; Kozu, Masujima & Majima 2020), this study revealed a remarkable level of acceptance and effective coping among women despite the intense emotional struggles they endured. These findings from this study suggest women showed exceptional resilience in challenging circumstances, and these findings have yet to be highlighted in prior studies.

Although the women did not discuss their partners' experiences extensively, they indicated that their partners provided good support. Future studies could explore partners' needs, experiences, and impact on parenthood. Participants emphasised the need for specialised childcare support during treatment, particularly in the postpartum period when placing a newborn in daycare is challenging. Access to specific daycare services, especially when family support is unavailable, can significantly aid recovery and provide peace of mind.

In summary, these findings enhance our understanding of the impact of mental health and well-being on women diagnosed with pregnancy-associated cancer. Organisations such as the Cancer Council Australia offer initial mental health support, including counselling and support groups (Cancer Council 2024). These services are valuable but may not be sufficient to address the individual needs of women with specific types of cancer. There remains a need for more comprehensive and personalised mental health services to support these patients throughout their cancer journey. Enhanced support for women can be achieved through several key strategies, including:

- a) Implementing early screening processes to identify psychological distress in pregnant and postpartum women with a cancer diagnosis.
- b) Appointing a designated midwife or early childhood nurse to provide personalised psycho-oncological support tailored to each woman's unique needs.
- c) Establishing specialised counselling services designed to address the distinct emotional requirements of these women, along with ensuring easy access to mental health professionals and adequate peer support.

By implementing these measures, we can significantly improve the support available to women in navigating the complexities of pregnancy-associated cancer. Future research investigating the long-term psycho-oncological aspects of women diagnosed with pregnancy-associated cancer would significantly enhance our understanding of the impact of gestational cancer on mental health.

7.7 Strengths and Limitations

The strength of this study lies in its exploration of the mental health journeys of women diagnosed with cancer during pregnancy or postpartum, which has received limited attention.

A fundamental limitation of this study was the need for more diversity of participants. Owing to certain constraints, this study included only English-speaking women, excluding voices from various ethnic or cultural backgrounds. More diverse participants might have uncovered additional themes and perspectives. Additionally, this study findings are not broadly applicable because of each participant's unique circumstances and personal experience. Despite these limitations, our study provides valuable insights into the significance of mental health experiences among women with pregnancy-associated cancer.

7.8 Conclusion

This study revealed that women with pregnancy-associated cancer experience significant stress and isolation. However, despite these challenges, they have demonstrated remarkable resilience. The notable gap in mental health support highlights the need for improved care. This study underscores the importance of enhancing mental healthcare for this population through early screening, involvement of designated midwives or nurses, specialised counselling services, accessible mental health professionals, and peer support networks. Further research is crucial to explore the long-term psycho-oncological effects of pregnancy-associated cancer to inform comprehensive care strategies for affected women.

7.9 Chapter summary

Chapter 7 addresses the question of how pregnancy-associated cancer impacts the well-being and mental health of affected women, providing a detailed exploration of the psycho-oncological challenges they face. The chapter demonstrates that mental health support for these women is insufficient, revealing a critical gap in the current healthcare system. Through this analysis, the chapter contributes to the broader study by uncovering the specific mental health needs of women during the perinatal period and identifying key areas where interventions are lacking. This chapter also answers questions about the types of mental health challenges experienced and their implications for care, placing the groundwork for future research to enhance mental health interventions and support pathways.

Table 7.1 Participant characteristics

No of women	Cancer diagnosis (pregnancy or postpartum)	Age at diagnosis (Y)	Type of cancer	Marital status	No of children	Residence
W1	Pregnancy	33	Breast cancer	Married	2	Regional
W2	Pregnancy	34	Hodgkin Lymphoma	De-facto	2	Metropolitan
W3	Postpartum	43	Non-Hodgkin Lymphoma	Separated	1	Regional
W4	Postpartum	40	Melanoma	Married	2	Metropolitan
W5	Pregnancy	38	Breast cancer	Divorced	2	Metropolitan
W6	Postpartum	32	Uterine choriocarcinoma	De-facto	1	Metropolitan
W7	Postpartum	41	Ovarian cancer	Married	1	Regional
W8	Postpartum	35	Bowel cancer	Married	2	Metropolitan
W9	Pregnancy	32	Oropharyngeal cancer	Married	2	Metropolitan
W10	Pregnancy	35	Melanoma	Married	2	Metropolitan
W11	Postpartum	39	Breast cancer	Married	2	Regional
W12	Pregnancy	29	Thyroid cancer	Married	3	Regional
W13	Postpartum	33	Breast cancer	Married	2	Metropolitan
W14	Postpartum	35	Breast cancer	Married	1	Regional
W15	Postpartum	36	Breast cancer	Married	2	Metropolitan
W16	Pregnancy	40	Breast cancer	Married	2	Metropolitan
W17	Postpartum	25	Melanoma	De-facto	2	Metropolitan

Table 7.2 Additional quotes

Themes	Quotes
1. Alone on the road	<i>"It really felt incredibly isolating... living with uncertainty is pretty tough, I'll be honest." (W12, thyroid cancer)</i>
	<i>"So, I felt that the first bit was quite stressful because the diagnosis was delayed, and I don't know how something like that could be sorted out. We did feel a little bit lost and alone during that period." (W3, non-Hodgkin lymphoma)</i>
	<i>"I think that's the support that is lacking. A lot of people feel isolated because nobody gets it." (W10, melanoma)</i>
	<i>"I could not find any support or anyone to connect with who had gone through this before. I could not sit down and ask, 'Well, what did you do?' or 'What happened to you?' When someone has breast cancer, they have a mountain of support, whereas this particular cancer does not. It is so rare!" (W6, uterine choriocarcinoma)</i>
2. It was absolutely devastating; emotional turmoil and a deep fear of the unknown	<i>"The only way to know if it [cancer] has gone anywhere else is if something else out of the norm flares up, and it's just not great! If I get a sore back and it's not normal, okay, here you go. That's probably something every cancer patient goes through — that fear. So, only hope!" (W11, breast cancer)</i>
3. Autopilot; you have no choice	<i>"Everyone just looked at me and said, 'You're just amazing! How are you getting through this? You have kids, you have this, that,' and I'm just like if I didn't have the kids, I'm sure I would be curled up in a ball every day in my bed, but you can't. So, you just gotta keep going." (W11, breast cancer)</i>
	<i>"Look, you have days where you just like, 'Just leave me alone.' But you know, there's no choice. You don't have a choice. There's nothing you can do about it. So, you just have to make the most of it." (W15, breast cancer)</i>
	<i>"I was like, 'No, I'm going to watch this kid grow up, so let's make it happen, let's do it.' And I refuse to let it stop me from living my life and put a damper on my life or my kids' life. It's part of my life, but it is not my whole life, and I refuse to let it be." (W17, corneal, ocular, and uvular melanoma, diagnosed- postpartum)</i>

Chapter 8: Discussion

8.1 Chapter introduction

The management of pregnancy-associated cancer presents a complex and multifaceted challenge for both affected women and their healthcare professionals. As the incidence of pregnancy-associated cancer is continuously rising, there is a critical need for comprehensive research to understand maternal and neonatal outcomes, healthcare experiences, and the mental health and well-being of these women. A multi-method design was used in this thesis to explore these aspects, employing both quantitative and qualitative approaches across separate studies to provide a holistic perspective on this rare but significant condition.

The four studies presented in this thesis (Chapters 4, 5, 6, and 7) collectively strengthen the understanding of pregnancy-associated cancers by addressing critical gaps in the literature. These include insights into the incidence, outcomes and management of pregnancy-associated colorectal cancer (PACRC), perinatal outcomes after exposure to systemic treatment, communication experiences between women and healthcare providers (HCPs), and mental health challenges faced by women diagnosed with this condition.

This chapter synthesises the findings from these studies, explores their broader implications, and presents recommendations for future research and clinical practice. By integrating these findings, this chapter constructs a comprehensive narrative that highlights the complexities of pregnancy-associated cancer and underscores the need for tailored interventions and multidisciplinary care. This chapter concludes by highlighting the implications and recommendations of this work.

8.2 Key findings of this research and discussion

This research identified a significant annual increase in the incidence of PACRC, independent of maternal age. Women diagnosed with gestational CRC experienced higher rates of birth interventions, including induced labour, caesarean sections, and planned preterm births, along with maternal morbidities, such as cardiac arrest and cerebral oedema. Neonatal complications, including respiratory distress syndrome and transient tachypnoea, were significantly higher; however, no significant differences were observed in perinatal deaths and congenital anomalies between the neonates of women with and without gestational CRC.

A systematic review and meta-analysis revealed that systemic cancer treatment during pregnancy was associated with a significantly higher incidence of preterm births among infants exposed to these treatments in utero. However, no significant differences were reported in the rates of spontaneous abortion, congenital anomalies, stillbirth, intrauterine growth restriction, or small-for-gestational-age births between infants exposed to systemic therapy and those who were not.

A qualitative analysis of women's experiences with HCPs identified three overarching themes: "Scarcity of information," "Not involved in treatment decisions," and "Lack of resources and advocates." Furthermore, an exploration of the mental health impacts of pregnancy-associated cancer revealed three key themes: "Alone on the Road," "It was absolutely devastating; emotional turmoil and a deep fear of the unknown," and "Autopilot; you have no choice." These findings underscore the profound mental health challenges faced by women and highlight the critical gaps in communication and support systems.

8.2.1 The growing incidence of pregnancy-associated cancer: Younger women at risk

Recent trends indicate a notable shift in cancer epidemiology, with an increasing incidence among younger populations, particularly women (Kehm et al. 2019). This research identified a significant annual increase in pregnancy-associated colorectal cancer (PACRC), independent of maternal age. Furthermore, an increasing number of PACRC cases have been observed among younger individuals, aligning with broader trends in colorectal cancer epidemiology (Kasi et al. 2018; Levine & Zbuk 2019; Munteanu et al. 2019). These findings highlight the importance of understanding cancer risk in the younger population.

Historically, cancer diagnoses were predominantly associated with older adults; however, recent decades have witnessed a rise in cancer incidence among younger individuals (Brinton et al. 2008; Di Martino et al. 2022). This trend, particularly pronounced in colorectal cancer, poses unique challenges for its prevention, early detection, and treatment (Ben-Aharon et al. 2023; Stoffel & Murphy 2020). Hypotheses linking this trend to lifestyle changes, such as increased consumption of processed foods, reduced physical activity, and rising obesity rates, are supported by studies emphasising their role in cancer development (Ben-Aharon et al. 2023; Dannenberg & Berger 2013; Gupta et al. 2020; Stoffel & Murphy 2020; Ugai et al. 2022).

The growing prevalence of cancer among women is of particular concern. The risk of developing cancer during pregnancy or postpartum is expected to increase as the likelihood of many malignancies increases with advancing maternal age (Ruiz et al. 2017; Troisi et al. 2018). This trend is primarily attributed to the growing prevalence of delayed childbearing observed in recent years (Eastwood-Wilshere et al. 2019; Maggen et al. 2019; Wolters et al. 2021). Among women, specific reproductive health factors, including age at menarche, age at first childbirth, and prolonged use of hormonal contraception, may also play a role in the diagnosis of pregnancy-associated cancer (Gierisch et al. 2013; Kapil et al. 2014). Prolonged exposure to oestrogen in women who delay childbirth or use oral contraceptives for extended periods is associated with an increased risk of certain cancers such as breast, cervical, colorectal and endometrial cancers (Gierisch et al. 2013). Hormonal changes during pregnancy or postpartum are hypothesised to influence the risk of cancer (Froehlich et al. 2019; Troisi et al. 2018). However, these associations with pregnancy-associated cancer remain inconclusive.

To date, research has explored potential links between PACRC and factors such as advanced maternal age, obesity, pregnancy-related growth factors, genetic predispositions, and environmental influences (Araujo et al. 2022; Predescu D et al. 2020; Samadder et al. 2020). However, the specific aetiology of PACRC remains complex and multifactorial, and no single factor has been definitively identified as causative. This underscores the need for further investigation of the interplay of genetic, hormonal, and environmental factors in the pathogenesis of PACRC.

While it appears that genetic and hormonal factors combine with lifestyle and environmental exposure to increase cancer risk, the role of the social determinants of health, including access to healthcare, education, and socioeconomic status, should also be considered (Akinyemiju & Noor 2012; Korn et al. 2023). Increased access to antenatal care and cancer screening may contribute to higher detection rates of pregnancy-associated cancer (Cottreau et al. 2019; Esposito et al. 2024; Ndlela et al. 2018); however, these factors alone are unlikely to explain the observed trends comprehensively. The rising incidence of cancer in younger populations, particularly among women during pregnancy and the postpartum period, emphasises the importance of targeted prevention strategies, improved early detection methods, and tailored interventions to address the unique challenges posed by cancer.

8.2.2 Delayed diagnosis of pregnancy-associated cancer

Delayed diagnosis of cancer during pregnancy and the postpartum period presents a significant challenge in maternal healthcare, with profound implications for cancer outcomes and maternal-

neonatal health. Despite advancements in diagnostic technologies and medical practices, this issue persists, resulting in adverse outcomes for women and their newborns.

A key finding of this thesis is that two-thirds of the women with PACRC were diagnosed during the postpartum period. This observation is consistent with the results of the previous studies suggesting that many cases of pregnancy-associated cancer were identified postpartum due to missed diagnostic opportunities during pregnancy (Andersson et al. 2015; Dalmartello et al. 2020). The qualitative findings further highlight that women frequently reported that their symptoms were dismissed or misattributed to regular pregnancy-related changes, which subsequently contributed to delays in diagnosis. Symptoms, such as fatigue, nausea, weight loss, and abdominal pain, which are expected in both pregnancy and cancer, are often overlooked (Johansson et al. 2019; Maggen et al. 2019; Shemer et al. 2022). This issue is particularly pronounced in rare cancers such as colorectal or gastric cancer, where early warning signs can easily be misinterpreted as pregnancy-related symptoms (Kocián et al. 2019; Munteanu et al. 2019; Shemer et al. 2022). The symptom overlaps between pregnancy-related changes and cancer can obscure the clinical picture, making it difficult for both patients and healthcare providers to differentiate between what is "Normal" for pregnancy and what may be indicative of a severe underlying condition such as cancer (Esposito et al. 2024; Johansson et al. 2019).

A significant factor contributing to delayed diagnosis is the limited awareness and medical training of HCPs regarding pregnancy-associated cancer (Hepner et al. 2019; Johansson et al. 2019; Rajagopal, Liamputtong & McBride 2019; Stafford et al. 2022). Due to the relative rarity of pregnancy-associated cancer, many healthcare providers lack sufficient experience or knowledge to identify its clinical signs or navigate the complexities of diagnostic and treatment decisions effectively (De Haan et al. 2016; Hepner et al. 2019; Rajagopal, Liamputtong & McBride 2019; Salani, Billingsley & Crafton 2014; Stafford et al. 2022). Although clinical guidelines for managing cancer during pregnancy exist, oncologists and obstetricians often face challenges due to a lack of consensus on the safest and most effective diagnostic and therapeutic approaches due to the lack of comprehensive standardised guidelines (De Haan et al. 2016; Esposito et al. 2024; Hepner et al. 2019; Silverstein et al. 2020; Stafford et al. 2022).

Several theoretical frameworks have been proposed to explain why delayed diagnosis occurs more frequently in women, particularly during pregnancy. Healthcare systemic biases and structural inequalities further compound delays in cancer diagnosis (Williams, Murchie & Bond 2019). Delayed cancer diagnosis is a well-documented issue in healthcare and is frequently highlighted in studies concerning gender disparities in medical practice (Thompson & Blake 2020). Gender biases within the

medical field have been well documented, with women's complaints often being underestimated or not taken as seriously as those of men (Kent, Patel & Varela 2012; Thompson & Blake 2020). Gendered medical practices contribute to the under-recognition of symptoms in pregnant women, with healthcare providers often attributing unexplained symptoms to hormonal changes or emotional stress (Kent, Patel & Varela 2012; Thompson & Blake 2020). This phenomenon, commonly referred to as medical gaslighting (Khan & Majeed 2024), reflects a broader issue in healthcare systems where women's health concerns are frequently dismissed. This dismissal can fail to investigate symptoms thoroughly, leading to diagnostic delays and unequal access to treatment and care for women, potentially leading to worse health outcomes, including higher complications and mortality rates (Alspach 2017; Khan & Majeed 2024).

Another theory centres around the medicalisation of pregnancy, where pregnancy symptoms are seen as "normal" or "expected," thus leading to the under-recognition of warning signs of more severe conditions like cancer (De Haan et al. 2016; Gomes, Sand & Girardon-Perlini 2021; Khangura et al. 2015). Cultural expectations about the physical and emotional toll of pregnancy further exacerbate this tendency, creating an environment in which women's complaints are often under-prioritised (Kent, Patel & Varela, 2012; Thompson & Blake, 2020). Healthcare access disparities may also play a significant role in delayed cancer diagnosis during pregnancy and the postpartum period (Yee et al. 2020). Women in rural or socioeconomically disadvantaged areas face numerous barriers, including limited access to specialised diagnostic services, long appointment waiting times, the need to travel long distances for care and financial constraints, all of which contribute to delayed diagnosis (Abd-Allah et al. 2019; Akinyemiju & Noor 2012; Menvielle et al. 2018). These access disparities highlight the intersectionality of gender, geography, and socioeconomic status in shaping health outcomes.

The consequences of delayed diagnosis have been far-reaching. Advanced-stage cancer diagnoses during pregnancy are associated with more aggressive treatment regimens, which pose significant risks to maternal and neonatal health (Maggen et al. 2019; Pereg, Koren & Lishner 2008; Wolters et al. 2021). Five-year survival rates for breast and colorectal cancer decline markedly when diagnosed at advanced stages, as these cancers are more likely to have metastasised and become less responsive to conventional treatments (Khangura et al. 2015; Lee, Burge & Eastgate 2019; McPhail et al. 2015). In pregnancy, advanced cancer treatments, such as chemotherapy, carry heightened risks for foetal outcomes, including preterm birth, small for gestational age and intrauterine growth restriction (Capozza et al. 2024; Garofalo et al. 2017; Maggen et al. 2019). This risk creates a clinical dilemma in which maternal treatment must be balanced against foetal safety, further complicating care.

The mental health and psychological toll of delayed cancer diagnosis warrant attention. Women diagnosed with advanced cancer during or after pregnancy face not only the physical challenges of managing their illness but also profound mental health impacts (Leung, Bryant & Stafford 2020; Roberts & Andrewes 2022). The findings of this study reveal the need for improved support systems to address the psychological burden for women and their families.

8.2.3 Maternal and neonatal outcomes in pregnancy-associated cancer

Increased birth intervention and maternal outcomes

Cancer diagnosis and treatment during pregnancy present unique challenges, significantly impacting maternal health and pregnancy outcomes. The quantitative analysis conducted in this thesis (Study 1) found that women diagnosed with cancer during pregnancy experienced higher rates of birth interventions, including induced labour, caesarean sections, and planned preterm births. These findings align with the existing literature, which highlights that such interventions often arise from the need to balance maternal cancer treatment with the safe delivery of the infant (Kocián et al. 2019; Predescu D et al. 2020).

Women with pregnancy-associated cancer may also be more vulnerable to infections and inflammatory responses, potentially triggering preterm labour (Dahling et al. 2009; Gens & Barbosa 2017). This increased intervention rate underscores the complexity of managing pregnancy-associated cancer, which requires thorough clinical decision-making to navigate the dual priorities of maternal treatment and neonatal health (Safi et al. 2023). However, these interventions, such as caesarean sections and preterm deliveries, often place additional physical and emotional burdens on affected women. The time-sensitive nature of decisions regarding cancer treatment and delivery intensifies stress and anxiety, particularly as women must weigh concerns for their health and the well-being of their babies (Leung, Bryant & Stafford 2020; Roberts & Andrewes 2022). A particularly salient narrative across the qualitative interviews was that the role of communication in this context is critical. Poor communication between HCPs and fragmented care pathways further compounds this stress, leaving women feeling unsupported and confused (Hammarberg et al. 2018; Stafford, Sinclair, Gerber, Collins, et al. 2021). These narratives complement the quantitative findings, providing insight into how clinical outcomes such as caesarean section or preterm birth can carry psychological or mental health consequences when not accompanied by adequate support and shared decision-making.

An encouraging finding from the thesis (Study 1) was that pregnancy itself does not adversely affect the prognosis of women with PACRC. Women with PACRC were found to have survival rates comparable to non-pregnant women with colorectal cancer. This is reassuring for both clinicians and women. However, maternal morbidity in women with gestational CRC reinforces the need for tailored management strategies. These strategies should carefully balance the timing of cancer diagnosis and treatment with the safe delivery of the infant while also promoting heightened awareness among HCPs to ensure timely diagnosis and intervention.

Neonatal Outcomes

Pregnancy-associated cancer significantly increases the likelihood of preterm birth, particularly in infants exposed to systemic cancer treatments in utero. These findings align with the broader literature that consistently identifies preterm birth as a prevalent adverse outcome in pregnancies complicated by maternal systemic treatment (Esposito et al. 2021; Maggen et al. 2019; Momen et al. 2018; Shechter Maor et al. 2019). The observation of a higher incidence of preterm births among women receiving systemic therapy is likely attributable to iatrogenic factors such as the medical induction of labour to allow for the continuation of maternal cancer treatment (Capozza et al. 2024; Lucovnik et al. 2016). The decision to induce labour early highlights the clinical dilemma faced by HCPs in balancing maternal treatment needs with foetal safety.

Prematurity is a significant concern, as it is a leading cause of neonatal mortality and morbidity. (De Haan et al. 2018; Harrison & Goldenberg 2016; Lataifeh et al. 2011). The short-term consequences of preterm birth are well-documented and include respiratory complications, increased susceptibility to infections, feeding difficulties, extended neonatal intensive care unit (NICU) admissions, and an overall heightened risk of neonatal morbidity (Garofalo et al. 2017; Humberg et al. 2020; Patel 2016). Beyond these immediate risks, preterm birth carries significant long-term implications for neurodevelopment (Briana & Malamitsi-Puchner 2020; Crump 2020). Infants born early or late preterm are at exceptionally high risk for cognitive delays, speech or language disorders, developmental disabilities, and chronic health problems, including asthma and long-term respiratory issues (Srinivas Jois 2018; Vohr 2014). The association between preterm birth, small for gestational age, NICU admissions, and systemic therapy exposure remains inconclusive, warranting caution in making definitive recommendations for treatment during pregnancy (Capozza et al. 2024; Garofalo et al. 2017; Van Assche et al. 2022).

The long-term effects of in-utero exposure to systemic cancer treatments, including chemotherapy, remain poorly understood. While studies have documented neurodevelopmental risks associated with

preterm birth, such as cognitive delays, speech disorders, and chronic respiratory issues, the specific impact of maternal cancer treatment requires further exploration (Amant et al. 2012; Briana & Malamitsi-Puchner 2020; Cardonick et al. 2015). While some studies suggest that early interventions, such as physical therapy and early childhood education programs, may mitigate developmental challenges, the specific impact of maternal cancer treatment on neurodevelopment remains poorly understood (Korakiti et al. 2020; Van Assche et al. 2022).

The research highlights the complexity of managing pregnancy-associated cancer, underscoring the need for coordinated decision-making between oncology and obstetric teams. The higher rate of preterm births among women exposed to systemic therapy reinforces the need for vigilant monitoring and meticulous planning to improve neonatal outcomes. Encouragingly, recent data indicate a reduction in iatrogenic preterm delivery rates, possibly due to extended systemic therapy courses during pregnancy, which allow for delayed delivery and, consequently, improved neonatal outcomes (De Haan et al. 2018). Importantly, studies suggest that the risks associated with systemic therapy during pregnancy can be managed through careful timing and interdisciplinary collaboration, as systemic therapy administered during the second and third trimesters did not indicate significantly worse neonatal outcomes, reinforcing the critical role of treatment timing in minimising potential adverse effects (Esposito et al. 2016; Garofalo et al. 2017; Hepner et al. 2019; Maggen et al. 2019).

Limited research has been conducted to date; therefore, more robust longitudinal studies are required to thoroughly evaluate the long-term impact of in-utero exposure to chemotherapy and other systemic therapies on neonatal health (Capozza et al. 2024; Van Assche et al. 2022). Such research will be instrumental in advancing understanding of the long-term effects of cancer treatments on both mothers and their children, ultimately informing clinical guidelines and improving care delivery in pregnancy-associated cancer.

8.2.4 Communication in cancer care during pregnancy and postpartum

Effective communication plays a pivotal role in the cancer care experiences of pregnant and postpartum women (Kozu, Masujima & Majima 2020; Stafford, Sinclair, Gerber, Collins, et al. 2021). Findings from this thesis underscore that communication gaps significantly impact women's ability to understand their treatment options, make informed decisions, and feel confident in managing their care during a highly stressful period. Many women reported that healthcare professionals often failed to explain the risks associated with cancer treatments during pregnancy or postpartum. The lack of comprehensive information left women overwhelmed and disempowered, highlighting the critical need for improved communication strategies tailored to this unique context.

Importance of good communication in building trust, alleviating anxiety, and informing decisions

Effective communication builds trust between patients and HCPs, reduces anxiety, and facilitates informed decision-making (Keslar 2023; Ward 2018). This is particularly crucial in the perspective of pregnancy-associated cancer, where women face complex and emotionally challenging decisions that affect both their health and their unborn child (Ferrari et al. 2018; Hurren et al. 2023; Roberts & Andrewes 2022). This gap is particularly concerning given the emotional and psychological vulnerability associated with a dual diagnosis of pregnancy and cancer. Clear and empathetic communication plays a critical role in alleviating the anxiety that often accompanies the psychological and mental health burden of a cancer diagnosis during this vulnerable time (Ferrari et al. 2018; Keslar 2023; Roberts & Andrewes 2022).

By providing accurate and accessible information, healthcare providers empower women to understand their treatment options and make decisions aligned with their values, fostering a sense of control over their care during a highly stressful period (Hunter et al. 2019; Stafford et al. 2022). Establishing a therapeutic relationship through clear and empathetic communication provides essential support, fostering an environment where women feel comfortable discussing sensitive topics, such as the potential risks of cancer treatments for their baby (Hammarberg et al. 2018; Hurren et al. 2023; Keslar 2023).

Conversely, poor communication exacerbates the psychological burden of a cancer diagnosis, intensifying uncertainty and distress (Hammarberg et al. 2018). In this thesis, women highlighted that lacking comprehensive, timely, and accurate information from HCPs left them feeling isolated and unsupported. Studies consistently show that respectful and empathetic communication not only improves patient satisfaction but also enhances clinical outcomes by fostering a collaborative approach to care (Ferrari et al. 2018; Roberts & Andrewes 2022; Stafford, Sinclair, Gerber, Collins, et al. 2021). In this context, effective communication is not just a component of quality care; it is a cornerstone of support for women navigating the dual challenges of pregnancy and cancer.

One pressing concern raised by women in this study was the perceived lack of HCP preparedness and confidence, which often led to delays in diagnosis and inconsistent communication. This challenge is likely compounded by the relative rarity of pregnancy-associated cancer and the limited clinical experience of many HCPs in managing cancer during pregnancy (Rajagopal, Liamputtong & McBride 2019; Stafford et al. 2022). Addressing this issue requires systematic interventions, including targeted

training and the development of standardised communication guidelines, to ensure that HCPs are equipped to provide accurate and empathetic care.

Decision-making in cancer care during pregnancy: process and challenges

Decision-making in cancer care during pregnancy is multidisciplinary, involving oncologists, obstetricians, and other specialists working collaboratively to balance the best interests of both mother and foetus (Silverstein et al. 2020; Sorouri et al. 2023; Voulgaris, Pentheroudakis & Pavlidis 2011). However, findings from this thesis reveal variability in women's experiences with decision-making. While some women felt actively involved in discussions, others described feeling excluded, with decisions being made unilaterally by healthcare teams.

This variation in experience can be attributed to several factors, including the urgency of treatment, the complexity of the cancer diagnosis, and cultural or personal preferences (Swainston et al. 2012). The urgency of treatment often determines the level of women's involvement. Women diagnosed with advanced-stage cancer may face time-critical decisions, leaving little opportunity for thorough discussions about risks and benefits (Brown et al. 2012; Christoffersen et al. 2018; Maggen et al. 2019; Voulgaris, Pentheroudakis & Pavlidis 2011). Conversely, women with earlier-stage cancer may have more time to engage in shared decision-making, allowing for a deeper exploration of treatment options and their implications (Brown et al. 2012; Christoffersen et al. 2018). Regardless of the clinical context, clear and compassionate communication remains central to ensuring women feel informed, supported and respected throughout the decision-making process (Hunter et al. 2019; Stafford et al. 2022).

Women's knowledge, choices, and involvement in decision-making

This thesis highlights a significant lack of women's involvement in treatment decisions, with many participants reporting that HCPs did not adequately discuss their preferences, values, and concerns. This exclusion from the decision-making process often results in increased anxiety and diminished sense of control, which is particularly distressing during pregnancy. These findings resonate with existing literature, emphasising respecting patient autonomy and integrating women's values into treatment planning (Amant et al. 2013; Hammarberg et al. 2018).

Women diagnosed with cancer during pregnancy or postpartum often experience significant emotional distress, including shock, fear, and anxiety, which can influence their level of involvement in decision-making (Kozu, Masujima & Majima 2020; Mazzocco et al. 2019). For some women, these

overwhelming emotions lead to a preference for relying on HCPs to guide treatment decisions, as they feel ill-equipped to evaluate complex medical information or weigh the potential risks and benefits (Kozu, Masujima & Majima 2020; Roberts & Andrewes 2022; Swainston et al. 2012). This reliance on clinicians is often rooted in a perceived lack of knowledge or confidence in making decisions about their care (Swainston et al. 2012), and some women feel unprepared to navigate the complexities of balancing their own health needs with those of their unborn children (Hammarberg et al. 2018; Roberts & Andrewes 2022). The uncertainty surrounding medical treatments and their potential impact on maternal and foetal outcomes further compounds these feelings. In such cases, women often trusted HCPs to make decisions on their behalf that aligned with their best interests and prioritised optimal outcomes for both mother and baby (Kozu, Masujima & Majima 2020; Roberts & Andrewes 2022).

Despite this, integrating women's preferences and values into decision-making is a fundamental principle of patient-centred care and essential for improving emotional and clinical outcomes (Linkeviciute et al. 2024; Sorouri et al. 2023). Women's participation in decision-making fosters a sense of agency and control, which can be incredibly empowering during pregnancy (Chan et al. 2021; Linkeviciute et al. 2024). Ensuring women feel informed, engaged, and respected throughout their treatment journey is a cornerstone of effective cancer care, and it has been shown to mitigate some of the psychological burdens associated with a cancer diagnosis during pregnancy (Chan et al. 2021). Pregnancy and birth decisions are profoundly personal and heavily influenced by women's focus on mothering and the well-being of their unborn child (Coxon 2014; Yuill et al. 2020).

Women often prioritise their babies' health and safety, even when faced with significant risks to their health (Coxon 2014; Yuill et al. 2020). Under typical circumstances, women are the primary decision-makers during pregnancy; however, a cancer diagnosis introduces added complexity, requiring decisions that intersect with medical, ethical, and psychosocial considerations (Kozu, Masujima & Majima 2020; Silverstein et al. 2020; Zagouri et al. 2016). Women may need to decide whether to continue or terminate the pregnancy, delay treatment until after childbirth, or accept potential risks to the foetus in order to prioritise their health (Kozu, Masujima & Majima 2020; Maggen et al. 2019; Silverstein et al. 2020).

The information provided by HCPs plays a pivotal role in shaping these profoundly personal decisions. Factors such as the urgency of treatment, the complexity of the clinical situation, and the alignment of care with women's values and priorities are all heavily influenced by the quality of communication

between women and their clinicians (Hurren et al. 2023; Stafford, Sinclair, Gerber, Collins, et al. 2021). Effective and empathetic communication ensures that women are fully informed about their options and the associated risks, enabling them to make decisions that align with their values and priorities (Hammarberg et al. 2018; Stafford, Sinclair, Gerber, Collins, et al. 2021; Stafford et al. 2022).

8.2.5 Mental health challenges in women with pregnancy-associated cancer

This thesis highlights the substantial mental health challenges confronted by women diagnosed with pregnancy-associated cancer. Emotional responses included shock, anxiety, fear, and uncertainty about the future, which were common (Roberts & Andrewes 2022; Stafford, Sinclair, Gerber, Collins, et al. 2021). These emotions were further exacerbated by the complexity of decision-making around cancer treatment during pregnancy, concerns about the baby's health, and feelings of stigma or isolation while expecting or caring for an infant (Leung, Bryant & Stafford 2020; Silverstein et al. 2020).

A cancer diagnosis significantly impacts an individual's psychological and emotional well-being, creating profound challenges that extend beyond physical health (Grassi et al. 2023; Niedzwiedz et al. 2019). Among women, the mental health effects of cancer are particularly pronounced, as they often intersect with critical life stages, such as reproductive health, caregiving responsibilities, and societal expectations (Linden et al. 2012; Logan et al. 2019). Research indicates that women diagnosed with cancer frequently experience heightened levels of anxiety, depression, and emotional distress, which can persist throughout their cancer journey and beyond (Kulpa, Owczarek & Stypula-Ciuba 2013; Logan et al. 2019; Sobota & Ozakinci 2014). These psychological challenges are often compounded by the complexity of treatment decisions, concerns about prognosis, changes in body image, and the potential impact on fertility and family dynamics (Miaja, Platas & Martinez-Cannon 2017; Sobota & Ozakinci 2014). Additionally, the stigma surrounding mental health and cancer intensifies feelings of emotional isolation, leaving women without adequate support during an already challenging time (Kulpa, Owczarek & Stypula-Ciuba 2013; Wells & Kelly 2008).

The mental health challenges associated with pregnancy-associated cancer are particularly severe, as women must navigate the dual burden of managing cancer alongside preparing for childbirth or caring for a newborn (Ferrari et al. 2018). Studies reveal that women face heightened risks of anxiety, depression, and post-traumatic stress disorder (PTSD) during their reproductive years (Ghamari et al. 2023; Linden et al. 2012; Tung et al. 2018). These challenges were particularly pronounced for those diagnosed with rare cancers, where limited support intensified emotional distress. Tailored emotional

and mental health support is essential for these women to feel understood and supported throughout their journey (Faccio et al. 2020; Ferrari et al. 2018; Ives, Musiello & Saunders 2016).

The importance of early identification of mental health needs has been emphasised in recent research. Hurren et al. (2023) advocate for better collaboration between oncology and obstetric teams to provide holistic care that prioritises the mental well-being of women (Hurren et al. 2023). This integrated approach ensures that women receive timely and comprehensive mental health support, which is critical in managing the unique challenges posed by pregnancy-associated cancer.

Women often report feeling isolated in general cancer support groups, as their experiences as pregnant or new mothers differ significantly from those of other patients (Hammarberg et al. 2018). Women advocate for expanding peer support programs tailored to their unique needs. Although research has shown that peer networks enhance emotional well-being and mental health (Hoey et al. 2008; Meyer, Coroiu & Korner 2015; Moulton et al. 2013), existing peer support programs often fail to meet the specific needs of women dealing with rare pregnancy-associated cancers. Developing targeted support groups allows women to connect with others facing similar struggles, providing emotional validation and shared understanding.

The emotional toll of pregnancy-associated cancer is significant, ranging from initial shock and anxiety to fear of the unknown. Balancing the need for treatment with concerns for their unborn baby's well-being intensifies these feelings. Approximately one-third of cancer patients experience mental health conditions such as anxiety or depression, and this rate is likely higher for women with pregnancy-associated cancer (Mental Health Foundation 2018). Postpartum depression, anxiety and fear of cancer recurrence (FCR) emerged as significant concerns, affecting the quality of life, parenting, and overall mental health of women diagnosed with pregnancy-associated cancer (Faccio et al. 2020; Ferrari et al. 2018; Kozu, Masujima & Majima 2020).

The mental health of women diagnosed with pregnancy-associated cancer directly impacts maternal and foetal outcomes. Studies link maternal stress, anxiety, and depression to adverse pregnancy outcomes, including preterm birth, low birth weight, and intrauterine growth restriction (Grote et al. 2010; Lewis, Austin & Galbally 2016; Liou, Wang & Cheng 2016). The emotional well-being of the pregnant woman directly influences foetal development. Maternal stress can lead to elevated levels of cortisol, a stress hormone that can affect the developing foetus, potentially leading to neurodevelopmental issues, impaired immune function, or premature delivery (Grote et al. 2010; Liou, Wang & Cheng 2016; Talge, Neal & Glover 2007). Additionally, anxiety and depression during pregnancy are associated with poorer maternal-infant bonding, potentially affecting children's

emotional and long-term social development (Fisher & O'Connor 2012; Fitch, Bunston & Elliot 1999; Kuswanto et al. 2018).

Interestingly, this thesis found that motherhood served as a coping mechanism for many women, offering resilience and hope. Caring for newborns or other children provides a sense of purpose and motivation for survival, contrasting with previous studies that emphasise fears about parenting and concerns for children's well-being after cancer treatments (Faccio et al. 2020; Ferrari et al. 2018; Kozu, Masujima & Majima 2020). This nuanced finding underscores the dual role of motherhood as both a source of emotional strain and a significant source of strength.

These findings contribute to a deeper understanding of the mental health challenges faced by women with pregnancy-associated cancer. They underscore the critical need for comprehensive, personalised mental health support as an integral component of care pathways for women navigating cancer during pregnancy or the postpartum period. Tailored interventions addressing both emotional well-being and practical needs are essential to improving outcomes for both mother and child.

8.2.6 Person-centred care: A holistic approach to pregnancy-associated cancer

Person-centred care is a holistic and innovative approach to healthcare that emphasises understanding patients as unique individuals and empowering them to participate actively in their treatment decisions (Giusti et al. 2020; Loonen et al. 2018). This approach extends beyond addressing physical health to encompass psychological, social, and existential dimensions, ensuring that patient's values, preferences, and needs are respected and integrated into their care plans (Giusti et al. 2020). This approach is particularly significant for women navigating the dual challenges of a cancer diagnosis during pregnancy or postpartum. Person-centred care supports these women's mental health and well-being by fostering trust, enhancing communication, and reducing the emotional burden of their circumstances (Linkeviciute et al. 2024).

The literature consistently underscores the positive impact of person-centred care on the quality of reproductive healthcare by prioritising an individual's unique needs and preferences, which ultimately leads to improved outcomes (Attanasio et al. 2022; Giusti et al. 2020). Effective communication is central to this model of care, as it ensures women are informed, their concerns are acknowledged, and they feel supported throughout their treatment journey (Giusti et al. 2020; Williams et al. 2020). Respectful and empathetic communication fosters shared decision-making, enabling women to regain control over their care (Williams et al. 2020). This is crucial in mitigating feelings of helplessness and

anxiety, which are often exacerbated by the uncertainty of a cancer diagnosis and treatment (Williams et al. 2020).

The association between person-centred care and mental health outcomes is particularly significant (Attanasio et al. 2022). Person-centred care can alleviate distress, promote emotional resilience, and enhance overall well-being by addressing the mental health, psychological and social dimensions of care (Linkeviciute et al. 2024). In the context of pregnancy-associated cancer during pregnancy or postpartum, person-centred care ensures that women's unique needs as both patients and expectant mothers are at the forefront of care. This approach integrates maternal health considerations with the unborn child's well-being, aligning clinical decision-making with the patient's values and priorities.

Advocacy and the role of communication in person-centred care

Advocacy is the cornerstone of person-centred care and is essential in addressing the complex needs of women diagnosed with cancer (Thomas et al. 2021; Thomas et al. 2023). Effective advocacy relies on clear communication between women and HCPs (Hagan et al. 2017). However, findings from this thesis highlight significant communication gaps, compounded by insufficient support systems, leaving many women feeling excluded from decision-making and struggling to advocate for their own needs.

For person-centred care to be effective, women must feel heard and understood, and healthcare providers need to deliver precise and accessible information (Giusti et al. 2020; Loonen et al. 2018). Self-advocacy, where women voice their needs and preferences, similarly depends on open and responsive communication channels (Hagan et al. 2017; Thomas et al. 2021). Women in this study emphasised the potential benefits of dedicated advocates, such as nurses or midwives, who can enhance their understanding of treatment options, improve communication, and foster a more person-centred approach to care. By providing accurate and timely information, advocates reduce feelings of isolation and confusion, helping women navigate the complexities of pregnancy-associated cancer.

Integrating advocates such as nurses or midwives into care teams bridges gaps between oncology and obstetric care, promoting transparent communication and ensuring that women receive comprehensive and coordinated care (Hagan et al. 2017; Thomas et al. 2023). This approach empowers women to make informed decisions aligned with their values, reducing feelings of helplessness and improving their overall well-being (McCormack & McCance 2006; Thomas et al. 2021; Waddell et al. 2021).

The role of multidisciplinary teams in advocacy and person-centred care

Multidisciplinary teams play a pivotal role in managing pregnancy-associated cancer as women face complex and multifaceted challenges that are associated with both cancer treatment and pregnancy or postpartum care (Silverstein et al. 2020). Cancer care is inherently multidisciplinary, typically involving surgical, medical, and radiation oncologists, oncology nurses, psycho-oncologists, and allied health professionals. However, in the context of pregnancy, the integration of obstetric professionals, such as maternal-foetal medicine specialists, obstetricians, midwives, and neonatal teams, is also critical to ensure coordinated care for both the mother and infant (Hunter et al. 2019; Walpole et al. 2019). Evidence suggests combining multidisciplinary care with a person-centred approach improves outcomes in complex healthcare settings (Linkeviciute et al. 2024; Sorouri et al. 2023). However, this thesis identifies ongoing challenges in coordinating multidisciplinary teams. These challenges include fragmented communication, unclear roles across specialties, and inconsistent referrals between teams. As discussed in Chapter 6, these systemic gaps adversely affect women's experiences and delay timely decision-making during critical treatment periods.

To address this, multidisciplinary models should evolve to include not only traditional oncology team members but also obstetric and neonatal care specialists working together (Hunter et al. 2019; Sorouri et al. 2023; Walpole et al. 2019). Embedding obstetric professionals within established oncology care structures rather than developing parallel systems can facilitate timely, collaborative decision-making and reduce fragmentation (Linkeviciute et al. 2024; Sorouri et al. 2023). This model is supported by international guidelines on the care of cancer during pregnancy and aligns with best practices in integrated cancer care models (Linkeviciute et al. 2024; Sorouri et al. 2023; Walpole et al. 2019)

Furthermore, including patient advocates within these teams can address these challenges further by fostering continuous communication, improving care coordination and addressing women's emotional and psychological needs (Abbasinia, Ahmadi & Kazemnejad 2020; Sorouri et al. 2023). Advocates can ensure continuity of care, especially in complex care pathways where patients interact with multiple services. This thesis highlights that such advocacy is not currently standard practice but could significantly enhance the patient experience.

Integrating advocacy, centralised resources, multidisciplinary care, and person-centred care is essential for enhancing the experience of women diagnosed with pregnancy-associated cancer (Abbasinia, Ahmadi & Kazemnejad 2020; Sorouri et al. 2023). Dedicated advocates are vital resources, bridging communication gaps, reducing emotional stress, and facilitating informed decision-making (Abbasinia, Ahmadi & Kazemnejad 2020). This integrated approach places women's needs at the centre of care,

addressing the dual priorities of maternal and foetal health while fostering a sense of empowerment and resilience throughout their cancer journey.

8.3 Implications

The diagnosis of pregnancy-associated cancer assigns a significant burden to affected women, their families, and HCPs. This thesis has highlighted critical gaps in the understanding of the incidence, maternal and neonatal outcomes, and psychosocial impacts of pregnancy-associated cancer. These findings have implications for clinical practice, healthcare systems, HCPs, and future research, underscoring the need for improved guidelines, communication strategies, and holistic care models.

8.3.1 Implications for clinical practice

This thesis revealed that women with pregnancy-associated cancer face significant challenges, including an increased risk of preterm birth due to systemic therapies. These findings highlight the need for individualised treatment plans that balance maternal efficacy with foetal safety. Clinicians should exercise caution, particularly when administering chemotherapy during the first trimester, and prioritise collaborative decision-making with patients.

The findings also indicate significant communication gaps between women and their HCPs. To address this, patient-centred communication should be implemented to ensure that patients receive clear, consistent, and timely information about their diagnosis and treatment options. Patient-centred communication training for HCPs should emphasise active listening and empathetic engagement, empowering women to participate in treatment decisions.

To address patients' physical and mental health needs, mental health assessments and support should be integrated into routine care with multidisciplinary teams involving oncologists, obstetricians, and mental health professionals. This approach aligns with the findings of the study that highlight the emotional toll of pregnancy-associated cancer and the need for tailored mental health support.

8.3.2 Implications for the healthcare system

The rising incidence of pregnancy-associated cancer, particularly PACRC, calls for enhanced cancer screening protocols in prenatal care, especially in high-risk populations. Healthcare systems should invest in training programs for HCPs to recognise early symptoms of PACRC and adopt appropriate screening practices.

The findings from this thesis indicate fragmented communication and care pathways for women with pregnancy-associated cancer. Dedicated patient advocates or navigators integrated into care teams could help bridge these gaps, ensuring seamless coordination between oncology and obstetrics. Establishing specialised units or services focused on pregnancy-associated cancer would also improve outcomes by centralising expertise and resources.

Mental health services should be prioritised as part of routine care, ensuring that mental health support is available from diagnosis through postpartum recovery. Policymakers should consider developing programs tailored to the unique mental health challenges faced by women with pregnancy-associated cancer, as highlighted in this study.

8.3.3 Implications for healthcare professionals

The findings of this thesis highlight the importance of tailoring care to the complex and multidisciplinary nature of pregnancy-associated cancer. Healthcare professionals (HCPs) from both obstetric and oncology disciplines have distinct yet interconnected roles in providing patient-centred care.

Implications for Obstetric Care Providers

Obstetricians, midwives, and maternal-foetal medicine specialists are central to coordinating pregnancy care for women diagnosed with cancer. This thesis highlights the need for:

- Ongoing education and training in the impact of systemic cancer therapies during pregnancy, including the timing of delivery, and about maternal treatment protocols.
- Strengthened skills in shared decision-making, particularly regarding birth interventions, preterm delivery planning, and maternal health monitoring.
- Enhanced awareness of psychosocial risks, including the emotional toll of treatment decisions and potential impacts on bonding, birth experience, and postpartum adjustment.

Implications for Oncology Professionals

Oncologists, cancer nurses, and psycho-oncology teams are key in managing the maternal cancer diagnosis and treatment. Findings suggest a need for:

- Greater integration of pregnancy-specific considerations into oncology care plans, including foetal risks, gestational timelines, and maternal comorbidities.
- Training in perinatal communication, to ensure compassionate and appropriate conversation with patients facing concurrent cancer and pregnancy.

Enhancing Multidisciplinary Collaboration

This thesis underscores the value of a multidisciplinary approach involving both obstetric and oncology professionals, as well as health practitioners. Embedding mental health screening and support pathways within oncology and maternity care services to identify and address emotional distress early. By recognising the unique but overlapping responsibilities of each specialty and fostering stronger collaboration, these implications aim to improve both clinical outcomes and women's experiences of care throughout the perinatal cancer journey.

HCPs play a pivotal role in the care of women with pregnancy-associated cancer. This thesis highlights the need for ongoing professional development to ensure HCPs have up-to-date knowledge of systemic therapy during pregnancy, effective communication strategies, and multidisciplinary care approaches. Training programs should focus on patient-centred care and respect for patient autonomy, ensuring that women are actively involved in treatment decisions.

This study also underscores the importance of recognising and addressing mental health issues in women with pregnancy-associated cancer. HCPs should be trained to identify signs of emotional distress and to refer patients to appropriate mental health support services. Building empathy and communication skills through training programs can help HCPs deliver care with greater sensitivity and understanding.

8.3.4 Implications for research

This thesis highlights critical gaps in the understanding of pregnancy-associated cancer, particularly in areas such as the long-term effects of systemic therapy on children exposed in utero and the impact of mental health on women. Future research should focus on the following aspects.

PACRC risk factors and prevention: Research should investigate the underlying factors contributing to the increasing incidence of PACRC beyond maternal age. Studies exploring genetic, environmental, and pregnancy-related factors may lead to improved screening and prevention strategies.

Long-term outcomes of systemic therapy: Longitudinal studies are needed to examine developmental, cognitive, and psychological effects on children exposed to chemotherapy in utero. These studies would provide valuable insights into late-onset complications and safer treatment protocols.

Communication interventions: This thesis identifies the significant communication challenges faced by women with pregnancy-associated cancer. Future research should develop and evaluate interventions to improve HCP-patient communication, including tools such as decision aids, telemedicine platforms, and training programs for HCPs.

Mental health interventions: Tailored mental health programs for women with pregnancy-associated cancer should be developed and evaluated, focusing on therapies such as cognitive-behavioural therapy, peer support networks, and mindfulness-based approaches. Longitudinal studies can provide insights into the effectiveness of these interventions in mitigating mental health challenges.

8.4 Recommendations

8.4.1 Prenatal screening

A robust prenatal screening protocol is essential to optimise maternal and neonatal outcomes. The following recommendations are proposed:

1. *Targeted screening for high-risk groups:* Implementing enhanced prenatal screening for women with known risk factors, including family history of cancer or symptoms overlapping with common pregnancy-related changes. Given the rising incidence of PACRC, integrating colorectal cancer screening in high-risk populations, especially for women in their reproductive period, could provide early detection benefits.
2. *Safe and tailored imaging:* Advanced imaging techniques such as MRI should be prioritised for high-risk pregnancies because of their safety profile. Developing imaging guidelines during pregnancy can ensure timely diagnosis without compromising foetal safety.

3. *Patient-centred communication*: Clear, empathetic communication about the purpose, risks, and benefits of prenatal screening should be standard practice. All the information resources should be available after diagnosis.

8.4.2 Postnatal follow-up

Effective postnatal care for women diagnosed with pregnancy-associated cancer is essential to ensure long-term health and well-being for both mother and child. The following recommendations are proposed for postnatal screening to optimise outcomes in women diagnosed with pregnancy-associated cancer:

1. *Structured postnatal follow-up*: Develop personalised postnatal care protocols with regular follow-ups during the first two years postpartum, focusing on recurrence monitoring through imaging and biomarker surveillance. Tailor monitoring frequency based on cancer type and treatment history.
2. *Enhancing postnatal mental health support through integrated care*: Postnatal care providers should be supported to identify psychological distress and collaborate with psycho-oncology services to ensure women receive timely and appropriate mental health support following pregnancy-associated cancer. Screening protocols, clear referral pathways, and interprofessional training are recommended to promote continuity of care and reduce service fragmentation.
3. *Lactation counselling and support*: For women who wish to breastfeed, lactation counselling should be provided with special consideration given to the effects of cancer treatment on milk production and safety. Some treatments may necessitate cessation of breastfeeding, while others may be compatible. Counselling should be personalised based on the patient's treatment history and current health status, ensuring that mothers are fully informed about their options.
4. *Long-term child health monitoring*: Regular developmental assessments for children exposed to systemic therapy in utero are vital. These assessments should address neurodevelopmental and cognitive milestones, ensuring early intervention for any identified concerns.

5. *Women's education and empowerment:* Empowering women's knowledge of their condition and the importance of postnatal screening is vital. Healthcare providers should ensure that women are well informed about the need for ongoing monitoring, the signs and symptoms of recurrence, and the importance of adhering to follow-up appointments. Providing written materials and access to resources such as support groups or educational seminars can enhance patient engagement and compliance with postnatal care recommendations.

8.4.3 Health care providers (HCPs)

The findings of this thesis underscore the critical role of both obstetric and oncology healthcare providers in supporting women diagnosed with pregnancy-associated cancer.

For the obstetric care team:

1. *Enhanced training programs:* Provide specialised training to obstetric clinicians to improve their ability to recognise symptoms of pregnancy-associated cancer and manage its unique complexities. Training should include symptom recognition, safe treatment timing, and decision-making strategies.
2. *Communication skills development:* Strengthen obstetric clinicians' ability to deliver empathetic, clear, and patient-centred communication. Workshops and case-based simulations should focus on managing challenging conversations and fostering shared decision-making.
3. *Fertility option:* Obstetric clinicians should actively enquire about and consider women's concerns regarding fertility, including the potential impact of cancer treatment on their ability to have more children. They should stay informed by reviewing relevant research that addresses these issues and provide empathetic guidance when discussing future reproductive options and decisions regarding subsequent pregnancies.

For the oncology team:

1. Oncologists should be trained in treatment decision-making that balances maternal and foetal outcomes. Study results highlighted the emotional burden women felt when treatment decisions were not explained clearly or tailored to their perinatal context.

2. Oncology clinicians should undertake training in psycho-oncology, with a focus on identifying and addressing mental health concerns in perinatal women with cancer. Early recognition of distress and referral to appropriate services should be embedded in standard cancer care protocols.

8.4.4 Healthcare system

A well-coordinated, multidisciplinary approach is essential for improving outcomes for women with pregnancy-associated cancer. This thesis identifies the following priorities:

1. *Integrated multidisciplinary care models:* Strengthen collaboration between oncology and obstetric teams by integrating obstetric professionals such as maternal-foetal medicine specialists, obstetricians, and midwives into existing oncology MDTs. This integration should involve joint treatment planning meetings, clearly defined roles across disciplines, and the use of shared documentation platforms to ensure continuity of care. Embedding obstetric care within the cancer multidisciplinary team will facilitate timely and coordinated decision-making, particularly in areas such as treatment scheduling, delivery planning, and neonatal care.
2. *Development of clinical pathways:* Create evidence-based clinical care pathways that delineate the roles, responsibilities, and communication protocols across oncology, obstetrics, mental health, and neonatal care. These pathways should reflect the complexities of managing concurrent maternal and fetal health needs and be adaptable to local healthcare system structures.
3. *Centralised resource development:* Healthcare systems should develop and provide centralised, accessible resources for women diagnosed with cancer during pregnancy or postpartum. This can include information on treatment options, support services, and decision-making tools.
4. *Integration of mental health services:* Mental health services should be integrated into standard care for women diagnosed with pregnancy-associated cancer. This includes routine mental health assessments and the availability of counselling services throughout cancer treatment and the postpartum period.

8.4.5 Peer support networks

Peer support plays a crucial role in enhancing mental health, well-being and overall outcomes of women diagnosed with pregnancy-associated cancer. Shared experiences and mutual understanding among peers can provide emotional comfort, reduce feelings of isolation, and empower patients to participate in their care actively. The following recommendations are proposed to integrate and optimise peer support as a critical component of care for women with pregnancy-associated cancer.

1. *Specialised peer support programs:* Develop targeted peer support programs connecting women with similar experiences to foster mutual understanding and shared coping strategies. These programs can include pregnancy-specific peer support sessions or virtual communities that connect women across geographical boundaries.
2. *Digital peer support platforms:* To address resource limitations and geographic isolation, digital or online peer support platforms could be piloted in collaboration with cancer support organisations. These platforms may offer moderated forums or group video sessions, reducing the burden on clinical staff while offering accessible emotional support.

8.4.6 Future research

To understand and manage pregnancy-associated cancer, it is essential to prioritise future research to address the current gaps in knowledge and enhance clinical practice.

1. *Longitudinal studies on maternal and child outcomes:* Examine the long-term effects of systemic therapies on children exposed in utero, focusing on developmental and cognitive trajectories.
2. *Effectiveness of Screening Protocols:* Investigate the effectiveness of integrated prenatal and postnatal screening protocols in diverse healthcare settings to refine best practices.
3. *Development of Targeted Therapeutic Strategies:* Future research should prioritise the development of targeted therapeutic strategies that minimise risks to the foetus while effectively treating maternal cancer. This includes investigating the safety and efficacy of new chemotherapeutic agents, immunotherapies, and personalised medical approaches during pregnancy. Research should also explore the optimal timing and dosing of these treatments to balance the maternal and foetal outcomes.

4. *Mental Health Interventions*: Develop and evaluate targeted mental health interventions, such as cognitive-behavioural therapy and mindfulness programs, tailored to the unique needs of women with pregnancy-associated cancer.
5. *Communication strategies*: Research on effective communication interventions to enhance interactions between women and their HCPs, ensuring patient-centred and culturally sensitive care delivery.

8.5 Strengths and limitations

8.5.1 Strengths

A major methodological strength of this thesis is the use of a multi-method research design, which employed both quantitative and qualitative methodologies in distinct but complementary studies. Rather than integrating findings across methodological paradigms, each study addressed a specific research objective aligned with the overarching aim of exploring the maternal, perinatal, and psychosocial implications of pregnancy-associated cancer. This approach allowed for a comprehensive and layered understanding of the phenomenon, capturing both population-level patterns and the lived experiences of affected women.

Large-Scale, population-based data (Study 1)

The strengths of Study 2 lie in its extensive, population-based, linked data approach, which spans two decades (1994-2013) and captures the entire cohort of women giving birth in New South Wales (NSW). The extensive timeframe data provided a robust foundation for analysing trends in pregnancy-associated colorectal cancer (PACRC) incidence and outcomes. This large-scale dataset enhances the generalisability of the findings and allows for a more nuanced understanding of the factors that influence maternal and neonatal outcomes in this population.

Innovative comparative analysis (Study 2)

To the best of my knowledge, Study 2 is the first systematic review to compare perinatal outcomes between women who were exposed to systemic therapy following a cancer diagnosis during pregnancy or postpartum and those who were not exposed. This analysis sheds light on the varying outcomes of treatment exposure and establishes a foundation for future research in this area. The insights gained from this study have the potential to significantly influence clinical practice and provide crucial guidance for decision-making in the management of pregnancy-associated cancer.

Exploration of communication experiences (Study 3)

The strength of Study 3 lies in its exploration of the communication experiences between HCPs and women diagnosed with pregnancy-associated cancer. By including a diverse range of participants in terms of age, cancer diagnosis, and the timing of diagnosis, this study sheds light on the specific communication challenges faced by this unique group of patients. This study provides a critical foundation for understanding the nuanced demands and needs of women navigating cancer diagnosis and treatment during pregnancy. This area has yet to be explored in the existing literature. The data generated are novel and valuable, offering new insights into the complexities of patient-provider communication in this context.

Identification of gaps in mental health support (Study 4)

Study 4 identified a significant gap in mental health support for women with pregnancy-associated cancer, an area that has received limited attention in previous studies. These findings underscore the critical need for targeted interventions to improve the mental health and well-being of these patients. This study highlights the importance of integrating specialised psycho-oncological care into clinical practice, contributing to the ongoing discourse on comprehensive cancer care.

Unique opportunity for participant reflection

A distinctive strength of this research is the opportunity it provided for most of the women with pregnancy-associated cancer interviewed in this study to debrief and reflect on their experiences. For many participants, narrating their stories without constraints allowed them to articulate their distress, recovery, and goals for the future, both for themselves and for future generations of women. This reflective process enriched the data collected and contributed to the participants' psychological processing and healing.

Professional experience

A final strength is my decades of experience as a health professional. This background provided me with a profound understanding of women's challenges, the perspectives of healthcare providers, and the complexities of health systems. While this expertise has enriched my comprehension of the issues, I have remained careful to align with specific healthcare professionals, specialties, disciplines, and health services relevant to this research, ensuring an unbiased and objective approach.

8.5.2 Limitations

Study 1

While Study 1 benefited from being a population-based study spanning 20 years (1994-2013), it was limited by a lack of detailed information on the treatment of pregnancy-associated colorectal cancer (PACRC). As a result, this study could not provide a more comprehensive analysis of the impact of specific treatments on maternal and neonatal outcomes. Additionally, the dataset did not include information on early pregnancy loss, which limits the ability to capture the incidence of PACRC fully and may lead to underestimation of the number of cases.

Study 2

The key methodological limitation of this study is that most of the included studies and the exposure of the systematic therapies examined occurred before 2013. Additionally, most of the drugs investigated were cytotoxic agents, and no studies have reported specific neonatal outcomes following exposure to newer targeted therapies or non-cytotoxic medications during pregnancy. As a result, newer targeted therapies and non-cytotoxic treatments that are increasingly used in contemporary oncology practice were not represented. This limits the generalisability of the findings to current treatment contexts, particularly for clinicians seeking guidance on neonatal outcomes following exposure to modern cancer therapies during pregnancy.

Another methodological limitation were the small sample sizes in most of the included studies and the lack of long-term follow-up data for infants and children exposed to systemic therapy during gestation. Furthermore, the included studies may have been subject to biases, such as reporting or selection bias, mainly because some data were collected via questionnaires. In contrast, other data were derived from cancer and pregnancy registries.

Study 3 & 4

The limitations of Studies 3 and 4 are primarily related to the lack of diversity within the sample. All participating women were English speakers; therefore, we did not capture their experiences from diverse ethnic and cultural backgrounds. A more diverse sample could have uncovered additional themes and insights, thus enriching the study's findings. The generalisability of the findings is also limited by the relatively small sample size and inherent variability in patient information needs, which are influenced by their unique circumstances and personal experiences. Additionally, interviews were conducted and analysed by a single researcher, which may influence interpretation despite efforts to enhance rigour through reflexive journaling, supervision, and peer debriefing. Double coding was not

conducted due to practical constraints, which may limit the reliability of thematic interpretation. Nevertheless, themes were cross-checked with supervisors and iteratively reviewed to strengthen credibility. A methodological limitation is the potential for recall bias, particularly for participants reflecting on experiences many years ago. Additionally, the study did not explore the experiences and needs of partners, which could have provided a more comprehensive understanding of family dynamics and support systems for managing pregnancy-associated cancer.

One limitation and methodological consideration in this thesis was the expansion of the inclusion criteria for Studies 3 and 4 to include women diagnosed with cancer in the postpartum period. While this was initially unplanned, the decision was made in response to slow recruitment and the ethical imperative to include women with relevant and valuable experiences. The protocol amendment (Appendix 7) was approved, and data from women diagnosed postpartum were analysed alongside those diagnosed during pregnancy.

Despite these methodological limitations, the study offers valuable insights into the importance of effective communication between women, healthcare providers, and cancer care nurses or midwives. This research highlights the mental health experiences of women with pregnancy-associated cancer, underscoring the need for more comprehensive and personalised mental health services. These findings contribute to a deeper understanding of the unique challenges faced by this population and critical areas for improvement in their care.

8.6 Chapter summary

Chapter 8 presents a thorough discussion of the essential findings and offers a comprehensive approach to managing pregnancy-associated cancer, focusing on developing tailored treatment plans that enhance the outcomes for both mothers and their babies. This chapter highlighted the critical role of effective communication and mental health support in the care of women with pregnancy-associated cancer. It also outlines the implications and recommendations for the healthcare system, research, and healthcare professionals while clearly defining the strengths and limitations of the study. The next chapter provides the concluding statements for this thesis.

Chapter 9: Conclusion

This thesis presents a comprehensive analysis of pregnancy-associated cancer, shedding light on the challenges and critical needs in managing and caring for affected women and their unborn children. The increasing incidence of pregnancy-associated cancer, particularly PACRC, highlights the complexities in oncologic and obstetric management. While congenital anomalies and perinatal deaths were not observed among babies born to women with PACRC, higher rates of birth interventions and maternal and neonatal morbidities underscore the urgent need for evidence-based guidelines. Developing these protocols requires multidisciplinary collaboration and further research, particularly to address gaps in treatment data for women with PACRC.

Although chemotherapy is generally well-tolerated after the first trimester, the systematic review identifies an associated increase in preterm birth rates. However, the limited number of studies comparing outcomes between exposed and non-exposed infants undermines the strength and validity of this association. Additionally, the effects of newer cancer therapies, including non-cytotoxic chemotherapy and immunotherapy during pregnancy, remain largely unexplored, highlighting the need for further investigation.

This thesis also explores the communication experiences of women with pregnancy-associated cancer, uncovering consistent challenges across both pregnant and postpartum populations. These findings emphasise the critical need for effective communication, targeted education, and robust support systems for healthcare providers. Developing tailored resources and advocacy initiatives, mainly through coordinated multidisciplinary care and the involvement of dedicated nurses or midwives, is essential for improving healthcare experiences and outcomes.

Moreover, this research enhances our understanding of the profound impact of pregnancy-associated cancer on women's mental health and well-being. While initial mental health support is available through organisations in Australia, there is an urgent need for more comprehensive and personalised services throughout the cancer journey. Addressing these unique challenges can significantly improve the mental health and overall well-being of women and their families, leading to better long-term outcomes.

In conclusion, this thesis underscores the importance of addressing both clinical and psychosocial aspects of pregnancy-associated cancer. By advancing multidisciplinary care, enhancing communication and education, and prioritising mental health support, healthcare providers can better meet these women's and their families' needs, ultimately improving maternal and neonatal outcomes.

Appendices

Appendix 1 Search strategy for literature review

Search Focus	Search Terms	Purpose
Pregnancy-associated cancer and population	("pregnancy-associated cancer" OR "gestational cancer") AND ("pregnancy" OR "postpartum") AND ("incidence" OR "prevalence" OR "epidemiology")	To retrieve articles focusing on the occurrence and frequency of pregnancy-associated cancer during pregnancy or the postpartum period.
Pregnancy-associated cancer, health services and women's experiences	("pregnancy-associated cancer" OR "gestational cancer") AND ("healthcare providers OR "health services") AND ("women's experience" OR "patient experience"), AND ("communication" OR "mental health" OR "well-being")	To identify articles exploring how healthcare providers interact with women diagnosed with pregnancy-associated cancer, with a focus on communication, mental health, and overall well-being.
Pregnancy-associated cancer, Interventions, and maternal outcomes	("pregnancy-associated cancer" OR "gestational cancer") AND ("caesarean section" OR "labour complications" OR "obstetric complications") AND ("maternal outcomes" OR "perinatal mortality" OR "stillbirth" OR "neonatal death")	To identify articles examining the relationship between pregnancy-associated cancer and pregnancy outcomes with a specific emphasis on labour and delivery complications such as caesarean sections, obstetric complications, and adverse maternal and neonatal outcomes.
Pregnancy-associated cancer and neonatal outcomes	("pregnancy-associated cancer" OR "gestational cancer") AND ("neonatal outcomes" OR "premature birth" OR "low birth weight" OR "small for gestational age") AND ("neonatal intensive care unit" OR "Apgar score" OR "congenital abnormalities")	To identify articles focusing on neonatal outcomes related to pregnancy-associated cancer, such as premature birth, low birth weight, the need for neonatal intensive care, or the presence of congenital abnormalities.
Broad search across multiple topics	("pregnancy-associated cancer" OR "gestational cancer") AND ("incidence" OR "obstetric complications" OR "mental health") AND ("communication" OR "pregnancy outcomes" OR "infant mortality")	To capture a broad range of articles that address various aspects of pregnancy-associated cancer, including its incidence, obstetric complications, women's communication, mental health experiences, and both maternal and neonatal outcomes.

Appendix 2 Supplementary table Details of the NHW health linked data

Linked data source	Data availability	Data records
PDC (Perinatal Data collection)	Data is available from 1990	Its a population-based surveillance system covering all births, including stillbirths (at least 20 weeks of gestation or 400 grams birth weight, either in hospitals or labour at home in NSW. It was used as a primary data set for both mothers and babies (1994-2013).Physicians or midwife collected data and recorded the medical and obstetric information on the mother, labour and delivery details and neonatal information.
NSWCR (the NSW Cancer Registry)	Data is availbe for invasive primary cancer cases (1972-2018)	NSWCR is a population based cancer registry that includes data regarding demographic, diagnosis, staging, histological grading and spreading of cancer and death information as well of all people in NSW. Data that related to the degree of spread of cancer was obtained from the NSWCR and generally spreading of cancer used for categorised colorectal cancer; 1= localised to tissue of origin, 2= regional spread to the adjacent organs, 3= regional spread to lymph nodes, 4= distant metastasis, 6= carcinoma in situ and 9=unknown. In our data set we did not include carcinoma in situ stage.
APDC (NSW Admitted Patient Data Collection)	Data is available from July 2001 onwards.	APDC records the information regarding discharges, transfers and deaths of patients from all hospitals, including other multipurpose services and day procedure centres in NSW
RoCC (the Register of congenital conditions)	Data is available from 2009	RoCC is a population based surveillance system to monitor congenital conditions detected during pregnancy or birth.
PDR (Perinatal Death Review)	Data is available from 2001 to 1016	This database annually includes perinatal death (stillbirth or neonatal death) in NSW.
RBDM (Register of Births, Deaths and Marriages)	Data is available from 1995	RBDM is a permanent record of all registered birth in NSW, including stillbirths. It includes the details of the biological mother , father/other parent and the childs name. we obtained RBDM by CheReL to facilitate high quality linkage to PDC.
COD URF (Cause of Death Unit Record File)	Data is availbe from 2007	The COD URF contain death information registered in coded form by ABS (Australian Bureau of Statistics) in NSW. Due to the coding process, this data is always available after the RBDM death registration data.
CHeReL (The NSW Centre for Health Record Linkage)	The CHeReL was established in 2006	system linked all these data sources and converts consistently collected data into a potent research resource and evaluation. The linkage process for the data sources are available on CheReL website.

Appendix 3 Components of MMOI and NAOI

The MMOI included the following maternal morbidities (acute abdomen, acute renal failure, acute psychosis, cardiac arrest/failure/infarction, cerebral oedema or coma, disseminated intravascular coagulopathy (DIC), cerebrovascular accident, major complications of anaesthesia, obstetric embolism, shock, sickle cell anaemia with crisis, status asthmaticus, status epilepticus, uterine rupture), and the following procedures (assisted ventilation, curettage in combination with general anaesthetic, dialysis, evacuation of haematoma, hysterectomy, procedures to reduce blood flow to the uterus, reclosure of disrupted CS wound, repair of bladder or cystostomy, repair of intestine, repair ruptured or inverted uterus, transfusion of blood or coagulation factors) (Roberts et al. 2008).

The NAOI included the following diagnoses (respiratory distress syndrome, seizure, intraventricular haemorrhage, cerebral infarction, periventricular leukomalacia, birth trauma, hypoxic-ischaemic encephalopathy, necrotising enterocolitis, bronchopulmonary dysplasia, sepsis/septicaemia, pneumonia, other respiratory: primary atelectasis, respiratory failure) and the following procedures (resuscitation, ventilatory support (mechanical ventilation and/or CPAP), central venous or arterial catheter, transfusion of blood or blood products, pneumothorax requiring an intercostal catheter, any body cavity surgical procedure, any intravenous fluids) (Lain et al. 2012).

Appendix 4

Search strategy (MEDLINE 2001-current)

- #1. Exp Pregnancy/ (1,003,967)
- #2. Exp Pregnancy Outcome/ (85,533)
- #3. Gestational.ti, ab. (137073)
- #4. Prenatal.ti, ab. (108,593)
- #5. Antenatal.ti, ab. (43,332)
- #6. In-Utero.ti, ab. (30,886)
- #7. Inutero.ti, ab. (20)
- #8. Exp Immunotherapy/ (332,003)
- #9. Exp Antineoplastic agents/ (1,243,314)
- #10. Targeted therapy. ti, ab. (32,058)
- #11. Hormonal therapy.ti,ab. (10,327)
- #12. Systemic therapy. ti, ab. (16,512)
- #13. Chemotherapy.ti, ab. (428,622)
- #14. 1 or 2 or 3 or 4 or 5 or 6 or 7 (1,097,819)
- #15. 8 or 9 or 10 or 11 or 12 or 13 (1,809,056)
- #16. 14 and 15 (38,106)
- #17. Congenital, Hereditary, and Neonatal Diseases and Abnormalities/ (891)
- #18. Abnormalities, Drug-Induced/ (14,738)
- #19. Abnormalities, Radiation-Induced/ (862)
- #20. Neonatal outcome*. ti, ab. (13,265)
- #21. Perinatal Outcome*. ti, ab. (10,950)
- #22. 17 or 18 or 19 or 20 or 21 (39,140)
- #23. 16 and 22 (2,024)
- #24. limit to 2001 to 2022 (650)

Search strategy (EMBASE 2001-current)

- #1. exp pregnancy/ (1003,967)
- #2. exp pregnancy outcome/ (85,533)
- #3. Gestational.ti, ab. (137,073)
- #4. Prenatal.ti, ab. (108,593)
- #5. Antenatal.ti, ab. (43332)
- #6. In-Utero.ti, ab. (30,886)
- #7. Inutero.ti, ab. (20)
- #8. exp immunotherapy/ (332,003)
- #9. exp antineoplastic agent/ (1243,314)
- #10. Targeted therapy.ti,ab. (32,058)
- #11. Hormonal therapy.ti,ab. (10,327)
- #12. Systemic therapy.ti,ab. (16,512)
- #13 chemotherapy.ti,ab. (428,622)
- #14. drug induced malformation/ (0)
- #15. radiation induced malformation/ (0)
- #16. congenital malformation/ (2,987)
- #17. neonatal outcome*. ti,ab. (13,265)
- #18. Perinatal outcome*. ti,ab. (10,950)
- #19. 1 or 2 or 3 or 4 or 5 or 6 or 7 (1097,819)
- #20. 8 or 9 or 10 or 11 or 12 or 13 (1809,056)

#21. 14 or 15 or 16 or 17 or 18 (25,817)
 #22. 19 and 20 and 21 (302)
 #23. limit 2001 to current (272)
 Search strategy (COCHRANE 2000-current)
 #1 MeSH descriptor: [Pregnancy] explode all trees (31,117)
 #2 MeSH descriptor: [Pregnancy Outcome] explode all trees (5,118)
 #3 (gestational):ti,ab,kw (22,423)
 #4 (prenatal):ti,ab,kw (8,358)
 #5 (antenatal):ti,ab,kw (5,581)
 #6 (in-utero):ti,ab,kw (802)
 #7 (inutero):ti,ab,kw (123)
 #8 Mesh descriptor: [Immunotherapy] explode all trees (11,696)
 #9 MeSH descriptor: [Antineoplastic Agents] explode all trees (16,553)
 #10 (targeted therapy):ti,ab,kw (14,382)
 #11 (hormonal therapy):ti,ab,kw (10,567)
 #12 (systemic therapy):ti,ab,kw (33,627)
 #13 (chemotherapy):ti,ab,kw (89,865)
 #14 (prenatal outcome):ti,ab,kw (3,817)
 #15 (neonatal outcome):ti,ab,kw (11,634)
 #16 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 (51,938)
 #17 #8 OR #9 OR #10 OR #11 OR #12 OR #13 (152,311)
 #18 #14 OR #15 (14,460)
 #19 #16 AND #17 AND #18 (53)

Search strategy (CINAHL 2000-current)

#1 (MH pregnancy+) (226,305)
 #2 (MH "Pregnancy Outcomes") (28,118)
 #3 TI gestational OR AB gestational (45,904)
 #4 TI prenatal OR AB prenatal (32,418)
 #5 TI antenatal OR AB antenatal (18,145)
 #6 TI in-utero OR AB in-utero (5190)
 #7 TI inutero OR AB inutero (10)
 #8 (MH "Immunotherapy+") (54,736)
 #9 (MH "Antineoplastic Agents+") (137,573)
 #10 TI targeted therapy OR AB targeted therapy (15,375)
 #11 TI hormonal therapy OR AB hormonal therapy (2,851)
 #12 TI systemic therapy OR AB systemic therapy (9,973)
 #13 TI chemotherapy OR AB chemotherapy (83,231)
 #14 (MH "Congenital, Hereditary, and Neonatal Diseases and Abnormalities") (151)
 #15 (MH "Abnormalities, Drug-Induced") (1,128)
 #16 (MH "Abnormalities, Radiation-Induced") (74)
 #17 TI neonatal outcome OR AB neonatal outcome (9,599)
 #18 TI perinatal outcome OR AB perinatal outcome (6,751)
 #19 1 or 2 or 3 or 4 or 5 or 6 or 7 (264,050)
 #20 8 OR 9 OR 10 OR 11 OR 12 OR 13 (250,168)
 #21 14 or 15 or 16 or 17 or 18 (16,620)
 #22 19 AND 20 AND 21 (147)
 #23 Limit 2001- current (131)

Search strategy (GOOGLE SCHOLAR 2000-current)

Cancer AND Pregnancy AND ("antenatal outcome" OR "perinatal outcome" OR "neonatal outcome" OR) AND systemic therapy

Appendix 5

The following data were extracted:

Publication details: title, authors, journal, city, year of publication, country of publication, type of publication, and funding source.

Methods: study design, aim of the study, data collection methods, recruitment and sampling methods, sample size, and eligibility (inclusion and exclusion criteria).

Study participant details: age, cancer type, stages, and trimester at cancer diagnosis.

Details of systemic treatment: type, duration, number of cycles, dose reduction/delay, and overall timing of

systemic therapy administration for women diagnosed with cancer (e.g., cytotoxic or non-cytotoxic drugs in

all trimesters, methotrexate, and imatinib in first trimesters).

Outcome data: Data on perinatal outcomes included spontaneous abortion, pregnancy termination, intrauterine growth restrictions (IUGR), stillbirth (a baby is born without signs of life after the 20th week of

pregnancy), Intrauterine foetal death (a baby dies in the mother's womb before birth), neonatal mortality,

preterm birth (<37 weeks), birth weight, respiratory support at birth, Apgar score at five minutes, small for

gestational age (SGA), low birth weight, congenital anomalies or congenital disability, and admission to

neonatal intensive care (NICU) were extracted. Data relating to infant death before one year and long-term

infant and child outcomes (cognitive skill and academic achievement) following systemic therapy were also

collected.

Limitations: Information regarding selection bias, response bias, information bias, and any limitations reported by study authors was collected.

Appendix 6 Excluded studies

Article 1

Abdel-Hady, E.S., Hemida, R.A.H., Gamal, A., El-Zafarany, M., Toson, E. & El-Bayoumi, M.A. 2012, 'Cancer during pregnancy: Perinatal outcome after in utero exposure to chemotherapy', *Archives of Gynecology and Obstetrics*, vol. 286, no. 2, pp. 283-6.

Article 2

Amant, F., Vandenbroucke, T., Verheecke, M., Fumagalli, M., Halaska, M.J., Boere, I., Han, S., Gziri, M.M., Peccatori, F., Rob, L., Lok, C., Witteveen, P., Voigt, J.-U., Naulaers, G., Vallaey, L., Van Den Heuvel, F., Lagae, L., Mertens, L., Claes, L. & Van Calsteren, K. 2015, 'Pediatric Outcome after Maternal Cancer Diagnosed during Pregnancy', *The New England journal of medicine*, vol. 373, no. 19, pp. 1824-34.

Article 3

Anderka, M.T., Lin, A.E., Abuelo, D.N., Mitchell, A.A. & Rasmussen, S.A. 2008, 'Reviewing the evidence for mycophenolate mofetil as a new teratogen: case report and review of the literature', *American Journal of Medical Genetics. Part A*, vol. 149A, no. 6, pp. 1241-8.

Article 4

Berger, J.C. & Clericuzio, C.L., 'Pierre Robin sequence associated with first trimester fetal tamoxifen exposure', *American Journal of Medical Genetics. Part A*, vol. 146A, no. 16, pp. 2141-4.

Article 5

Bozkurt, M., Antonoff, M., Jaramillo, S., Sagebiel, T. & Murphy, M.B. 2019, 'Gastroesophageal Cancer During Pregnancy: a Case Report and Review of the Literature', *journal of gastrointestinal cancer*, vol. 50, no. 3, pp. 634-40.

Article 6

Cardonick, E., Bhat, A., Gilmandyar, D. & Somer, R. 2012, 'Maternal and fetal outcomes of taxane chemotherapy in breast and ovarian cancer during pregnancy: Case series and review of the literature', *Annals of Oncology*, vol. 23, no. 12, pp. 3016-23.

Article 7

Cardonick, E., Gilmandyar, D. & Somer, R.A. 2012, 'Maternal and neonatal outcomes of dose-dense chemotherapy for breast cancer in pregnancy', *Obstetrics and Gynecology*, vol. 120, no. 6, pp. 1267-72.

Article 8

Chakravarty, E.F., Murray, E.R., Kelman, A. & Farmer, P. 2011, 'Pregnancy outcomes after maternal exposure to rituximab', *Blood, The Journal of the American Society of Hematology*, vol. 117, no. 5, pp. 1499-506.

Article 9

Cheon, J., Ahn, J.W., Park, K.M., Lee, G. & Jo, Y.S. 2016, 'Teratogenic effect of radotinib: Case report', *Anticancer Research*, vol. 36, no. 12, pp. 6599-601.

Article 10

Choi, J.G., Baek, S.W., Jang, T.S. & Cho, D.Y. 2018, 'Adjuvant chemotherapy and radiation therapy in the first trimester of a pregnant woman with breast cancer: A case report'.

Article 11

Danet, C., Araujo, M., Bos-Thompson, M.A., Portolan, G., Gautier, S., Vanlemmens, L., Bonenfant, S., Jonville-Bera, A.P., Cottin, J., Vial, T., Bavoux, F., Montastruc, J.L., Damase-Michel, C., Benevent, J., Bourgeois-Mondon, I. & Lacroix, I., 'Pregnancy outcomes in women exposed to cancer chemotherapy', *Pharmacoepidemiology & Drug Safety*, vol. 27, no. 12, pp. 1302-8.

Article 12

Dawson, A.L., Riehle-Colarusso, T., Reefhuis, J. & Arena, J.F. 2014, 'Maternal exposure to methotrexate and birth defects: A population-based study', *Birth Defects Research Part A - Clinical and Molecular Teratology*, vol. 100 (5), p. 423.

Article 13

de Haan, J., Verheecke, M., Van Calsteren, K., Van Calster, B., Shmakov, R.G., Mhallem Gziri, M., Halaska, M.J., Fruscio, R., Lok, C.A.R., Boere, I.A., Zola, P., Ottevanger, P.B., de Groot, C.J.M., Peccatori, F.A., Dahl Steffensen, K., Cardonick, E.H., Polushkina, E., Rob, L., Ceppi, L. & Sukhikh, G.T. 2018, 'Oncological management and obstetric and neonatal outcomes for women diagnosed with cancer during pregnancy: a 20-year international cohort study of 1170 patients', *Lancet Oncology*, vol. 19, no. 3, pp. 337-46.

Article 14

Dobashi, M., Isonishi, S., Morikawa, A., Takahashi, K., Ueda, K., Umezawa, S., Kobayashi, Y., Iwashita, M., Takechi, K. & Tanaka, T. 2012, 'Ovarian cancer complicated by pregnancy: Analysis of 10 cases', *Oncology Letters*, vol. 3, no. 3, pp. 577-80.

Article 15

Donoway, T., Mandeville, J. & Gauer, R. 2012, 'When a foetus survives methotrexate exposure', *Journal of Family Practice*, vol. 61, no. 3, pp. E1-E4.

Article 16

Fanale, M.A., Uyei, A.R., Theriault, R.L., Adam, K. & Thompson, R.A. 2005, 'Treatment of metastatic breast cancer with trastuzumab and vinorelbine during pregnancy', *Clinical breast cancer*, vol. 6, no. 4, pp. 354-6.

Article 17

Farhadfar, N., Cerquozzi, S., Hessenauer, M.R., Litzow, M.R., Hogan, W.J., Letendre, L., Patnaik, M.M., Tefferi, A. & Gangat, N. 2017, 'Acute leukemia in pregnancy: a single institution experience with 23 patients', *Leukemia and Lymphoma*, vol. 58, no. 5, pp. 1052-60.

Article 18

Fischer, D., Ahr, A., Schaefer, B., Veldman, A. & Schloesser, R., 'Outcome of preterm and term neonates of mothers with malignant diseases diagnosed during pregnancy', *Journal of Maternal-Fetal & Neonatal Medicine*, vol. 19, no. 2, pp. 101-3.

Article 19

Gadducci, A., Cosio, S., Fanucchi, A., Nardini, V., Roncella, M., Conte, P.F. & Genazzani, A.R. 2003, 'Chemotherapy with Epirubicin and Paclitaxel for Breast Cancer during Pregnancy: Case Report and Review of the Literature', *Anticancer Research*, vol. 23, no. 6 D, pp. 5225-9.

Article 20

Garofalo, S., Degennaro, V.A., Salvi, S., De Carolis, M.P., Capelli, G., Ferrazzani, S., De Carolis, S. & Lanzone, A. 2017, 'Perinatal outcome in pregnant women with cancer: are there any effects of chemotherapy?', *European Journal of Cancer Care*, vol. 26, no. 6.

Article 21

Germann, N., Goffinet, F. & Goldwasser, F. 2004, 'Anthracyclines during pregnancy: embryo–fetal outcome in 160 patients', *Annals of oncology*, vol. 15, no. 1, pp. 146-50.

Article 22

Ghaemmaghani, F., Abbasi, F. & Abadi, A.G.N. 2009, 'A favorable maternal and neonatal outcome following chemotherapy with etoposide, bleomycin, and cisplatin for management of grade 3 immature teratoma of the ovary', *Journal of Gynecologic Oncology*, vol. 20, no. 4, pp. 257-9.

Article 23

Goodyer, M.J., Ismail, J.R., O'reilly, S.P., Moylan, E.J., Ryan, C.A.M., Hughes, P.A. & O'Connor, A. 2009, 'Safety of trastuzumab (Herceptin®) during pregnancy: two case reports', *Cases journal*, vol. 2, no. 1, p. 9329.

Article 24

Granzow, J.W., Thaller, S.R. & Panthaki, Z. 2003, 'Cleft palate and toe malformations in a child with fetal methotrexate exposure', *The Journal of craniofacial surgery*, vol. 14, no. 5, pp. 747-8.

Article 25

Greenlund, L.J.S., Letendre, L. & Tefferi, A. 2001, 'Acute leukemia during pregnancy: A single institutional

experience with 17 cases', *Leukemia and Lymphoma*, vol. 41, no. 5-6, pp. 571-7

Article 26

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Article 27

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Article 28

Hermel, D.J., Chiu, V., Hermel, M.H., Tulpule, A. & Akhtari, M., 'Cardiac birth defects in a twin infant born to a woman with chronic myeloid leukemia on dasatinib', *Journal of Oncology Pharmacy Practice*, vol. 25, no. 3, pp. 699-702.

Article 29

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Article 30

Isaacs, R., Hunter, W. & Clark, K. 2001, 'Tamoxifen as systemic treatment of advanced breast cancer during pregnancy—case report and literature review', *Gynecologic oncology*, vol. 80, no. 3, pp. 405-8.

Article 31

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Article 32

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Article 33

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Article 34

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Article 35

Lasica, M., Willcox, A., Burbury, K., Ross, D.M., Branford, S., Butler, J., Filshie, R., Januszewicz, H., Joske, D., Mills, A., Simpson, D., Tam, C., Taylor, K., Watson, A.M., Wolf, M. & Grigg, A. 2019, 'The effect of tyrosine kinase inhibitor interruption and interferon use on pregnancy outcomes and long-term disease control in chronic myeloid leukemia', *Leukemia and Lymphoma*, vol. 60, no. 7, pp. 1796

Article 36

Lataifeh, I.M., Masri, M.A., Barahmeh, S., Otay, L., Obeidat, N., Badran, O., Darwazeh, G. & Jaradat, I. 2011, 'Management of cancer during pregnancy obstetric and neonatal outcomes', *International Journal of Gynecological Cancer*, vol. 21, no. 6, pp. 1159-64.

Article 37

Lewden, B., Vial, T., Elefant, E., Nelva, A., Carlier, P. & Descotes, J. 2004, 'Low dose methotrexate in the first trimester of pregnancy: Results of a French collaborative study', *Journal of Rheumatology*, vol. 31, no. 12, pp. 2360-5.

Article 38

Li, J., Wang, L.j., Zhang, B.z., Peng, Y.p. & Lin, Z.q. 2011, 'Neoadjuvant chemotherapy with paclitaxel plus platinum for invasive cervical cancer in pregnancy: two case report and literature review', *Archives of Gynecology and Obstetrics*, pp. 1-5.

Article 39

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Article 40

Marnitz, S., Köhler, C., Oppelt, P., Schmittl, A., Favero, G., Hasenbein, K., Schneider, A. & Markman, M. 2010, 'Cisplatin application in pregnancy: first in vivo analysis of 7 patients', *Oncology*, vol. 79, no. 1-2, pp. 72-7.

Article 41

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Article 42

Mohamed, K.E.H. & Mirghani, S. 2017, 'Breast cancer case using tamoxifen during pregnancy: a case report and literature review', *Sudan Journal of Medical Sciences*, vol. 12, no. 2, pp. 114-8.

Article 43

Morris, P.G., King, F. & Kennedy, M.J., 'Cytotoxic chemotherapy for pregnancy-associated breast cancer: single institution case series', *Journal of Oncology Pharmacy Practice*, vol. 15, no. 4, pp. 241-7.

Article 44

Mukhopadhyay, A., Dasgupta, S., Kanti Ray, U., Gharami, F., Bose, C.K. & Mukhopadhyay, S. 2014, 'Pregnancy outcome in chronic myeloid leukemia patients on imatinib therapy', *Irish Journal of Medical Science*, pp. 1-6.

Article 45

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Article 46

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Article 47

Piggott, K.D., Sorbello, A., Riddle, E. & DeCampli, W. 2011, 'Congenital cardiac defects: A possible association of aminopterin syndrome and in utero methotrexate exposure?', *Pediatric Cardiology*, vol. 32, no. 4, pp. 518-20.

Article 48

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Article 49

Rivas, G., Llinas, N., Bonilla, C., Rubiano, J., Cuello, J. & Arango, N. 2012, 'Use of erlotinib throughout pregnancy: A case-report of a patient with metastatic lung adenocarcinoma', *Lung Cancer*, vol. 77, no. 2, pp. 469-72.

Article 50

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Article 51

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Article 52

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Article 53

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Article 54

Van Calsteren, K., Heyns, L., De Smet, F., Van Eycken, L., Gziri, M.M., Van Gemert, W., Halaska, M., Vergote, I., Ottevanger, N. & Amant, F. 2010, 'Cancer during pregnancy: An analysis of 21 5 patients emphasizing the obstetrical and the Neonatal outcomes', *Journal of Clinical Oncology*, vol. 28, no. 4, pp. 683-9.

Article 55

Vaux, K.K., Kahole, N.C. & Jones, K.L., 'Cyclophosphamide, methotrexate, and cytarabine embryopathy: is apoptosis the common pathway?', *Birth Defects Research*, vol. 67, no. 6, pp. 403-8.

Article 56

Verheecke, M., Halaska, M.J., Lok, C.A., Ottevanger, P.B., Fruscio, R., Dahl-Steffensen, K., Kolawa, W., Gziri, M.M., Han, S.N., Van Calsteren, K., Van den Heuvel, F., De Vleeschouwer, S., Clement, P.M., Menten, J. & Amant, F. 2014, 'Primary brain tumors, meningiomas and brain metastases in pregnancy: Report on 27 cases and review of literature', *European Journal of Cancer*, vol. 50, no. 8, pp. 1462-71.

Article 57

Zhang, Y.P., Duan, J., Zhu, X.W., Li, J. & Shi, Y. 2019, 'Maternal and neonatal outcomes of cancer during pregnancy: A multi-center observational study', *Journal of Cancer*, vol. 10, no. 23, pp. 5727-34

Appendix 7 Ethics approval documents

On 22/3/19, 12:58 pm, "Research.Ethics@uts.edu.au" <Research.Ethics@uts.edu.au> wrote:

Dear applicant

RE: HREC Approval Granted - ETH18-2362

[External Ratification: NSW Population & Health Services Research Ethics Committee, HREC approval AU RED Reference: HREC/17/CIPHS/11 Cancer Institute NSW

Reference: 2017/HRE0301 - 23/11/2017 to 23/11/2022]

The UTS Human Research Ethics Expedited Review Committee has reviewed your application titled, "Cancer and Reproductive Outcomes for Women: a population-based cohort study" and agreed that the application meets the requirements of the NHMRC National Statement on Ethical Conduct In Human Research (2007). I am pleased to inform you that your external ethics approval has been ratified.

Your approval number is UTS HREC REF NO. ETH18-2362.

Approval will be for the period specified above and subject to the provision of annual reports and evidence of continued support from the above-named Committee. Please note that the ethical conduct of research is an on-going process. The National Statement on Ethical Conduct in Research Involving Humans requires us to obtain a report about the progress of the research, and in particular about any changes to the research which may have ethical implications. This report form must be completed at least annually, and at the end of the project (if it takes more than a year). The Ethics Secretariat will contact you when it is time to complete your first report.

I also refer you to the AVCC guidelines relating to the storage of data, which require that data be kept for a minimum of 5 years after publication of research. However, in

NSW, longer retention requirements are required for research on human subjects with potential long-term effects, research with long-term environmental effects, or

research considered of national or international significance, importance, or controversy. If the data from this research project falls into one of these categories, contact University Records for advice on long-term retention. You should consider this your official letter of approval. If you require a hardcopy please contact Research.Ethics@uts.edu.au.

To access this application, please follow the URLs below:

* if accessing within the UTS network: <https://rm.uts.edu.au>

* if accessing outside of UTS network: <https://vpn.uts.edu.au> , and click on " RM6 – Production" after logging in.

We value your feedback on the online ethics process. If you would like to provide feedback please go to: <http://surveys.uts.edu.au/surveys/onlineethics/index.cfm>. If you have any queries about your ethics approval, or require any amendments to your research in the future, please do not hesitate to contact Research.Ethics@uts.edu.au.

Yours sincerely,

Associate Professor Beata Bajorek

Chairperson

UTS Human Research Ethics Committee

C/- Research & Innovation Office

University of Technology, Sydney

On 20/05/20, 8:13 am, "Research.Ethics@uts.edu.au" <Research.Ethics@uts.edu.au> wrote:

Dear Applicant,

Re: ETH19-4526 - "Cancer in pregnancy: mothers' Reflections and healthcare Experiences (CaRE)"

Thank you for your response to the Committee's comments for your project. The Committee agreed that this application now meets the requirements of the National Statement on Ethical Conduct in Human Research (2007) and has been approved on that basis. You are, therefore, authorised to commence activities as outlined in your application.

You are reminded that this letter constitutes ethics approval only. This research project must also be undertaken in accordance with all [UTS policies and guidelines](#) including the Research Management Policy.

Your approval number is UTS HREC REF NO. ETH19-4526.

Approval will be for a period of five (5) years from the date of this correspondence, subject to the submission of annual progress reports.

The following special conditions apply to your approval:

1. The researcher is requested to mention in the Participant Information Sheet (PIS) that participation is voluntary.
2. The researcher is requested to include a data confidentiality section in their verbal script. This can be taken from their PIS.

The following standard conditions apply to your approval:

- Your approval number must be included in all participant material and advertisements. Any advertisements on Staff Connect without an approval number will be removed.
- The Principal Investigator will immediately report anything that might warrant review of ethical approval of the project to the Ethics Secretariat (Research.Ethics@uts.edu.au).
- The Principal Investigator will notify the UTS HREC of any event that requires a modification to the protocol or other project documents and submit any required amendments prior to implementation. Instructions on how to submit an amendment application can be found [here](#).
- The Principal Investigator will promptly report adverse events to the Ethics Secretariat. An adverse event is any event (anticipated or otherwise) that has a negative impact on participants, researchers or the reputation of the University. Adverse events can also include privacy breaches, loss of data and damage to property.
- The Principal Investigator will report to the UTS HREC annually and notify the HREC when the project is completed at all sites. The Principal Investigator will notify the UTS HREC of any plan to extend the project's duration past the approval period listed above through the progress report.
- The Principal Investigator will obtain additional approvals or authorisations as required (e.g. from other ethics committees, collaborating institutions, supporting organisations).
- The Principal Investigator will notify the UTS HREC of his or her inability to continue as Principal Investigator, including the name and contact information for a replacement. This research must comply with the Australian Code for the Responsible Conduct of Research and the National Statement on Ethical Conduct in Human Research. You should consider this your official letter of approval. If you require a hard copy, please contact the ethics secretariat.

If you have any queries about your ethics approval or require any future research amendments, please don't hesitate to contact the Ethics Secretariat and quote the ethics application number (e.g. ETH20-xx) in all correspondence.

Yours sincerely,

Prof Meera Agar and Dr Tim Luckett
Chairperson

UTS Health and Medical Research Ethics Committee
C/- Research Office University of Technology Sydney
E: Research.Ethics@uts.edu.au

On 2/2/21, 8:59 am, "Research.Ethics@uts.edu.au" <Research.Ethics@uts.edu.au> wrote in response to amendments:

Dear Applicant,

Re: ETH20-5565 - "Cancer in pregnancy: mothers' Reflections and healthcare Experiences (CaRE)"

The UTS Human Research Ethics Executive Review Committee reviewed your amendment application for your project and agreed that the amendments meet the requirements of the NHMRC National Statement on Ethical Conduct in Human Research (2007). I am pleased to inform you that the Committee has approved your request to amend the protocol as follows:

"Recruitment The original project recruited women who were diagnosed with cancer during pregnancy. During this process, we have had a few women contact us who had been diagnosed with cancer after pregnancy, usually in the post-partum period. They were keen to be involved, and we would like to include them in our study. Methods Regarding methodological changes, we'd also like to advertise that women are welcome to write their stories down and send them to us. We would still consent women in the same way and would send them the interview guide to use as a guide. Participant material Participant materials will be changed to reflect these changes."

This amendment is subject to the standard conditions outlined in your original approval letter. You are reminded that this letter constitutes ethics approval only. This research project must also be undertaken in accordance with all [UTS policies and guidelines](#) including the Research Management Policy. You should consider this your official letter of approval. If you require a hard copy, please contact the Ethics Secretariat.

To access this application, please [click here](#), a copy of your application has also been attached to this email. If you wish to make any further changes to your research, please contact the Research Ethics Secretariat on 02 9514 2478. In the meantime, I take this opportunity to wish you well with the remainder of your research.

Yours sincerely,

The Research Ethics Secretariat, on behalf of the Human Research Ethics Executive Review Committees

C/- Research Office

University of Technology Sydney
Research.Ethics@uts.edu.au | [Website](#)
PO Box 123 Broadway NSW 2007

Ref: E41

Appendix 8

Advertisement for social media



Cancer in pregnancy or after giving birth: mother's Reflections and healthcare Experiences (CaRE)



Were you diagnosed with cancer during pregnancy or up to 6 months after giving birth? Would you like to tell your story and be part of our study?

Have you been diagnosed with cancer during pregnancy or up to six months after giving birth? If so, we would love to speak with you about that experience.

We are conducting a research project because there is very little information available about women with cancer during or just after pregnancy. It is essential to know about women's experiences to understand better the needs of pregnant women and new mothers with cancer.

The study is being conducted by the University of Technology Sydney (UTS) as part of a more extensive study funded by The Cancer Council NSW. If you'd like to take part in this research project, it will involve participating in a phone or Zoom conversation with an interviewer to talk about your experiences, or if you'd prefer, writing your story down and sending it to us (we will provide a guide). All information collected will be de-identified, so your name and details will be kept confidential, and privacy is assured.

Participation either involves being interviewed or If you would like to know more about the study or may be interested in participating, please contact us by email: Jane.frawley@uts.edu.au or sultana.farhana@student.uts.edu.au

Cancer in pregnancy: mothers' Reflections and healthcare Experiences (CaRE) Interview guide

Consent

1. Prior to the interview, check that consent has been received. If no written consent has been received, you will need to seek oral consent using the verbal consent protocol.
2. Remind the participant that the aim of the research is to learn about the healthcare experiences of mothers diagnosed with cancer during pregnancy.
3. If prior consent was received, confirm that the participant read and understood the Participant Information Sheet and the Consent Form. Answer any questions the participant may have arising from the Participant Information Sheet. Confirm that they consent to participate in the study.
4. If prior consent was not received, follow the verbal consent protocol
5. Ask permission to record the interview.
6. Ask the participant to choose a pseudonym.

Demographic information

Demographic questions

Place of residence	Metropolitan	Regional	Rural/Remote	
Relationship status during pregnancy	Married/Defacto	Single	Divorced/Separated	
Relationship status now	Married/Defacto	Single	Divorced/Separated	
Level of education	Primary School	Secondary School	Trade Certificate	Tertiary
Occupation				
Number and ages of children				
Age now				
Age at diagnosis				
Year of diagnosis				
Gestation (in weeks) at diagnosis				
Diagnosis/condition				
Private or public obstetric services	Private	Public		
Private or public oncologist	Private	Public		
Number of pregnancies prior to pregnancy with a cancer diagnosis				
Was this pregnancy naturally conceived or an assisted conception (ART, IUI etc.)				
Outcome of pregnancy with cancer diagnosis	Live Birth	Stillbirth	Miscarriage	Termination
Gestation (weeks) at birth (if gave birth)				
Mode of birth (if gave birth)	Vaginal	Assisted Vaginal (Forceps Etc.)	Caesarian Section	
Were you admitted to a higher level of care in the peripartum period (HDU, ICU, CCU)?	No	Yes		
Were you transferred after the birth to a general hospital for medical care? If yes, were you separated from your baby?	No	Yes, baby came with me	Yes, I was separated from my baby	

Focal story (Let participant tell her story without asking direct questions)

E.g. "Tell me about when you were diagnosed, how it happened and what happened during your pregnancy."

Experience of health care (unless covered in the focal story ask about)

Participant's views about their care at the time of and after the diagnosis (for the duration of treatment i.e. probably beyond birth), whether this met their needs, what worked and what did not work, and how things could be improved in terms of:

- What was the interaction between your doctors, midwives and other healthcare professionals?
- How would you rate the quality of the information you were given?
- How consistent was the information you were given from different people (and was there any conflict in advice/information between health care professionals)?
- Do you feel that you received emotional/psychological support when you were diagnosed with cancer in pregnancy? Was it helpful? (If not already specified, who provided this support (professional support, family support, community support etc.?)
- Did your healthcare providers include your partner or family/friends in consultations?
- Did you receive any advice regarding future pregnancies, including pregnancy spacing or fertility preservation?
- Was your baby well? Did your baby need a higher level of care and for how long? Did the baby remain in the hospital after you were discharged? Were you able to breastfeed?
- [If livebirth] What happened when you came home with your baby? (Cancer treatment (commence or re-commencing)? Was your baby pre-term? Managing a newborn and being unwell etc.).
- [if livebirth] How did the family/partner/friends organise to support you when you came home with the baby?
- Manage at home caring for a newborn baby, or were you able to help to care for your baby?
- [If livebirth] What structured health and community services did you access in the first year after coming home from the hospital with your baby? Who provided this support (midwives, psychologists, counsellors, breast cancer care nurses, mother's group, early childhood nurse, GP, etc.)?
- What services would you have liked? What kind of services would enhance your quality of life and overall experiences?

PARTICIPANT INFORMATION SHEET
Cancer in pregnancy: mothers' Reflections and healthcare Experiences (CaRE)
(UTS HREC REF NO. ETH19-4526)

INTRODUCTION

We are inviting you to take part in a research study examining the health care experiences of women who have been diagnosed with cancer during pregnancy.

Before you decide whether you wish to participate in this study, it is important for you to understand why the research is being conducted and what it will involve. Please take the time to read the following information carefully and discuss it with others if you wish.

WHO IS DOING THE RESEARCH?

The study is conducted by Professor Elizabeth Sullivan, Doctor Jane Frawley and Ms Sultana Farhana. This research study will form part of Ms Sultana Farhana's PhD.

WHAT IS THIS RESEARCH ABOUT?

Cancer is the leading cause of death in women of reproductive age, and the rates of some cancers in pregnant women are increasing. Currently, it is estimated that 1 in 1,000 pregnancies are affected by cancer.

Managing cancer and pregnancy is complex. Treatment is a balancing act that seeks to maximise the benefits of cancer therapy for the mother while minimising the risks of harm to the baby.

Pregnant women with cancer and their babies are at higher risk of adverse outcomes. Pregnant women with cancer may also have more complicated patient experiences, often due to the complexity of care coordination and the challenges of aligning therapeutic strategies with their personal perspectives.

The aim of this study is to better understand the experiences of women diagnosed with cancer in pregnancy and develop recommendations to support women who experience gestational cancer in the future.

More specifically, we would like to:

- describe the impact of cancer diagnosed during pregnancy on the patterns and experiences of cancer and pregnancy care,
- recognise opportunities to enhance the care provided for women with cancer during pregnancy and to inform appropriate interventions, patient information and counselling materials to improve outcomes for women and their infants.

To achieve this outcome, we will interview several women who have been diagnosed with cancer during pregnancy about their healthcare experiences. These interviews will be analysed, and the findings will be used to develop resources.

FUNDING

Funding for this project has been received from Cancer Council NSW.

WHY HAVE I BEEN ASKED?

You are invited to participate in this study because you have experienced a diagnosis of cancer during pregnancy

IF I SAY YES, WHAT WILL IT INVOLVE?

I will invite you to take part in a conversation with a researcher about your healthcare experiences as a woman who experienced cancer during pregnancy.

You will be asked if it is all right if the conversation is recorded; just let the researcher know if you're comfortable with this or if you'd like the researcher to take written notes instead.

You will also be asked to choose a "pseudonym"—a name used for the interview to protect your identity. The researcher will ask you some background questions (such as age, where you live etc.). They will then ask you questions about your diagnosis of cancer and your experience of the health care provided during your pregnancy. Finally, you will be asked if there's anything else you'd like to add.

The interview will be conducted by telephone and will take at least twenty minutes but can last up to an hour, depending on how much you'd like to tell us.

DO I HAVE TO SAY YES?

Participation in this study is voluntary. It is entirely up to you whether you decide to participate. You can say "NO".

If you decide not to participate, it will not affect any ongoing treatment or care you receive or your relationship with the researchers, doctor or staff caring for you.

If you choose to participate in the interview, you can still decline to answer any questions you find distressing or terminate the interview at any time.

WHAT WILL HAPPEN IF I SAY NO?

You are free to withdraw from this study at any time without consequence.

The researcher will thank you for your time and won't contact you about this research again.

If you withdraw from the study, the audio recordings will be erased. However, it may not be possible to withdraw your data from the study results if you have already had your identifying details removed.

ARE THERE ANY RISKS/INCONVENIENCE/COSTS?

This interview will ask about your experience of having cancer during pregnancy. This is a sensitive issue, and talking about it may cause discomfort or distress. The researcher can stop the interview whenever you desire and recommend an appropriate counselling service if required.

There is also the inconvenience of giving up your time.

There are not expected to be any other risks or costs associated with participating in this study.

HOW WILL INFORMATION FROM THE STUDY BE USED TO HELP OTHERS AND ME?

There will be no clear benefit to you from your participation in this research, but we hope that it may improve the future care of women with cancer during pregnancy.

For the wider community to benefit from the study, we plan to produce reports and/or articles that are publicly available. We will ensure that any publication or presentation of these reports and information is presented in a non-identified and summary form so that you or anyone else cannot be identified. Your privacy will be always protected.

CONFIDENTIALITY

By signing the consent form, you consent to the research team collecting and using your personal information for the research project. All this information will be treated confidentially. You will also be asked to choose a “pseudonym” – a name used for the interview to protect your identity. Your information will only be used for this research project and destroyed once the study is complete.

WHAT IF I HAVE CONCERNS OR A COMPLAINT?

This study has been approved by the University of Technology Sydney Human Research Ethics Committee [UTS HREC]. If you have any concerns or complaints about any aspect of the conduct of this research, please contact the Ethics Secretariat at +61 2 9514 2478 or email Research.Ethics@uts.edu.au and quote the UTS HREC reference number. Any matter raised will be treated confidentially and investigated, and you will be informed of the outcome.

Any issues you raise will be treated in confidence and investigated thoroughly, and you will be informed of the outcome. Furthermore, if you have concerns about the research, please contact Dr Jane Frawley at jane.frawley@uts.edu.au. Thank you for taking the time to consider this study. If you wish to participate, please sign the attached consent form. You will be given a copy of this form to keep

CONSENT FORM

**Cancer in pregnancy: mothers' Reflections and healthcare Experiences (CaRE)
(UTS HREC REF NO. ETH19-4526)**

I _____ (participant's name) agree to participate in the research project '*Cancer in pregnancy: mothers' Reflections and healthcare Experiences (CaRE)*' (UTS HREC REF NO. ETH19-4526) being conducted by Professor Elizabeth Sullivan, Professor of Public Health, University of Technology Sydney. Email: elizabeth.sullivan@uts.edu.au

I have read the Participant Information Sheet, or someone has read it to me in a language I understand.

I understand the research's purposes, procedures and risks as described in the Participant Information Sheet. I understand that if I choose to participate in the interview, I can decline to answer any questions that I find distressing.

I have had an opportunity to ask questions, and I am satisfied with the answers I have received.

I understand that the purpose of this study is to understand the healthcare experiences of women diagnosed with cancer during pregnancy.

I understand that I have been asked to participate in this research because I have been diagnosed with cancer during pregnancy and that my participation in this research will involve having a conversation with a researcher about my thoughts and experiences of having cancer in pregnancy.

I understand the interview will be recorded and transcribed and that I will be asked to choose a "pseudonym" – a name that will be used for the interview to protect my identity. I understand this is a sensitive issue, and I can stop the interview anytime. I also understand that aside from requiring up to an hour of my time, there are not expected to be any other risks or costs associated with taking part in this study.

I understand that I will be given a signed copy of this document to keep.

I agree to be audio recorded:

(please check the box if you agree)

I agree that the research data gathered from this project may be published in a form that does not identify me in any way:

(please check the box if you agree)

I am aware that I can contact Elizabeth Sullivan if I have any concerns about the research. I also understand that I am free to withdraw my participation from this research project at any time I wish, without consequences and without giving a reason. I agree that Elizabeth Sullivan (or delegate) has answered all my questions fully and clearly.

Name and Signature [participant]

____/____/____
Date

Name and Signature [researcher or delegate]

____/____/____
Date

NOTE:

This study has been approved by the University of Technology Sydney Human Research Ethics Committee [UTS HREC-4526]. If you have any concerns or complaints about any aspect of the conduct of this research, please contact the Ethics Secretariat at +61 2 9514 2478 or email Research.Ethics@uts.edu.au and quote the UTS HREC reference number. Any matter raised will be treated confidentially and investigated, and you will be informed of the outcome.

Any issues you raise will be treated in confidence and investigated fully, and you will be informed of the outcome.

CONSENT FORM

Cancer in pregnancy: mothers' Reflections and healthcare Experiences (CaRE)
UTS HREC REF NO. ETH20-5565

I _____ (participant's name) agree to participate in the research project '*Cancer in pregnancy: mothers' Reflections and healthcare Experiences (CaRE)*' UTS HREC REF NO. ETH20-5565 is being conducted by Professor Elizabeth Sullivan, Professor of Public Health, University of Newcastle, email: e.sullivan@newcastle.edu.au and Doctor Jane Frawley, Senior Lecturer at the University of Technology Sydney, email jane.frawley@uts.edu.au.

I have read the Participant Information Sheet, or someone has read it to me in a language I understand.

I understand the research's purposes, procedures and risks as described in the Participant Information Sheet. I understand that if I choose to participate in this research, I can decline to answer any questions that I find distressing.

I have had an opportunity to ask questions, and I am satisfied with the answers I have received.

I understand that the purpose of this study is to understand the healthcare experiences of women diagnosed with cancer during or just after pregnancy.

I understand that I have been asked to participate in this research because I have been diagnosed with cancer during or just after pregnancy and that my participation in this research will involve having a conversation with a researcher about my thoughts and experiences of having cancer during pregnancy or in the six months after I'd given birth.

If interviewed, I understand the interview will be recorded and transcribed and that I will be asked to choose a "pseudonym" – a name that will be used for the interview to protect my identity. I understand this is a sensitive issue, and I can stop the interview anytime. I also understand that aside from requiring up to an hour of my time, there are not expected to be any other risks or costs associated with taking part in this study.

I understand that I will be given a signed copy of this document to keep.

I agree to be audio recorded:

(please check the box if you agree)

I agree to write my story down and send it in:

(please check the box if you agree)

I agree that the research data gathered from this project may be published in a form that does not identify me in any way:

(please check the box if you agree)

I am aware that I can contact Elizabeth Sullivan if I have any concerns about the research. I also understand that I am free to withdraw my participation from this research project at any time I wish, without consequences and without giving a reason.

I agree that Elizabeth Sullivan (or delegate) has answered all my questions fully and clearly.

Name and Signature [participant]

____/____/____
Date

Name and Signature [researcher or delegate]

____/____/____
Date

NOTE:

This study has been approved by the University of Technology Sydney Human Research Ethics Committee [ETH20-5565]. If you have any concerns or complaints about any aspect of the conduct of this research, please contact the Ethics Secretariat at +61 2 9514 2478 or email Research.Ethics@uts.edu.au and quote the UTS HREC reference number. Any matter raised will be treated confidentially and investigated, and you will be informed of the outcome.

Any issues you raise will be treated in confidence and investigated thoroughly, and you will be informed of the outcome.

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