Flinders University

Supporting Self-Management of Cardiovascular Disease and its Risk Factors in People Diagnosed with Cancer

by

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CONTENTS

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DECLARATION

I certify that:

1. this thesis does not incorporate material which has been accepted for the award of any other degree or diploma

2. the research within this thesis will not be submitted for any other future degree or diploma without the permission of Flinders University

3. to the best of my knowledge and belief, this thesis does not contain any material previously published or written by another person except where due reference is made in the body of the thesis, and

4. this thesis has been completed without the use of generative artificial intelligence tools.

Signed.....Reegan Kate Knowles.....

Date...24/9/2025

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Directly from the doctoral research

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ABBREVIATIONS

6MWT	6 Minute Walk Test
ADT	Androgen Deprivation Therapy
BMD	Bone Mass Density
CAD	Coronary Artery Disease
CAR	Chimeric Antigen Receptor
CCA	Corrected Covered Area
CIO	Cancer Information Overload
COSA	Clinical Oncology Society of Australia
CTR-CVT	Cancer Therapy-Related Cardiovascular Toxicity
CVD	Cardiovascular Disease
DCE	Discrete Choice Experiment
EHA	European Hematology Association
ESC	European Society of Cardiology
ESMO	European Society of Medical Oncology
ESTRO	European Society for Therapeutic Radiology and Oncology
HBM	Health Belief Model
HER-2	Human Epidermal Growth Factor Receptor 2
HR	Hazard Ratio
HREC	Human Resources Ethics Committee
IC-OS	International Cardio-Oncology Society
IGF	Immune-like Growth Factor
JBI	Joanna Briggs Institute
NHANES	National Health and Nutrition Examination Survey
NSCLC	Non-Small Cell Lung Cancer
PBAID	Person-Based Approach to Intervention Development
PRISMA	Preferred Reporting Items for Systematic reviews and Meta-Analyses
PSA	Prostate Specific Antigen
QOL	Quality Of Life
RCT	Randomised Controlled Trial
RR	Risk Ratio
RTA	Reflexive Thematic Analysis
SCORE	Systematic Coronary Risk Evaluation
SMR	Standardised Mortality Rates
TFA	Theoretical Framework of Acceptability
TKI	Tyrosine Kinase Inhibitors

THESIS SUMMARY

This thesis describes the research program I have undertaken as my PhD candidature, including the experiences of the scholarly journey.

Chapter 1 presents an overview of the conceptualisation of the research program, a summary of the thesis and how the research journey evolved, particularly regarding how the original plan for subsequent studies within the program changed based on findings of previous studies. In Chapter 2, an introduction and presentation of relevant existing literature provides a background for the reader and generates rationale for the research program. In particular, the seriousness and prevalence of CVD risk in cancer is described and the existing relevant guidelines and interventions (e.g., cardio-oncology clinics) are presented with detail. The aim of the research program was to develop understanding of perspectives of cancer care providers and people with cancer to inform the codesign of a new approach to reduce the impact of CVD risk in people who have been diagnosed with cancer.

Chapter 3 presents a review of systematic reviews investigating the effectiveness of lifestyle interventions in older people with cancer. The findings strongly support the inclusion of information and support to optimise physical activity behaviour as an important and effective component of a resource to reduce the impact of CVD risk in cancer. Limited dietary data suggests some favourable outcomes for older people with cancer, but there is no review-level evidence for smoking and alcohol interventions.

Chapters 4 and 5 report the findings of two qualitative studies to examine the perspectives of cancer care providers and people diagnosed with cancer regarding CVD in cancer. Providers were aware of the issue of CVD care in cancer and perceived it important, but many people with cancer were unaware. Cancer care providers perceived they could not deliver CVD care alone due to time and role constraints. Both providers and people with cancer suggested a diverse range of possible solutions to improve CVD care in cancer including education. These findings suggest the need for a flexible and individualised approach to provide information and support to people affected by cancer to self-manage aspects of the CVD care.

The codesign and usability testing of the first website, ‘My Heart and Cancer’, to provide information and support for patients to self-manage CVD risk in cancer, is described in Chapter 6. The website is visually-appealing, easy-to-use and interactive, and provides information and support including CVD risk assessment, self-management and access to services and resources. After testing for feasibility and effectiveness, the website has the potential to contribute to reducing the impact of CVD in cancer, including mortality and morbidity, through providing information and support according to the preferences of people diagnosed with cancer and cancer care providers.

1 CHAPTER ONE: RESEARCH CONCEPTUALISATION, THESIS OVERVIEW AND EVOLUTION OF THE RESEARCH PROGRAM

This section provides an overview of the research program, how the direction of the research changed and evolved throughout the candidature and tells the overall 'story' of the candidature. It explains how unexpected findings and practical limitations informed subsequent aspects of the research program. A flexible and open-minded outlook meant the research program evolved authentically and organically, which - although feeling uncertain at times - ensured the development of the PhD candidate into an independent researcher. Summarising the overall research program and its evolution early in the thesis also assists to 'situate' the reader, particularly with regard to appreciating the relevance of literature discussed in this chapter.

1.1 Brief background/context

Cardiovascular disease (CVD) risk is an important issue for people who have been diagnosed with cancer, with many survivors experiencing significant cardiovascular-related morbidity and mortality as well as poorer cancer outcomes (1-5). Voluminous literature reports cardio-oncology research which has led to the development of guidelines, the most comprehensive of which are the ESC Guidelines on Cardio-oncology which provide evidence and expert consensus-informed recommendations to support clinicians to assess, monitor and manage CVD risk in cancer (6). Approaches to reducing the impact of CVD in cancer are developing, including cardio-oncology clinics and clinical pathways (7, 8). In addition, education, self-management, lifestyle behaviour optimisation and risk prediction models may be able to contribute to addressing the problem of CVD in cancer. However, despite evidence, guidelines and developing interventions in cardio-oncology, CVD risk remains a prevalent and significant issue facing the cancer population which requires a new approach to reduce adverse CVD-related outcomes in cancer. In addition, older people are likely at even greater risk/need given they are more likely to experience both cancer and CVD but have often been under-represented in research.

1.2 Initial PhD research program conceptualisation

In 2017, Flinders University researchers, including two of the PhD candidate's supervisors (BK and MM) developed a risk prediction model using data from older adults from the Australian Longitudinal Study of Ageing, in which five CVD risk factors (physical inactivity, smoking, stroke history, age and sex) were identified being able to predict 10-year CVD mortality risk in people affected by cancer (9, 10). In 2019, the PhD candidate joined the risk prediction model researchers to report further research which validated the model using data from the Australian Longitudinal Study on Women's Health (10). We found acceptable discrimination, with 30% of the variation in mortality being explained by the model. Study conclusions included that the model could underpin

the development of a clinical tool that could assist in identifying and managing CVD risk in people with cancer. These findings led to broader discussions about how digital health could assist in translating cardio-oncology evidence and guidelines for real-world outcomes. The PhD candidate and supervisors then conceptualised the PhD research program, in which the aim was to develop a new (potentially digital) approach to reduce the impact of CVD in older people with cancer, codesigned with people affected by cancer, cancer care providers and researchers. The initial concept for the research work of the PhD was to focus on older adults with the research to be informed by the existing evidence or risk reduction strategies in older adults and proposed qualitative work exploring perspectives of health care providers and cancer survivors, undertaken as part of the PhD program.

1.3 Summary of the literature review on risk reduction strategies (chapter 3)

The importance of lifestyle behaviour optimisation in managing CVD and cancer risk is well-established. However, there was less understanding around the impact of lifestyle interventions on improving outcomes in older people with cancer, with no previous review of reviews focusing on people aged 65 years or more who have been diagnosed with cancer. Given differences in biological factors (e.g., sarcopenia) and social barriers to healthy lifestyle behaviours (e.g., lack of social support) between younger and older people with cancer, data derived from younger people with cancer should not be generalised to the older population. Therefore, a review of systematic reviews was conducted to summarise and synthesise review-level data from studies examining the effectiveness of lifestyle interventions in people diagnosed with cancer aged 65 years or older.

The review of reviews found majority of included reviews examined the effectiveness of physical activity in older people with cancer, whilst there were limited reviews reporting outcomes of diet interventions in this population, and no reviews examining smoking or alcohol interventions in older adults. Review-level data reporting the effectiveness of physical activity interventions in older people with cancer found physical activity was associated with benefits across multiple physical outcomes (lean muscle mass, functional performance, strength) and improved fatigue, which aligns with findings in younger people with cancer (11, 12). In contrast to younger adults, there was no improvement in anxiety and mixed findings for quality of life and depression. Synthesis of the data from the four dietary intervention reviews showed improvements across multiple outcomes including reduced treatment toxicity and complications and body weight; whilst there was mixed primary-level evidence for the impact on QoL and hot flushes. There was no impact on fatigue, libido, length of hospital-stay or mortality. In comparison to findings across the adult age continuum, while there is also limited review-level data on dietary interventions in younger people with cancer, there is consistency in the available data regarding the favourable impact of dietary interventions on body weight and fat mass in both older and younger people with cancer (13, 14).

However, the findings for older people regarding QoL were mixed, which was in contrast to McHugh et al. (14) who concluded favourable impacts on QoL in people with cancer for which the age of the population were not reported.

In summary, the findings of the review of systematic reviews strongly supports the inclusion of information and support to optimise physical activity behaviour as an important and effective component of an approach to reduce the impact of CVD risk in cancer. Although the data is more limited, there is also review-level evidence that healthy diets should also be encouraged in both younger and older people with cancer. The paucity of literature for smoking cessation and alcohol moderation interventions in older people means there is no added support for inclusion as a component of an intervention to reduce CVD risk, but there is also no evidence to contradict inclusion of support to optimise these behaviours. Ultimately, the strength of evidence for the broad range of negative outcomes associated with these behaviours necessitates the inclusion of information and support to quit smoking and moderate alcohol intake in a new approach to manage CVD risk in cancer.

1.4 Summary of the qualitative study of perspectives of cancer care providers regarding CVD care in cancer (chapter 4)

Despite evidence-based guidelines recommending CVD risk factor management in people diagnosed with cancer, understanding is limited as to why CVD risk assessment and management is not routinely undertaken. A qualitative study was conducted to examine health care providers' perspectives of the management of CVD risk factors in cancer.

Participants' feedback led to the construction of four themes: a) Majority of cancer care providers were aware of CVD risk in cancer and consider it an important issue to address; b) Cancer care providers expressed concern about their individual abilities to address CVD risk in cancer; c) Cancer care providers perceived potential challenges for individuals with cancer to engage in CVD risk assessment and management; and d) A range of approaches could be used to assess and manage CVD risk in cancer. In summary, data suggest that although the importance of CVD risk in cancer is appreciated by cancer care providers, they experience barriers to delivering CVD care and suggest a wide diversity of strategies to mitigate these barriers and reduce the impact of CVD risk in cancer.

The findings support the need for new approaches to reduce the impact of CVD in cancer, however these approaches must acknowledge the barriers and diverse preferences of cancer care providers, e.g., a teams-based approach to address cancer care providers' concern around not being able to deliver care alone, and a flexible and multi-pronged approach to meet multiple preferences for care.

1.5 Changing focus in the research program in response to research findings

Existing evidence, including previous research by the PhD candidate and supervisory team to develop a CVD risk prediction model in people with cancer, informed the aim of the overall research program to develop a new (potentially digital) approach to reduce the impact of CVD in cancer. It was anticipated that qualitative study involving cancer care providers may involve discussion about the potential for the development of a digital tool to be used in clinical practice to operationalise the team's risk prediction model. In fact, the original topic guide developed for this qualitative research included a focus on eliciting participants' perspectives around the development of a digital risk prediction tool. However, in the first focus group, the discussions about what could be done to improve cardio-oncology care remained broad in scope, with participants wanting to discuss many options for a new approach (rather than focus only on a risk prediction tool). The research team discussed how the data emerging from the first focus group highlighted the importance of being guided by stakeholders' perspectives and avoiding assumptions that a risk prediction tool would definitely be the outcome of the research program. To ensure this, the topic guide was amended to reduce the number of prompts related to risk prediction tools, to allow for broader discussions about potential approaches. This was a critical learning experience for the candidate and emphasised the importance of flexible thinking to ensure that the ultimate aim of developing a feasible and effective intervention aligning with stakeholder preferences was not compromised in order to adhere to preconceived ideas of what the research program might entail.

Another evolution in the overall research program related to the initial plan to focus on the CVD in *older* people diagnosed with cancer. This focus on older people also stemmed, in part, from the fact that the risk prediction model developed by the research team had been validated in older people with cancer originally. In addition, both cancer and CVD rates increase with age. Although, a focus on older people was encouraged throughout qualitative sessions with cancer care providers and people affected by cancer, it was clear that participants contributed perspectives about CVD risk in people with cancer of all ages. Therefore, it was determined that a new approach to reduce the impact of CVD in *all* people diagnosed with cancer would be developed, but that the special requirements of older people would be considered throughout all stages of approach development.

1.6 Summary of the qualitative study of perspectives of people diagnosed with cancer regarding CVD care in cancer (chapter 5)

There was a lack of qualitative data from patients to aid in understanding CVD care in cancer. Therefore, individual interviews with 15 people affected by cancer were conducted to examine experiences and perspectives regarding CVD risk to inform the development of future approaches. Participants' feedback led to the construction of two themes (with the second theme consisting of

four sub-themes): a) there was limited awareness of the importance of CVD risk in cancer; and b) there were diverse preferences on how to prioritise and deliver CVD risk management (sub-themes: prioritisation of dealing with cancer over CVD care; perception that a range of cancer care providers could deliver CVD care; diverse preferences for timing, content and manner of information provision about CVD risk; and diverse preferences for the mode and components of an approach to facilitate CVD care in cancer). The findings of this research support the need for a new approach to reduce the impact of CVD care in cancer, which should include information provision about CVD risk given participants' lack of awareness.

It is critical to consider both cancer care providers' and people affected by cancer's perspectives regarding CVD care in cancer together (i.e., the findings of both qualitative studies conducted as part of this research program). Differences in findings included that majority of people diagnosed with cancer were unaware or only somewhat aware of the increased risk of CVD in cancer, whilst all cancer care providers were aware. In addition, cancer care providers identified multiple barriers to the provision of CVD care, including perceived conflicts with role identity and lack of time and training. In contrast, people who diagnosed with cancer identified very few barriers to engaging in CVD care were identified (financial and psychological barriers were mentioned briefly). This may reflect patients' lack of awareness of CVD risk in cancer, meaning they likely have not considered potential barriers, and may perhaps also reflect health care consumers' trust in the Australian health care system. A finding common to the two qualitative studies was that both cancer care providers and people diagnosed with cancer contributed diverse ideas for solutions to optimise CVD care, highlighting that future approaches to CVD care in cancer must be flexible and individualizable and must be conceptualised and developed involving a broad range of stakeholders including people diagnosed with cancer, cancer care providers and researchers.

1.7 Refining the focus of subsequent studies in the research program

The previous work of the PhD candidate and supervisors to develop a CVD risk prediction model for older people with cancer influenced the conceptualisation and planning of the PhD research program. However, the qualitative studies with cancer care providers and people diagnosed with cancer were conducted in a way that facilitated participants to contribute ideas and preferences for any type of approach to reduce the impact of CVD in cancer. It became clear that cancer care providers did not believe that development of a risk prediction tool would be the best approach to improving CVD care in cancer, although there was no consensus between participants as to which specific intervention would be most feasible and effective, but rather a multitude of ideas about certain components/approaches that could favourably influence CVD outcomes.

Given the research program was informed by the development of the risk prediction model, early planning for the program had involved ideas to validate the risk prediction model in older men (as it had previously been externally validated in women), but the purpose of this study became

redundant due to the lack of support for the development of a digital tool to determine CVD risk. At this point, the research team discussed whether it was necessary to further examine preferences for an approach to reduce the impact of CVD in cancer through conducting a discrete choice experiment (DCE). A DCE is a quantitative methodology used to elicit preferences of participants acknowledging that decisions about healthcare involve individuals making trade-offs of particular aspects of that care (e.g., an individual may prefer to forego a particular aspect of care to receive overall care at a lower price). The research team also discussed the importance of bettering understanding around the importance of timing in CVD risk information provision and management in cancer. A secondary data analysis of a large dataset to examine the concept of the 'teachable moment' of cancer diagnosis in eliciting behaviour change. That is, is a cancer diagnosis a moment in time that leads to the patient being more likely to make lifestyle changes such as quitting smoking or optimising physical activity?

Ultimately, after a series of discussions, the research team determined the level of understanding of people with cancer and cancer care providers' perspectives and preferences for CVD care gained from the qualitative studies already conducted was sufficient to justify the next study being the codesign (with stakeholders) of a new digital approach to reducing the impact of CVD in cancer. The PhD candidate determined that a patient-facing website providing information and support for the self-management of CVD in cancer could address many of the needs and preferences of the stakeholders and would take into account the majority of barriers identified by study participants. First, information provision and education can be a key component of a patient-facing website, which addresses the finding that many people affected by cancer are unaware of CVD risk. In addition, participants specifically expressed support for education and information provision via a website. Second, a website could provide the specific types of information and support identified as important to people diagnosed with cancer, such as self-management support, tips for behaviour change, and support to understand what CVD signs and symptoms they should look for. Third, a website could cater for diverse preferences regarding the amount and detail of information provided, where information can be present in a general and simple way but with options to navigate to greater detail for those who prefer it. The use of videos, pictures, text and interactive activities could also create an individualised experience catering to user's different needs and preferences. Finally, a website may circumvent some barriers identified by cancer care professionals, including that they did not have the time and training to provide adequate CVD care, and that they felt their profession could not provide CVD care alone.

1.8 Summary of codesign and usability testing (chapter 6)

Two rounds of codesign (via focus groups and individual interviews) were conducted with people affected by cancer and cancer care providers to develop a website to support people affected by cancer to self-manage CVD risk. The website was developed iteratively based on feedback which

was grouped into five topics (content, design and interactivity, navigation, layout and need for the website). Initially a wireframe was developed based on preferences from the qualitative studies conducted as part of this research program and relevant literature more broadly and was used to prompt feedback in codesign round 1. The first prototype was then developed based on discussion amongst the research team about the data collected in codesign round 1. Codesign round 2 used the first prototype to generate further discussion which then informed the development of the second version of the website ready for usability testing. Usability testing generated further feedback also able to be separated into content, design and interactivity, navigation and layout. Twenty-seven changes were made to create the final website: ‘My Heart and Cancer’, which is the first website developed to support self-management of CVD risk factors in people diagnosed with cancer. It is anticipated that after further testing of feasibility, acceptability and effectiveness, the website could be made available publicly and may help to reduce the impact of CVD risk in cancer, which is associated with significant morbidity and mortality in this population.

2 CHAPTER TWO: INTRODUCTION

2.1 PART 1: Defining the Problem: Cardiovascular disease causes significant adverse effects in people diagnosed with cancer

This research program aimed to develop and implement an approach to reduce the impact of CVD in cancer. Therefore, it is necessary to define and describe the scope of the problem underpinning this aim, i.e., the substantial incidence and prevalence and adverse impacts of CVD in people diagnosed with cancer, including significant morbidity and mortality. This section summarises and synthesises the relevant literature in order to provide background and context to justify the need to improve CVD care for people diagnosed with cancer.

2.1.1 Cancer: Incidence and Prevalence and impact

It is estimated that 165,000 people were diagnosed with cancer in Australia in 2023, with the most common types of cancer diagnosed being prostate (25,500), breast (20,500) and melanoma (10,600) (15). Worldwide, it was estimated that in 2020, there were about 19.3 million new cases of cancer and 10 million deaths (16). Cancer is diagnosed more commonly in men (55% in 2023), in people experiencing social disadvantage (age-standardised rates were 5% higher in disadvantaged areas between 2012-2016 and mortality rates over 40% higher), and in First Nations people (12% higher than non-Indigenous Australians in 2014-2018) (15). It was estimated that around 30% of deaths in 2023 in Australia were caused by cancer (approximately 51,300 people) (15), and that cancer was responsible for 18% of the burden of ill health and 9% of health system expenditure in 2021 (17). It is estimated that around 1 million Australians have been diagnosed with cancer (18).

Cancer and anti-cancer treatment can have an array of acute and long-term consequences and may affect individuals and their family members and loved ones physically, psychologically, spiritually, socially and financially (19-23).

In addition, comorbidity is common in cancer, with US data suggesting that approximately 40% of people diagnosed with cancer had at least one other chronic disease such as cardiovascular disease (CVD), obesity, diabetes, musculoskeletal problems or mental ill health (24). Comorbidity can lead to worse outcomes for people with cancer (compared to those without another chronic disease), including poorer survival, post-operative complications, and potential not to receive standard anti-cancer treatment (25).

2.1.2 Cardiovascular disease in people with cancer: prevalence and impact

Given cancer and CVD are the most prevalent diseases in Australia (and many other countries), these diseases can often co-occur. In 2022, approximately 1.3 million Australian adults reported having a CVD (26), while approximately 456,200 people in Australia reported having cancer (27).

Understanding the co-occurrence of CVD and cancer is critical not only because they are the most prevalent diseases but also because they are leading causes of mortality and morbidity. Cancer was responsible for approximately 51,300 deaths in Australia in 2023 (15), whilst CVD caused 45,000 deaths in 2022 (26).

CVD is estimated to be the most common comorbidity experienced by individuals who have been diagnosed with cancer (24). CVD can be diagnosed pre-diagnosis of cancer or develop after cancer diagnosis. For example, a recent large retrospective analysis of linked health administration data from 17,389 people in South Australia and the Northern Territory, Australia who had been diagnosed with cancer and were receiving chemotherapy, found that approximately 50% developed CVD post-cancer diagnosis, and these people were significantly more likely than those without CVD to die in the next 12 months (1). Coexisting CVD and cancer have a strong and wide-ranging impact on mortality, with evidence suggesting people with cancer and CVD are more likely to die of CVD than those without cancer. For example, a systematic review and meta-analysis of 136 studies examining CVD mortality in cancer populations compared to non-cancer populations (reported as standardised mortality rates (SMRs)), found that of 876 CVD SMRs, 61% showed higher CVD mortality risk in people with cancer (2). A meta-analysis of the 876 SMRs were pooled (using random-effects model due to heterogeneity) and showed an increased CVD death risk in people with cancer compared to the general population (SMR = 1.55, CI = 1.40-1.72). There is also evidence of higher cancer-related mortality rates in people with coexisting cancer and CVD, compared to individuals with cancer but no CVD. For example, a prospective cohort study of National Health and Nutrition Examination Survey (NHANES) (1999-2016) data linked with Medicare and National Death Index, compared cancer mortality between individuals residing in the US with CVD and those without (3). Data from 44,591 participants with no history of cancer diagnosis at baseline was analysed. There was a significantly higher risk of cancer death in people who had been diagnosed with CVD compared to those with no CVD diagnosis (adjusted hazard ratio 1.37, $p = 0.01$) (3). Finally, there is also evidence that cancer survivors may be more likely to die from CVD-related causes than their cancer. Koczwara et al. conducted a retrospective cohort study of data from the South Australian Cancer Registry to examine mortality causes in people with cancer who were alive at least five years after diagnosis (4). Data from 32,646 people with a median follow-up of 17 years, were included in the analysis. There were 17,268 deaths, of which ischaemic heart disease was the most common cause of death accounting for 2,393 deaths. Although 45% of all deaths were due to any cancer, no one type of cancer caused more deaths than ischaemic heart disease – meaning that an individual cancer survivors 5 years post-diagnosis was more likely to die of ischaemic heart disease than any one type of cancer. At thirteen years post cancer diagnosis, CVD-related deaths exceeded mortality attributed to cancer (4).

There have not been studies examining differences in morbidity between people with cancer with CVD risk compared to those without CVD risk. However, there is some evidence that people with

cancer who have comorbidity (CVD or other chronic diseases including diabetes) have poorer QoL and higher healthcare costs than people with cancer and no comorbidity (5). There is also some evidence that (sometimes unwarranted) changes are made to anti-cancer treatment regimes in people with comorbidity, potentially adversely affecting outcomes (5).

Why are people with cancer at risk of cardiovascular disease?

Given the significant prevalence and serious adverse effects of CVD in cancer, it is critical to understand the mechanisms by which these diseases co-occur (28). High prevalence of both diseases means that there is an increased probability that the same people will experience both, but there are other mechanisms that increase the risk of co-occurrence, including the cardiotoxicity of anti-cancer treatment, shared risk factors and the effect of pathological and biological changes related to each individual disease and their risk factors, that can increase risk of the other disease also occurring (29).

2.1.2.1 Cardiotoxicity of anti-cancer treatment

Several anti-cancer treatment options are available to people diagnosed with cancer, including surgery, chemotherapy, targeted therapies, radiation therapy, hormone therapies and immunotherapy (30). Many anti-cancer treatments have side effects, e.g., nausea and fatigue, and some may increase CVD risk during, but also up to many years after treatment (31). Therapies that increase CVD risk may be referred to as cardiotoxic. Side effects (including CVD risk) should impact the specific therapeutic regime patients receive, along with clinical and pathological characteristics of the cancer/tumour and individual characteristics of the person being treated including age and preferences (6).

Cardiotoxicity may manifest in a wide range of cardiovascular diseases or risk factors, which may include myocardial dysfunction and heart failure; coronary artery disease (CAD); valvular disease; arrhythmias; arterial hypertension; thromboembolic disease; peripheral vascular disease and stroke; pulmonary hypertension; and pericardial complications (32). As new anti-cancer treatments are being developed all the time, and understanding of anti-cancer treatment cardiotoxicities expands, it is beyond the scope of this thesis to provide a comprehensive up-to-date description of all individual therapies and their likely cardiotoxic effects. However, Table 1 provides an overview of the evidence regarding cardiotoxic effects of types of anti-cancer treatments, including anthracyclines, monoclonal antibodies including Trastuzumab, tyrosine kinase inhibitors (TKIs) and radiotherapy. The risk of cardiotoxicity from anthracycline therapy is well-established in the literature. For example, a review and meta-analysis of incidence and clinical predictors of anthracycline cardiotoxicity reported that after a median follow-up of nine years approximately 6.3% of people receiving anthracycline treatment experienced clinical signs or symptoms of cardiac disease, and 17.9% had systolic dysfunction (33). Trastuzumab, a monoclonal antibody is used to improve survival rate in metastatic breast cancer and has been shown to cause heart

failure in 1-4% of patients, and a decline in left ventricular ejection fraction in 10% of those receiving the therapy (34). TKIs are used to treat a wide range of cancer types including breast, melanoma and lymphoma and have been shown to cause asymptomatic left ventricular dysfunction in 2.3% of patients receiving the therapy (35). TKIs have also been shown to be associated with higher risk of heart failure and myocardial dysfunction (36, 37). Radiation to the thoracic area may be used in treatment of breast or lung cancer, and lymphoma, and can cause direct damage to myocardial cells as well as induce CVD via the production of free radicals at the radiation site. Radiation therapy can increase risk of heart failure, pericarditis and myocardial infarction. There is limited evidence regarding the prevalence of cardiotoxicity from radiation therapy, however a recent systematic review and meta-analysis including 31 studies examining cardiovascular morbidity and mortality after radiotherapy for breast cancer showed increased risk of heart failure (HR: 1.37; 95% CI 1.20 to 1.57) and coronary artery disease (HR: 1.11; 95% CI 1.05 to 1.16) (38) . In addition, a large retrospective cohort analysis of lung cancer patients receiving radiotherapy found that 22.3% of patients experienced a cardiac event within the follow up period (median 73.7 months) (39). However, given lung cancer and CVD share risk factors, including smoking, this co-existence of CVD and lung cancer is unlikely to be solely attributable to the cardiotoxic effects of radiation therapy.

It is also beyond the scope of this thesis to provide a detailed description of mechanisms by which specific therapies affect the cardiovascular system. However, briefly, therapies may damage the cardiovascular system through increased levels of free radicals which cause oxidative stress injury, leading to the death of cardiac and endothelial cells (i.e., apoptosis); the direct activation of cell apoptosis by the therapy; interruption of pathways that protect the cardiovascular system; excessive and damaging immune cell activation; and changes to the physical structure of the heart (i.e., myocardial remodelling) (40). Understanding the mechanisms of cardiotoxic therapies is critical to inform future treatment approaches to protect from and manage CVD, especially through the isolation of biomarkers that can result in timely identification of CVD risk/damage (40).

Table 1 - Anti-cancer treatment and CVD risk (6, 36, 41)

Type of anti-cancer treatment (examples of specific agent/therapy)	**Examples of cardiovascular disease/condition associated with anti-cancer treatment**	**Examples of cancer types treated**
Anthracyclines (e.g., Doxorubicin, Daunorubicin, Mitoxantrone)	Heart failure, Left ventricular dysfunction, Arrhythmia	Breast, Prostate, Leukaemia, Lymphoma
Antimicrotubule agents (e.g., Docetaxel, Paclitaxel, Vinblastine)	Heart failure, Left ventricular dysfunction, Arrhythmia, Ischaemia	Breast, Lung, Prostate, Head and Neck,
Alkylating agents (e.g., Cisplatin, Clyclophosphamide, Melphalan)	Heart failure, Left ventricular dysfunction, Myopericarditis, Arrhythmia	Breast, Testicular, Lung, Neuroblastoma
Antimetabolites (e.g., Capecitabine, Fluorouracil, Decitabine)	Myocarditis, Arrhythmia, Left ventricular dysfunction, Heart Failure	Colon, Lymphoma, Leukaemia, Breast
Tyrosine kinase inhibitors (TKI) (e.g., Sunitinib, Ibrutinib, Cabozantinib)	Hyperlipidaemia, Stroke, Heart failure, Left ventricular dysfunction	Melanoma, Leukaemia, Breast, Renal,
Monoclonal antibodies (e.g., Trastuzumab, Pertuzumab, Rituximab)	Heart failure, Hypotension, Hypertension, Left ventricular dysfunction	Breast, Ovarian, Sarcoma, Leukaemia
Immune-checkpoint inhibitors (e.g., Nivolumab, Ipilimumab, Pembrolizumab)	Myocarditis, Arrhythmia, Left ventricular dysfunction, Pericarditis	Melanoma
Protease inhibitors (e.g., Carfilzomib, Bortezomib)	Hypertension, Heart failure, Left ventricular dysfunction, Venous thromboembolism	Multiple myeloma, Mantle cell lymphoma
Endocrine therapy (e.g., Tamoxifen, Flutamide, Anastrozole)	Hypertension, Hyperlipidaemia, Stroke, Heart failure	Breast, Endometrial, Prostate
Chimeric antigen receptor (CAR) T Cell therapy (e.g., Tisagenlecleucel, Axicabtagene ciloleucel)	Arrhythmia, Hypertension, Heart failure, Myocardial infarction	Leukaemia, Lymphoma
Radiotherapy (thoracic area)	Hypertension, Heart failure, Pericarditis, Myocardial infarction	Breast, Lymphoma, Lung
Haematopoietic Stem Cell Transplantation	Arrhythmia, Heart failure, Pericarditis, Myocarditis	Leukaemia, Lymphoma,

2.1.2.2 Cardiovascular disease and cancer have shared risk factors

Cancer and CVD share many of the same risk factors, including non-modifiable factors such as older age and male sex. In addition, modifiable risk factors such as poor lifestyle behaviours including physical inactivity, smoking, alcohol consumption and poor diet also determine cancer and CVD risk directly and indirectly (i.e., through increasing other disease risk factors including overweight and obesity, diabetes and hyperlipidaemia) (28). Socioeconomic disadvantage also increases risk, e.g., low income can adversely affect physical activity through reduced access to sport and activity facilities and reduced access to healthy diet due to high costs of many healthier food options (42). A summary of the prevalence of shared risk factors and their relationship to CVD and cancer is provided below, but it is important to note that these relationships are not linear, with complex interactions between risk factors and disease processes. Some factors have direct and/or indirect impacts on disease risk, e.g., poor diet increases disease risk through direct mechanisms, but also through increasing obesity risk (28).

Non-modifiable risk factors

2.1.2.2.1 Sex and age

In 2023, of those diagnosed with cancer in Australia, 55% were male (15) and in 2022, men were 1.3 times more likely to report having CVD than women (26). Men with co-existing disease were also more likely to die than women with both diseases (15, 26). Men are more likely than women to engage in lifestyle risk factors known to be associated with cancer and CVD, e.g., smoking (in 2021-22, about 12% of Australian men were smokers compared to 8% of women) (43) and unhealthy alcohol consumption (in 2021-22, about 36% of men exceeded the Australian Adult Alcohol Guideline compared to 18% of women) (44). Men are also more likely to be at an unhealthy weight, with approximately 71% of men in Australia being overweight or obese in 2022, compared to 61% of women (45). Differences in healthcare behaviours between men and women may also contribute to higher rates of disease and poorer outcomes. For example, men may be less likely than females to seek medical care which can lead to delayed diagnosis (46, 47). In addition, there are genetic factors that increase the risk of cancer in males (compared to females), including that men have higher testosterone levels, which may promote cell growth, and lower oestrogen levels, which have been shown to be protective against cancer (48). Immune responses vary in men and women and may also lead to increased risk for men compared to women (48). Furthermore, the male genetic profile influences the generation of enzymes involved in drug metabolism, which can affect anti-cancer treatment effectiveness (48). Similar to cancer risk, increased CVD risk can be due to genetic and molecular factors, which lead to differences in lipid metabolism, endothelial function and plaque formation (49).

The risk of both cancer and CVD increases with age. Although cancer can occur at any age, it is more common in older people with estimations for 2024 being that 88% of all cancers would be

diagnosed in people 50 years or older. It was estimated that in 2024, there would be 16 cases per 100,000 diagnosed in children younger than 10 years, whilst 2,800 per 100,000 would be diagnosed in people aged in their 80s. (15). Self-reported CVD also increases with age, with 28% of all Australians aged 75 years or older experiencing at least one CVD in 2022 (26). The mechanisms by which aging increases disease risk are similar for cancer and for CVD. Older people are more likely to be affected by other diseases including obesity and diabetes, which also increase CVD and cancer risk in their own right. Sex hormone levels decrease, some of which are known to be protective against both cancer and CVD. Oxidative stress and inflammation increase with age, which are known risk factor for both diseases, and has been specifically linked to functional and electrical problems in the cardiovascular system (50, 51). Cell damage accumulates over time and can lead to changes in DNA, thus increasing cancer risk (51).

2.1.2.2.2 Genetic predispositions

There is evidence that germline mutations can predispose individuals to cancer and CVD. Germline mutations are in the DNA of reproductive cells and are inherited by offspring (52). For example, mutations of the TTN genome can lead to altered production of the protein titin which impacts tumour microenvironment in many cancers including colorectal cancer (53), and can also increase cardiomyopathy risk (54). In addition, there is now emerging evidence that mutations in the TTN gene could increase risk of cardiotoxicity effects of anti-cancer therapy (55).

There is also evidence that cardiotoxicity of anti-cancer therapy is impacted by epigenetics. For example, mutations in transmembrane proteins that transport anti-cancer drugs can lead to an accumulation of the drug in cardiac cells leading to cardiac dysfunction (56). Mutations in the CRB3 gene have been shown to disrupt the metabolism of anti-cancer anthracycline therapy, leading to decreased left ventricular ejection fraction (57). Anti-HER2 therapy has also been implicated in the development of cardiotoxicity, where the drug-induced interruption in the HER2 pathway can lead to damage of cardiac cells (which are usually protected by the HER2 pathway) (58). A final example of the epigenetic impact of anticancer treatment is the immune dysfunction initiated by immune checkpoint inhibitors (a drug used to improve prognosis in many cancers). These changes to the immune system are associated with immune-related myocarditis (56).

Modifiable risk factors

2.1.2.2.3 Physical inactivity

Physical inactivity is a common risk factor for both cancer and CVD. In 2022, 37% of Australians aged between 18 and 65 did not meet the Australian Physical Activity Guidelines of 150 minutes of moderate to vigorous aerobic exercise each week (59). There is strong evidence that high levels of physical activity (vs lower levels) reduces the risk of many types of cancer, including bladder, breast, colon, endometrial, renal, and gastric with relative risk reductions ranging from 10-20% (60). A large systematic review and meta-analysis involving 136 studies, compared mortality in

people with cancer who engage in high levels of physical activity vs low levels, and found significantly lower mortality risk for higher physical activity (pre-diagnosis physical activity: HR = 0.82, 95% CI = 0.79 to 0.86; post-diagnosis: HR = 0.63, 95% CI = 0.53 to 0.75) (61). There is strong evidence that higher levels of physical activity are associated with a reduced incidence of CVD (62), and evidence suggests a 27% reduction in relative risk of cardiovascular-related mortality in people who are more physically active (63).

2.1.2.2.4 Smoking

Approximately 8% of Australian people reported being daily smokers in 2022/23. Smoking increases with age with around 500,000 Australians aged 60 years or more smoking daily (in 2022-23 (64). Smoking and other tobacco consumption has the greatest impact of all risk factors on disease burden and deaths in Australia, with 13% of all deaths and 8.6% of all disease burden in 2018 being attributed to smoking (65). It is well-established that smoking is a major risk factor for many cancers. For example, a large population-based cohort study involving data from 229,028 Australian residents reported that current smokers had an increased risk of all cancers combined of 1.42 (hazard ratio (HR)) (95% CI:1.34-1.51) (66). Current smokers were also more likely to die of cancer than those who have never smoked (HR: 3.23, $p<0.001$) (66). An Australian population-based cohort study involving 188,167 people also reported increased incident risk of all types of CVD in current vs never smokers of HR: 1.63 (CI: 1.56-1.71). A meta-analysis reported in the same paper indicated a relative risk of 2.75 for death from any CVD for current smokers (compared to never smokers) (67).

2.1.2.2.5 Alcohol consumption

In 2022-23, approximately 31% of people in Australia aged 14 years or older did not meet the Australian guidelines to reduce health risks from drinking alcohol, by either consuming 11 or more standard drinks per week, and/or consuming more than four standard drinks in one day at least once a month (68). People aged 70 years and over are the most likely to drink alcohol daily (69). A meta-analysis including 106 primary studies examining the relationship between alcohol consumption and cancer risk, reported that light to moderate (12.5-24.9 grams/day), moderate to high (25-49.9 grams/day), and heavy (>50 grams/day) consumption of alcohol significantly increased all-cause cancer risk (70). Risk of cancer increased with amount of alcohol consumed, with light to moderate consumption showing a Risk Ratio (RR) of 1.08 (95% CI, 1.04 to 1.12), moderate to heavy RR (95% CI, 1.13 to 1.27), and heavy RR 1.39 (95% CI, 1.29 to 1.49) (70). Likewise, a systematic review involving data from 1,579,435 individuals reported that higher intake of alcohol increases CVD risk and CV-related mortality (71).

2.1.2.2.6 Poor diet

In 2022, 56% of Australians aged 18 years or older did not eat the recommended two servings of fruit each day, and 94% did not eat at least five serves of vegetables. The proportion of energy

consumed through discretionary foods increased between 2018–19 and 2022–23 (72). The role of diet in cancer risk is less well-established in the literature compared to physical inactivity, smoking and alcohol consumption, but there is strong evidence that healthy dietary patterns reduce the risk of breast and colon cancer. There is limited evidence for unhealthy diet as a risk factor for upper digestive tract, pancreatic, ovarian, endometrial and prostate cancers. It is postulated that diet may impact cancer risk through overweight and obesity (73). Healthy dietary patterns also lead to reduced incidence of CVD, e.g., pooled RRs in an umbrella review indicated reduced risk (ranging from 0.55 (CI: 0.39-0.76) to 0.64 (CI: 0.53-0.79) for Mediterranean diets; and 0.70 (CI: 0.57-0.87) for high-quality diets) (74).

2.1.2.2.7 Overweight and obesity

In 2022, 66% of Australians were overweight or obese (75). Overweight and obesity is the second largest risk factor for disease after physical inactivity. A recent review reported that there is evidence that obesity is a risk factor for many cancers including breast, colon, endometrial, kidney and pancreatic cancers, and that body fat above healthy levels leads to up to 17% increased risk of cancer-related death (76). There is strong evidence that obesity increases risk factors of CVD including hypertension and dyslipidaemia, but it is also associated with the incidence of CVD and CVD-related mortality (independent of other CVD risk factors) (77).

2.1.2.2.8 Socioeconomic disadvantage

Socioeconomic disadvantage is commonly associated with poor health. In 2012-2016, cancer incidence was 5% higher in the most disadvantaged areas in Australia (compared to the least disadvantaged areas) (15). Similarly, cancer-related mortality rates were more than 40% higher in the most disadvantaged areas (185 deaths per 100,000) than the least disadvantaged (130 deaths per 100,000) (15). Survival was lower and mortality higher for people in the most disadvantaged areas compared with those in the least disadvantaged areas, with 5-year observed survival rates around 12 percentage points lower (56% compared with 68% in 2012–2016), and cancer mortality rates over 40% higher (185 deaths per 100,000 compared with 130 deaths per 100,000 in 2015–2019). In Australia, people aged 25 years or older living in the most socioeconomically disadvantaged areas were between 1.55 times (males) and 1.76 times (females) more likely to experience heart attack, and stroke incidence was 1.21 times (males) and 1.27 times (females) higher than those in advantaged areas (78). Socioeconomically disadvantaged people are more likely to experience poorer health due to the factors including early life experiences, housing, social capital, employment and social inclusion (i.e., these social determinants of health). The mechanisms through which disadvantage can impact health are multiple, and include education, health literacy, mental health and lifestyle behaviours (78). Population groups historically at higher risk of socio-economic disadvantage, including First Nations people, people living in rural and remote areas, and migrants, are also more likely to experience poor health, including cancer and CVD (15, 78).

2.1.2.3 Shared biological and pathological risk factors of CVD and cancer

Understanding is evolving regarding the biological and pathological processes that may increase the risk of cancer and CVD, including dysfunction affecting immune response, inflammation, platelet and coagulation, and endothelial and cell structure and function (28). These biological and pathological changes can impact the risk of co-existing cancer and CVD because they can a) be induced by an individual disease which then increases risk of the development of the other (e.g., an individual with cancer may experience the biological and pathological changes as a result of the presence of cancer, which in turn increases their risk of developing CVD); and/or b) occur as a result of some of the shared risk factors for both diseases which in turn increases the risk of both diseases developing (e.g., represent a mechanism by which risk factors increase likelihood of cancer and CVD). This section provides a brief overview of some of these processes, but it is beyond the scope of this thesis to describe each of these processes in detail.

Systemic inflammation and oxidative stress are well-established risk factors for CVD and cancer and are reported to be common in many risk factors including physical inactivity, high meat consumption, hypertension and obesity. Inflammation and oxidative stress are closely inter-related, with inflammatory cells releasing reactive species which contribute to oxidative stress, and oxidative stress causing increased transcription factors which lead to inflammation (79). Inflammation and oxidative stress can increase risk through damaging DNA, impacting cell communication, encouraging the growth of tumours, and have been specifically linked to functional and electrical problems in the cardiovascular system (50, 51, 80). Cancer cells also release inflammatory factors, which can promote CVD risk and progression (81).

Several risk factors increase risk of cancer and CVD through genotoxicity leading to changes to DNA including mutations, deletions and insertions. For example, a high-meat diet is thought to increase risk through the introduction genotoxic substances (28), inadequate folate intake can lead to genetic mutations impacting both cell division in the gastrointestinal tract and smooth muscle of blood vessels (28, 82), and acetaldehyde (alcohol metabolite) affects DNA repair and may impact folate and methionine metabolism (83).

Dysregulation in the production and function of hormones (including sex hormones, leptin and insulin), immune cells and cytokines (including interleukin-6) can occur in physical inactivity, poor diet, ageing, diabetes and obesity. There are multiple mechanisms through which these biological factors impact CVD and cancer risk, including for example, sex hormones are involved in increased systemic inflammation, leptin levels impact hepatocellular carcinoma risk via influencing telomerase reverse transcription, and excess interleukin-6 reduces apoptosis of cancer cells and increase resistance to anti-cancer drug therapy (84) and increases inflammatory markers important in CVD (85). Differences in hormone profile explains some of the increased risk in males (compared to females), including that men have higher testosterone levels which may promote cell

growth and lower oestrogen levels which have been shown to be protective against cancer (48). The presence of some CVDs can lead to increased secretions and changes in the immune system that may encourage tumour progression (86-88).

Finally, disordered fatty acid metabolism which can occur due to poor diet and activity behaviours, can lead to tumour growth impact cancer (89), and can impair cardiac function (81).

In summary, Part One has described the problem of reducing the impact of CVD in people with cancer including details of prevalence and incidence and serious outcomes of cancer, CVD and coexisting disease, and why these diseases may coexist. Existing approaches to cardio-oncology have been described. The next section focuses on potential solutions to the problem of CVD in people with cancer.

2.2 PART TWO: Addressing the Problem: Reducing the impact of CVD in people with cancer

This section focuses on how the problem of CVD in cancer can be addressed and includes a summary of the research literature. In particular, guidelines and recommendations for how to address CVD risk in cancer are discussed, including the European Society of Cardiology (ESC) Cardio-oncology guidelines (6), the European Society of Medical Oncology's (ESMO) consensus recommendations for the management of cardiac disease in cancer patients (36), and the ESC Position Paper on cancer treatments and cardiovascular toxicity (32). In addition, documents with a broader focus are discussed with regard to how they can be applied to CVD care in cancer, including Nekhlyudov et al.'s Cancer Survivorship Care Quality Framework (90), the Clinical Oncology Society of Australia (COSA) Model of Survivorship Care (91), and the Australian Cancer Plan (18). Next, existing and potential approaches to reducing the impact of CVD in cancer are discussed, including cardio-oncology clinics and clinical pathways; and factors/concepts that should shape new approaches including lifestyle behaviour optimisation, self-management, patient education, and CVD risk prediction tools. A summary of the gaps in literature is presented as well as a detailed description of what is needed to address these gaps. Finally, a description of the scope and approach (including methodology) of the research program reported in this thesis is provided.

2.2.1 Guidelines and recommendations for CVD care in cancer

Evidence for the impact of CVD in cancer has led to the development of guidelines and recommendations for best practice in the provision of CVD care in cancer. Most notable are the ESC Cardio-oncology guidelines (6), but other guidance documents include the Management of cardiac disease in cancer patients throughout oncological treatment: ESMO Consensus Recommendations (36), and the ESC Position Paper on cancer treatments and cardiovascular toxicity (32). More broadly, models, frameworks and plans have been developed that can be

applied to CVD care in cancer, including Nekhlyudov et al.'s Cancer Survivorship Care Quality Framework (90), the COSA Model of Survivorship Care: Critical Components of Cancer Survivorship Care in Australia (91), and the Australian Cancer Plan (18). Cancer survivorship refers to the focus on the health and wellbeing of people diagnosed with cancer from the point when they are diagnosed to the end of life (92), whilst supportive care in cancer refers to the provision of resources and care to assist the management of effects of cancer and anti-cancer therapy (93). A brief summary of these documents is provided below, with particular reference to cardio-oncology.

2.2.1.1 The ESC Cardio-oncology Guidelines

In 2022, the European Society of Cardiology (ESC) established a Task Force of cardio-oncology experts including those from the European Hematology Association (EHA), the European Society for Therapeutic Radiology and Oncology (ESTRO) and the International Cardio-Oncology Society (IC-OS). Together they developed the first ESC cardio-oncology guidelines (6). The guidelines were developed to assist clinicians to provide individualised CVD care to people with cancer through all stages of cancer treatment, with the main focus being on preventing and managing cancer therapy-related cardiovascular toxicity (CTR-CVT). In addition, these recommendations should be used to inform the conceptualisation, development and implementation of interventions and services to reduce the impact of CVD in cancer, increasing the likelihood of a consistent evidence-based approach across diverse health services. The comprehensive guidelines are presented using text, tables, graphics and videos in order to optimise user engagement, and supplementary resources (e.g., webinars, patient guidelines etc.) continue to be released to improve translation to practice. The ESC guidelines are well-established as the key guidance for addressing CVD risk in cancer, and this reflected in the voluminous literature describing how the recommendations inform clinical practice, research and policy.

The ESC guidelines provide 272 recommendations relating to CTR-CVT definitions, assessing CVD risk before anti-cancer therapy, preventing and monitoring cardiovascular risk during anti-cancer therapy, diagnosing and managing CVD and CVD risk during anti-cancer therapy, assessing CVD risk once anti-cancer therapy ceases, following up patients who have received cardiotoxic treatment to assess and manage CVD and CVD, considering individualised needs of special populations, providing information to and communicating with patients including supporting self-management, and how scientific organisations should be involved in reducing the impact of CVD (6). Table 2 shows the topics addressed in the ESC guidelines, along with examples of recommendations associated with each topic.

The recommendations were developed based on a thorough review of the relevant literature, including assessment of the quality and strength of evidence. Where evidence was unavailable to inform specific guidance regarding CVD risk assessment, treatment and prevention, the ESC

guidelines made recommendations based on expert consensus. An important limitation of the guidelines is that, of the 272 recommendations made in the ESC guidelines, only seven were supported by Level A evidence (i.e., data from multiple RCTs and meta-analyses). Fifty-seven had Level B evidence, which describes evidence from one RCT or a large non-randomised trial, and the remaining 208 (76%) of recommendations were supported by Level 3 evidence which is described as being low/very low level of evidence which comes from case studies, retrospective studies, or registries, or were developed based on expert opinion. The limited number of recommendations that are supported by data from high quality research may affect clinicians' confidence to make recommendations (94). Clinicians should be encouraged to continue to apply clinical judgement in their application of recommendations, and the guidelines must continually be updated as new evidence emerges (94). However, the ESC guidelines represent the most up-to-date and comprehensive set of recommendations to guide clinicians providing CVD care. The decision to develop recommendations based on low levels of evidence is reflective of the well-established need for clinician guidance in order to reduce the impact of CVD in cancer.

The ESC guidelines are targeted at clinicians (although a short and simple brochure has been developed for people diagnosed with cancer) and are therefore focused on guiding decision-making by health care providers, including advice about appropriate imaging choices for diagnosis and monitoring, and pharmacological intervention for management. There is a lack of detailed information and guidance about self-management (including self-management support to be provided by health care providers) and lifestyle interventions.

Table 2 - Summary of content of European Society of Cardiology Cardio-oncology Guidelines (6)

Section	**Purpose**	**Recommendations (example of recommendation)**
Chapter 3: Cancer therapy-related cardiovascular toxicity definitions	For consistency in terminologies and definitions related to CVRCT.	15 definitions related to CTR-CVT, myocarditis, vascular toxicity, arterial hypertension, and cardiac arrhythmias (e.g., Asymptomatic CTR-CVT definition: New left ventricular ejection fraction reduction to <40%).
Chapter 4: Cardiovascular toxicity risk stratification before anticancer therapy	To guide clinicians regarding how they should undertake CVD risk assessment and stratification before anticancer therapy, so that timely prevention strategies can be implemented.	• 8 recommendations for a general approach to CVD risk categorization. • 2 recommendations for electrocardiogram baseline assessment. • 1 recommendation for cardiac biomarker assessment prior to potentially cardiotoxic therapies. • 6 recommendations for cardiac imaging modalities in patients with cancer. *(Example recommendation: Cardiology referral is recommended in high-risk and very high-risk patients before anticancer therapy)*
Chapter 5: Prevention and monitoring of cardiovascular complications during cancer therapy	To guide clinicians regarding how to undertake tasks to improve primary prevention and monitoring of CVD-related complications.	• 6 recommendations for primary prevention of cancer therapy-related cardiovascular toxicity. • 1 recommendation for secondary prevention of cancer therapy-related cardiovascular toxicity. • 10 recommendations for baseline risk assessment and monitoring during anthracycline chemotherapy and in the first 12 months after therapy. • 10 recommendations for baseline risk assessment and monitoring during human epidermal receptor 2-targeted therapies and in the first 12 months after therapy. • 3 recommendations for baseline risk assessment and monitoring during fluoropyrimidine therapy. • 10 recommendations for baseline risk assessment and monitoring during vascular endothelial growth factor inhibitors. • 8 recommendations for baseline risk assessment and monitoring during second- and third-generation breakpoint cluster region–Abelson oncogene locus tyrosine kinase inhibitors. • 5 recommendations for baseline risk assessment and monitoring during Bruton tyrosine kinase inhibitor therapy. • 14 recommendations for baseline risk assessment and monitoring during multiple myeloma therapies.

		• 5 recommendations for baseline risk assessment and monitoring during combined rapidly accelerated fibrosarcoma and mitogen-activated extracellular signal-regulated kinase inhibitor therapy. • 6 recommendations for baseline risk assessment and monitoring during immunotherapy. • 4 recommendations for baseline risk assessment and monitoring during androgen deprivation therapy for prostate cancer. • 3 recommendations for baseline risk assessment and monitoring during endocrine therapy for breast cancer. • 3 recommendations for baseline risk assessment and monitoring during cyclin-dependent kinase 4/6 inhibitor therapy. • 6 recommendations for baseline risk assessment and monitoring during anaplastic lymphoma kinase and epidermal growth factor receptor inhibitors. • 4 recommendations for baseline risk assessment and monitoring in patients receiving chimeric antigen receptor T cell and tumour-infiltrating lymphocytes therapies. • 2 recommendations for baseline risk assessment of patients before radiotherapy to a volume including the heart. • 3 recommendations for baseline risk assessment in haematopoietic stem cell transplantation patients. *(Example recommendation: Baseline echocardiography is recommended before HER2-targeted therapies in all patients)*
Chapter 6: Diagnosis and management of acute and subacute cardiovascular toxicity in patients receiving anticancer treatment	To guide clinicians regarding how to diagnose and manage CVD related toxicities and complications during anti-cancer therapy.	• 1 recommendation for the management of cardiovascular disease and cancer therapy-related cardiovascular toxicity in patients receiving anticancer treatment. • 12 recommendations for the management of cancer treatment-related cardiac dysfunction during anthracycline chemotherapy. • 10 recommendations for the management of cancer treatment-related cardiac dysfunction during human epidermal receptor 2-targeted therapies. • 12 recommendations for the diagnosis and management of immune checkpoint inhibitor-associated myocarditis. • 3 recommendations for the diagnosis and management of Takotsubo syndrome in patients with cancer.

		• 7 recommendations for the management of acute coronary syndromes in patients receiving anticancer treatment. • 1 recommendation for the management of chronic coronary syndromes in patients receiving anticancer treatment. • 2 recommendations for the management of valvular heart disease in patients receiving anticancer treatment. • 10 recommendations for the management of atrial fibrillation in patients receiving anticancer treatment. • 8 recommendations for the management of long corrected QT interval and ventricular arrhythmias in patients receiving anticancer treatment. • 9 recommendations for the management of arterial hypertension in patients receiving anticancer treatment. • 5 recommendations for the management of venous thromboembolism in patients receiving anticancer treatment. • 4 recommendations for venous thromboembolism prophylaxis during anticancer treatment. • 1 recommendation for management of peripheral artery disease during anticancer treatment. • 3 recommendations for the management of pulmonary hypertension during anticancer treatment. • 7 recommendations for the management of pericardial diseases in patients receiving anticancer treatment. *(Example recommendation: Effective treatment of cancer therapy-induced arterial hypertension to prevent cancer treatment interruption and cardiovascular complications is recommended.)*
Chapter 7: End-of-cancer therapy cardiovascular risk assessment	To guide clinicians regarding CVD risk assessment at the end of anti-cancer therapy.	• 7 recommendations for end-of-cancer therapy cardiovascular risk assessment. *(Example recommendation: Educating and supporting patients with cancer to make appropriate healthy lifestyle choices is recommended.)*
Chapter 8: Long-term follow-up and chronic cardiovascular complications in cancer survivors	To guide clinicians about how to conduct long-term follow-up of people who have been treated with anti-cancer therapies, including to manage chronic CVD complications and to assess risk of those	• 5 recommendations for cardiovascular surveillance in asymptomatic adults who are childhood and adolescent cancer survivors. • 8 recommendations for cardiovascular surveillance in asymptomatic adult cancer survivors. • 2 recommendations for adult cancer survivors who develop cancer therapy-related cardiac dysfunction late after cardiotoxic cancer therapy.

	who have not been diagnosed with CVD yet but who may be at risk.	• 4 recommendations for adult cancer survivors with coronary artery disease. • 2 recommendations for adult cancer survivors with valvular heart disease. • 1 recommendation for adult cancer survivors with pericardial complications. • 5 recommendations for cardiovascular monitoring in cancer survivors during pregnancy. *(Example recommendation: Echocardiography may be considered every 5 years in asymptomatic moderate-risk adult cancer survivors.)*
Chapter 9: Special populations	To provide guidance to clinicians for how CVD care should be individualised for special populations who may have different characteristics and therefore different care needs compared to the typical cancer population.	• 4 recommendations for cardiovascular assessment and monitoring of pregnant women with cancer. • 6 recommendations for carcinoid valvular heart diseases. • 4 recommendations for amyloid light-chain cardiac amyloidosis diagnosis and monitoring. • 3 recommendations for risk stratification and monitoring for patients with cardiac implantable electronic devices undergoing radiotherapy. *(Example recommendation: Cardiac magnetic resonance is recommended in patients with suspected amyloid light-chain cardiac amyloidosis).*
Chapter 10: Patient information, communication, and self-management	To describe with what type of, and how, cancer survivors should be provided with information, support and communication, including supporting patients to self-manage aspects of their health and disease.	No specific recommendations.
Chapter 11: The role of scientific societies in the promotion and development of cardio-oncology in modern medicine	To describe the roles of scientific societies in clinical research, education and advocacy to promote and develop cardio-oncology care.	No specific recommendations.

Table Notes: CTR-CVT, Cancer Therapy-Related Cardiovascular Toxicity; HER-2, Human Epidermal Growth Factor Receptor 2.

2.2.1.2 Management of cardiac disease in cancer patients throughout oncological treatment: ESMO (European Society of Medical Oncology) Consensus Recommendations

In 2020, ESMO developed consensus recommendations which included a total of 39 recommendations for best practice for the care of people at risk of cardiotoxicity from anti-cancer treatment (36). The recommendations were informed by a comprehensive process involving an expert panel consisting of multidisciplinary representatives from cardiology and oncology. Over four years, a literature review of the evidence was conducted followed by a series of consensus discussions informing the development of 39 recommendations on prevention of cardiotoxicity, screening for CVD, monitoring and treatment. The recommendations addressed eight cardiotoxicity topics: collaborative approach, screening before anticancer therapy, primary prevention therapy, during cancer treatment: cardiac safety surveillance, asymptomatic, new laboratory abnormalities (or preclinical toxicity), clinical cardiac dysfunction, post-treatment: survivors of anticancer therapy and immune checkpoint inhibitor-associated CV toxicity. Levels of evidence and grades of recommendations were assigned, with 16 recommendations having an 'A' grade of recommendation (strong evidence for efficacy with a substantial clinical benefit, 'strongly recommended', and 12 based on Level 1 evidence (from at least one large RCT of good methodological quality or meta-analyses of good quality RCTs) (36). These ESMO consensus recommendations were developed to support and guide decision-making by clinicians which is critical to reduce the impact of CVD in cancer. Barriers to implementation of guidelines include that clinicians need adequate time and resources to engage with the guidelines and translate them into practice. Likewise, each setting is different and this can impact the transferability of recommendations. Finally, the recommendations focus on the impact of cardiotoxicity (with less focus on the impact of shared risk factors on the coexistence of cancer and CVD. Self-management (support) and lifestyle behaviour-change are not addressed in any meaningful way in the recommendations.

2.2.1.3 European Society of Cardiology Position Paper on cancer treatments and cardiovascular toxicity

In 2016, the ESC developed the first position paper regarding the cardiotoxicity of anti-cancer treatments. The position statements were developed by a Task Force for cancer treatments and cardiovascular toxicity of the ESC, which consisted of experts in cardiology and oncology from multidisciplinary professions who were involved in a comprehensive review of the literature as well as discussions regarding cardio-oncology practice. This document did not make specific recommendations and is not considered clinical practice guidelines. The aim was to guide clinicians by providing statements of expert consensus to support their application of clinical judgement. Position statements addressed cardiovascular complications of cancer therapy: pathophysiology and management, strategies for prevention and attenuation of cardiovascular complications of cancer therapy, and long-term surveillance programmes for cancer survivors. This

position paper did address information provision to patients, not how or by whom CVD care can be delivered.

2.2.1.4 Cancer Survivorship Care Quality Framework

In 2019, Nekhlyudov et al. (90) developed the comprehensive, evidence-based Cancer Survivorship Care Quality Framework in order to develop quality measures for survivorship care (90) (see Figure 1). A comprehensive process was undertaken to develop the framework involving a review of previous survivorship guidelines, disease-related guidelines, relevant United States (US) grants funded in the previous year, US state cancer control plans, and quality measures endorsed by US and European healthcare organisations. Cancer survivor network online communication was reviewed to identify any survivorship information not covered by the abovementioned literature reviews. Quality of care literature was reviewed through considering seminal papers. The final framework was developed after multiple and iterative rounds of the literature review and a series of discussions amongst the project team. As shown in Figure 1, the framework illustrates how policy, community, organisational, interpersonal and individual factors influence five key quality indicators of effective healthcare delivery in cancer, i.e., recurrences and new cancers, physical effects, psychosocial effects, health promotion and chronic conditions, which in turn impact health-related quality of life and function, emergency services and hospitalisations, costs and mortality outcomes. For each quality indicator, dot points add detail for how and what is involved in surveillance and management. In regard to cardio-oncology, the quality indicator of greatest relevance is chronic conditions in which the framework argues for the importance of evaluation and treatment of non-cancer medical conditions. In addition, health promotion is relevant to cardio-oncology, which references the importance of engaging in prevention activities including lifestyle behaviour optimisation (90).

Although it is possible to identify aspects of the Cancer Survivorship Care Quality Framework that are relevant to CVD care in cancer, it is also important to point out that cardio-oncology is not explicitly mentioned in the Framework and thus it could be argued that cardio-oncology is not yet a well-established component of what is considered to constitute survivorship care more broadly.

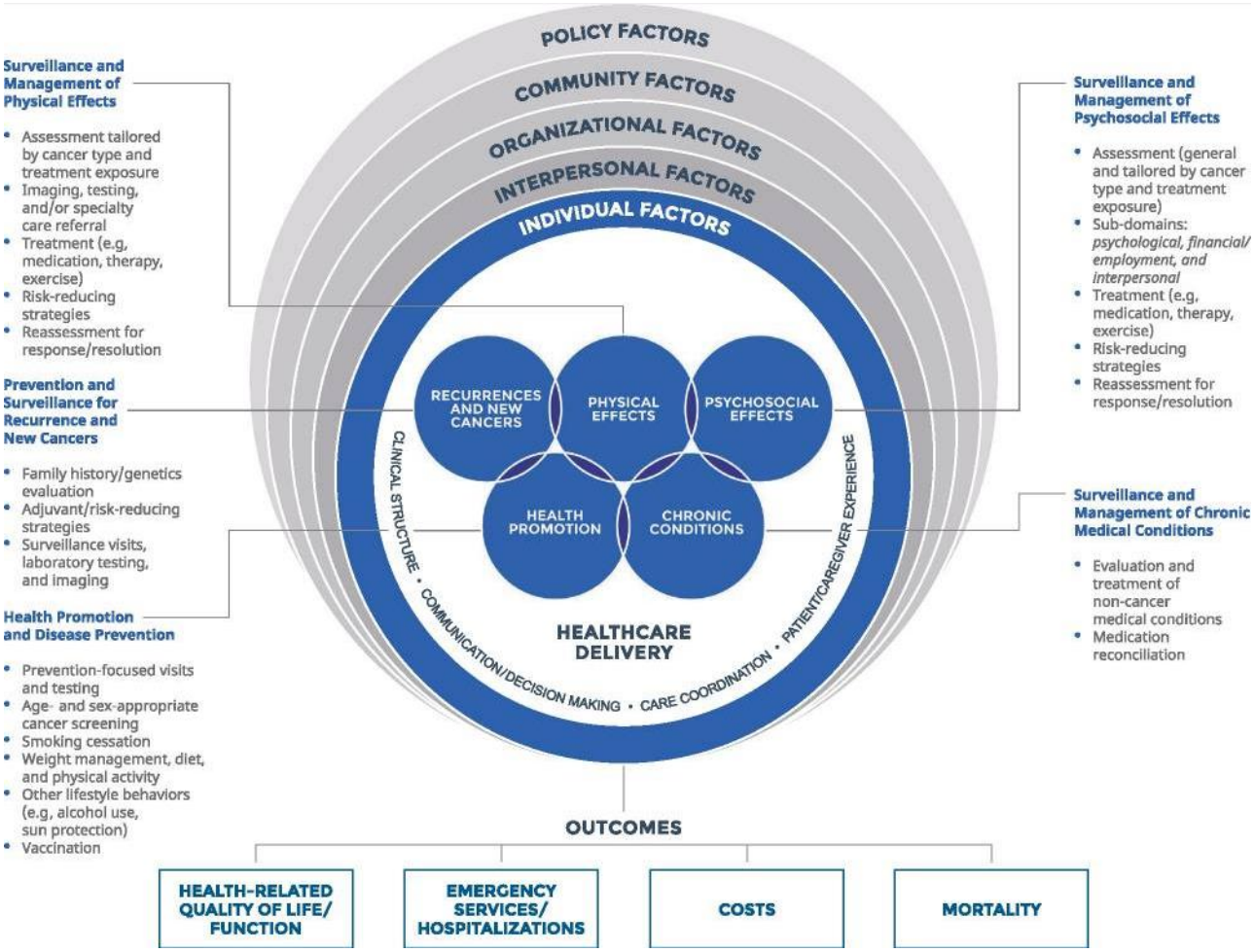


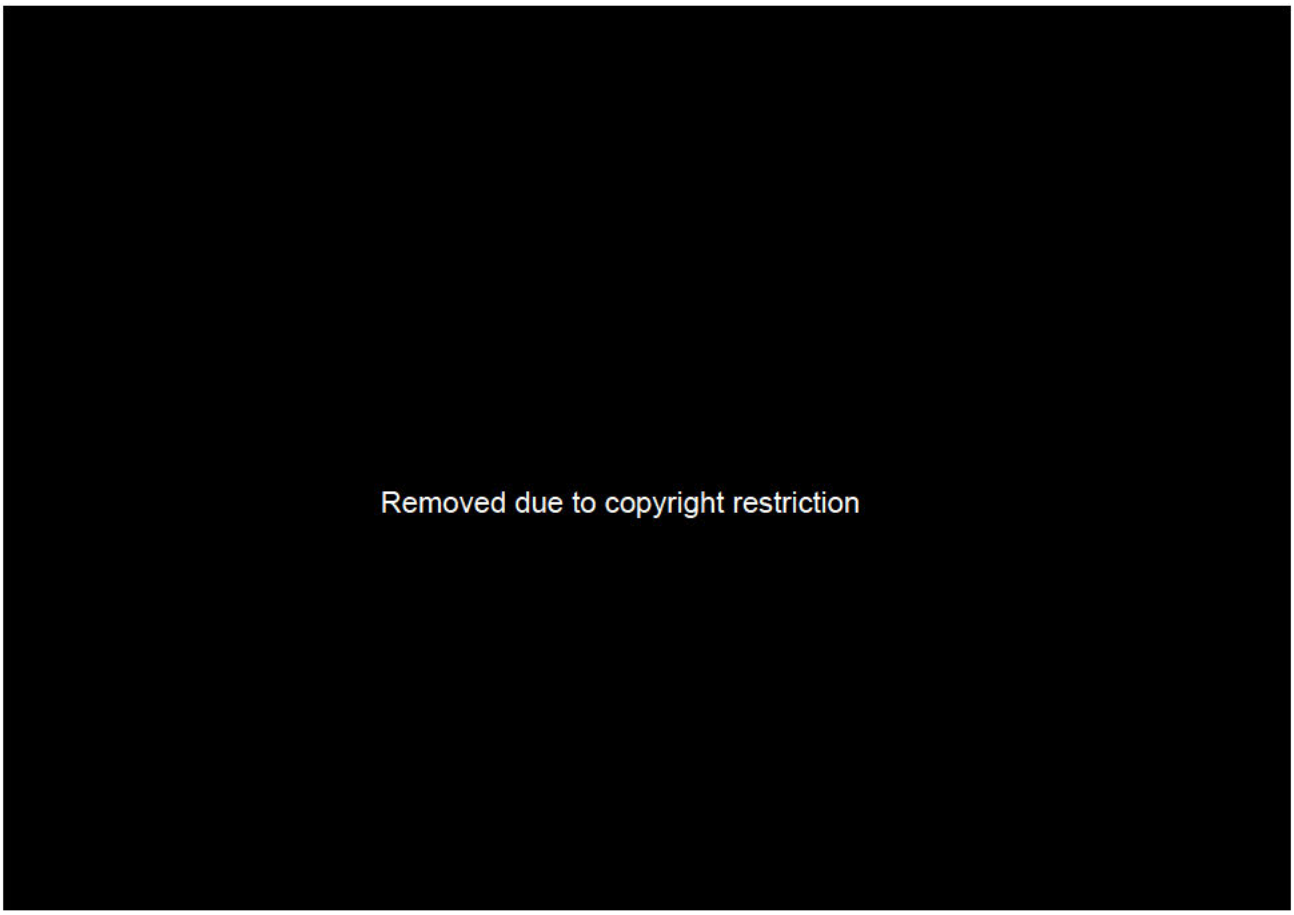
Figure 1 - Cancer Survivorship Care Quality Framework (90) (reproduced with permission from Oxford Academic)

2.2.1.5 COSA Model of Survivorship Care

In 2016, COSA undertook a comprehensive process to develop a model to guide survivorship care. As shown in Figure 2, the principles of the model include personalised care, wellness, survivorship care plan, access to services, and a multidisciplinary approach. The model recommends needs assessment to identify individuals' issues for which survivorship care is needed, risk stratification, development of a care plan to address needs, care coordination, and follow-up. The model highlights the importance of engagement of the individual diagnosed with cancer, the community and healthcare professionals as being critical in achieving quality survivorship care. The COSA model of survivorship care can be applied to the issue of CVD risk – where it is critical to assess needs for CVD care, stratify risk (the model specifies comorbidity as an example of risk stratification), develop a care plan based on needs and coordinate that care. Education and rehabilitation (addressing effects of anti-cancer treatment) are identified as critical after needs assessment, with lifestyle and behaviour being key examples (91). In line with cardio-oncology guidelines, care plans and coordination are determined by the level of risk and may include self-management, monitoring for changes and referral to appropriate professionals, e.g., cardiologist

for CVD management or allied health professionals to assist in behavioural change for prevention or management of CVD risk.

As per the Cancer Survivorship Care Quality Framework, it could be argued that although the application of guidance provided by the COSA Model of Survivorship Care could be applied to CVD risk management, the lack of cardio-oncology being explicitly mentioned in the model could be seen as an important gap affecting awareness and adequate care.



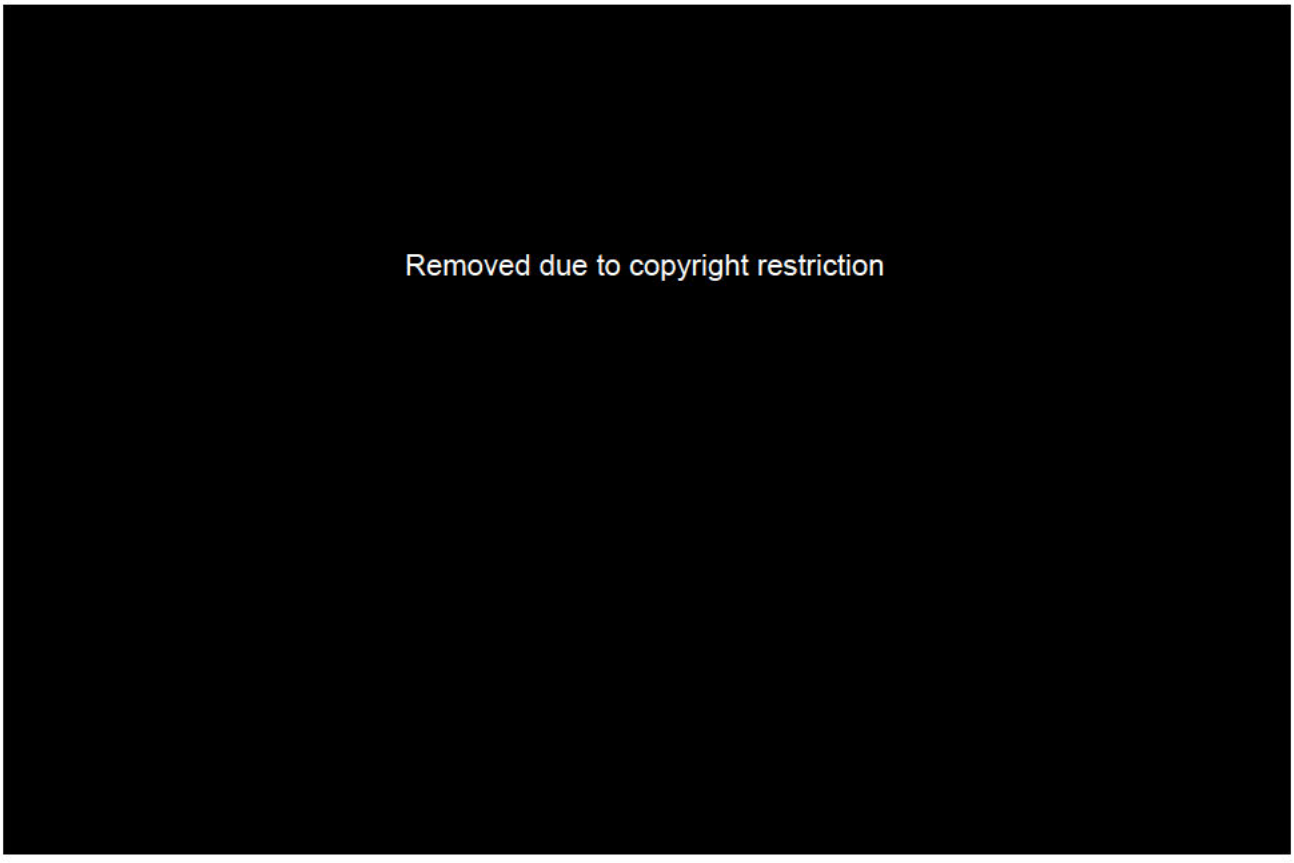


Figure 2 - COSA Model of Survivorship Care (91)

2.2.1.6 Australian Cancer Plan

Released in 2023, the Australian Cancer Plan (the Plan) defines a ten-year strategy to improve the care of people with cancer, with a key focus on equity of care. The Plan is informed by evidence and included rigorous and meaningful consultation with all key stakeholders in cancer, including researchers, clinicians, managers and patients. The Plan provides a structure that aims to guide a coordinated approach by all members of the cancer community to contribute to improved cancer care. The strategic objectives relate to improving cancer prevention and early detection, consumer experience, health systems, infrastructure, workforce and equity. As per all components of cancer care, the Australian Cancer Plan should inform the optimisation of CVD care for people with cancer through influencing the components addressed by the strategic objectives. In addition, the Australian Cancer Plan specifically highlights how comorbidities can adversely impact outcomes for people diagnosed with cancer and asserts the importance of ensuring care is individualised based on specific needs including comorbidity. However, there is no explicit mention of CVD risk in cancer or recommendations for management.

2.2.1.7 Summary of guidelines and recommendations for CVD care in cancer

Multiple evidence-informed guidelines and recommendations have been developed with a specific focus on the implementation of effective CVD care, including the 2022 ESC guidelines for cardio-oncology, the 2020 ESMO consensus recommendations for the management of cardiac disease in cancer patients throughout oncological treatment, and the 2016 ESC Position Paper on cancer treatments and cardiovascular toxicity. In addition, there are several guidance documents with a broader focus on cancer, supportive care and self-management, which can be applied to develop and implement approaches aiming to reduce the impact of CVD in cancer, including the Cancer Survivorship Care Quality Framework, the COSA Model of Survivorship Care and the Australian Cancer Plan. The existence of multiple guidelines underscores that CVD risk is appreciated as an important and significant issue for people who have been diagnosed with cancer and is a complex problem requiring a comprehensive, strategic and coordinated approach to reduce its impact.

However, despite the existence of multiple guidelines and models relevant to cardio-oncology (particularly the ESC guidelines), CVD risk remains a significant problem for people who have been diagnosed with cancer suggesting inadequate translation of evidence into practice. Knowledge translation requires effective dissemination of information to increase awareness, as well as the development and implementation of interventions and approaches which facilitate translation of evidence into practical actions in clinical settings. Although the cardio-oncology guidelines discussed in this section provide comprehensive guidance regarding the aspects of effective assessment and management of CVD risk, there remains a distinct gap (which is evident from the lack of explicit mention of cardio-oncology in models/frameworks for cancer survivorship, and in the Australian Cancer Plan) regarding the way in which these can be achieved in various contexts, i.e., when, how and by whom should tasks related to CVD care be implemented, and who

will be involved in the coordinate, monitor and evaluate if these have been enacted and successful. Interventions and approaches are required to facilitate the translation of evidence and guidance into clinical practice. Some existing and potential interventions (and components/principles to be included in interventions) are introduced below and are discussed with regard to their promise for contributing to an effective approach to reduce the impact of CVD in cancer.

2.2.2 Existing and potential approaches to CVD care in cancer

Several approaches have been reported in the cardio-oncology literature as having the potential to reduce the impact of CVD in cancer, including cardio-oncology clinics, referral pathways and models of care. In addition, lifestyle behaviour change, self-management, education and risk prediction tools have been earmarked as important components in effective CVD care. A brief description of existing and potential approaches to CVD care is provided below, along with discussion regarding potential benefits and challenges of their implementation.

2.2.2.1 Cardio-oncology clinics

Cardio-oncology clinics are specialised services which solely focus on managing CVD risk in people with cancer. This may involve assessing CVD risk before treatment, monitoring risk during treatment and providing support to manage risk (95). Cardio-oncology clinic workforces are typically multi-disciplinary and may consist of oncologists, cardiologists, nurses and allied health professionals including exercise and diet professionals who may have received specialised cardio-oncology training. The International Cardio-Oncology Society (ICOS) is the only organisation to provide certification for professionals who can then identify themselves as having up-to-date evidence-based knowledge and clinical experience in cardio-oncology. In addition, ICOS provides a certification of cardio-oncology services to indicate organisations that have expertise in providing CVD care to people with cancer. There are over 100 cardio-oncology organisations listed on the ICOS website, with over 70 that are ICOS-certified centres of excellence (95). In Australia, there are 10 centres of excellence and 11 clinicians recognised as cardio-oncologists as per the ICOS qualification requirements. There is a lack of evidence regarding the outcomes associated with receiving clinical services/intervention from cardio-oncology clinics (especially in comparison to usual care) (7). However, of the limited evidence it appears that cardio-oncology clinics can improve cardiovascular profile and reduce interruption/discontinuation of anti-cancer treatment (7). In addition, a qualitative study of patient's perceptions found that accessing a cardio-oncology clinic promoted information and understanding about CVD risk, that the cardio-oncology clinic service necessitated collaboration between multidisciplinary clinicians and this resulted in better care, and that patients felt more comfortable that their CVD risk was being managed so they could continue anti-cancer treatment (96).

Despite a growing number of cardio-oncology clinics and potential positive patient outcomes, the majority of cancer patients receive care through an oncology or cardiology service, or not at all (6).

Barriers to the development and implementation of cardio-oncology clinics include lack of funding, a lack of clinicians with expertise/interest in cardio-oncology, lack of infrastructure, and a lack of certainty in clinical standards and best practice (97). Enablers include education of staff/workforce, workplace support and cooperation, community outreach and effective referral pathways (97). In summary, although cardio-oncology clinics can provide patients with specialised care that may not be possible in oncology, cardiology or general practice settings, there are significant barriers to their implementation and the evidence base for improved outcomes may not be convincing enough to justify what is required to overcome significant cost, workforce and infrastructure barriers. In particular, more qualitative data derived from cancer stakeholders (including people affected by cancer, clinicians, and health system administrators and managers) is needed to understand if cardio-oncology clinics are viewed as promising once barriers and potential benefits are weighed against one another.

2.2.2.2 Cardio-oncology clinical care pathways

Clinical care pathways are developed and implemented in an attempt to improve particular health outcomes by applying evidence-based clinical guidelines in a local context. Clinical pathways are detailed descriptions or plans for how multidisciplinary care should be provided according to individual needs and organisational resources in order to provided standardised care for the target population (98). In the context of cardio-oncology, a clinical care pathway would include components of CVD risk assessment; risk stratification as low, medium or high risk of cardiotoxicity; monitoring for CV complications, and recommendations for CVD risk management according to risk (8). The specific aspects of the pathway will vary by health service. For example, Pons-Riverola et al. (8) presented a cardio-oncology clinical care pathway that specified that before treatment a complete CV risk assessment would include imaging and biomarker measurements to identify risk and pre-existing disease and findings would inform surveillance approach and anti-cancer therapy approach. During treatment all patients engage in CVD prevention and are monitored/reassessed for signs of CVD and CVD risk. Patients at high/very high risk of CVD (according to assessment before/during treatment) undergo increased surveillance for CVD, and risk/presence of CVD informs decisions regarding early CVD treatment and anti-cancer treatment interruption. Risk assessment is also conducted after anti-cancer treatment and managed via the clinic Survivorship Program (8). Benefits of cardio-oncology clinical care pathways are that they are tailored to the specific health service and context (e.g., available resources, workforce), they provide a standardised care for the service population and can make clinicians more confident given their role and tasks are well-defined. Well-defined clinical pathways can address common barriers to cardio-oncology care including variations across health services with regard to the availability of resources for cardio-oncology, and clinician's perceptions around lack of training and role definition. Barriers to cardio-oncology clinical care pathways are that they require the workforce and leaders to be aware of, and have time to follow, the pathway. In addition,

workforce and resources change over time making existing pathways inappropriate for new circumstances. Clinical care pathways require effective communication amongst members of the workforce, which can be affected by lack of time and clinicians working at different sites (8). Unfortunately, the literature is limited with regard to the prevalence and details of clinical pathways being implemented to improve CVD care in cancer. In summary, clinical care pathways have the potential to facilitate a teams-based approach to CVD care in which clinicians have well-defined roles, but in order to work effectively they need to be specific to the context/setting in which they are being implemented and rely on communication and a stable workforce. Although there is a lack of evidence for their effectiveness in cardio-oncology, clinical care pathways could represent a promising approach if clinicians, administrators and managers are engaged in their development and implementation.

2.2.2.3 Lifestyle behaviour optimisation

Optimisation of lifestyle behaviours including physical activity, diet, smoking, alcohol consumption and stress management is posited as a critical component in approaches to reduce the impact of CVD in cancer. For example, the ESC guidelines on cardio-oncology recommend educating and supporting patients with cancer to make appropriate healthy lifestyle choices, including managing hypertension, dyslipidaemia, smoking cessation, weight loss where needed, and exercise. However, this recommendation was derived from Level 3 evidence, which is described as low/very low level of evidence which comes from case studies, retrospective studies, or registries, or developed based on expert opinion. However, multiple randomised studies demonstrated benefits on cardiovascular outcomes, including cardiorespiratory fitness, cardiac and vascular function and the reduction of CVD risk factors, in a range of cancer populations (99). Limited observational data exists for all lifestyle behaviours, , such as Cao et al.'s. analysis of data from 432,700 people contributing to UK Biobank which reported that a healthy lifestyle (calculated as an index based on smoking, physical activity, diet, alcohol consumption and sleep behaviours) significantly reduced the risk of CVD development in people with cancer (100). In summary, although ESC recommendations to optimise lifestyle behaviour are based predominantly on observational data showing healthy lifestyle reduces CVD risk in cancer, there is evidence from experimental studies showing benefits of exercise in CVD outcomes in cancer. In addition, there is strong evidence that healthy lifestyle is linked to prevention, management and improved outcomes in each of these diseases when examined separately.

2.2.2.4 Self-management

Self-management can be defined as "the individual's ability to manage the symptoms, treatment, physical and psychosocial consequences and lifestyle changes inherent in living with a chronic disease" (101). In the context of cancer, this may include managing symptoms of cancer and anti-cancer treatment toxicities, optimise their lifestyle-related behaviours including physical activity and diet, coping with psychological difficulties arising from the experience of cancer and managing

therapeutic/follow-up regimes (102). In addition, people who have been diagnosed with cancer are expected to be involved in managing comorbidity, including CVD risk (102). Self-management has been shown to reduce physical and psychological symptom severity and improve QoL and self-efficacy in cancer (103-105).

Although the ESC guidelines on cardio-oncology do not specifically use the term self-management, several recommendations related to risk assessment, monitoring and management align with self-management principles. For example, cancer survivors are encouraged to measure their own blood pressure daily, and to monitor for CVD symptoms and report them to their healthcare team (6). In addition, although there is a lack of evidence reporting the effectiveness of self-management interventions to reduce the impact of CVD in cancer, the importance of self-management is well-established in the broader cancer (and general chronic disease) literature. A recent systematic review of 42 studies evaluating the impact of self-management interventions in cancer found that self-management improves patient experience of physical and psychological symptoms including pain, fatigue and emotional distress, and improves QoL (106). Strong evidence for the role of self-management in cancer led to a 'call-to-action' from cancer self-management experts in which they put forth priority areas for optimising self-management in order to improve outcomes for cancer survivors (102). A comprehensive approach to improving CVD care in cancer should aim to incorporate all six priority areas: preparation of patients to engage in self-management; enable patients to be involved in shaping how cancer care providers provide self-management support; prepare the workforce to enable self-management; identify and implement approach to evaluate self-management support; better understand self-management and self-management support through research; and increase access to self-management support programs that are individualised according to patient need (106). However, the literature outlines that there are challenges to engaging in self-management for people with cancer including lack of confidence, reductions in function and managing multiple chronic diseases concurrently (107-109).

2.2.2.5 Patient education

Patient education increases awareness and understanding, is a key component of many healthcare interventions, and has been shown to improve patient satisfaction, mood, coping and communication (110). There is evidence that some people with cancer lack understanding and awareness of CVD risk and management, highlighting the appropriateness of education interventions to improve patient outcomes. For example, in a 2020 analysis of survey data from 6,391 of people living in the US who have been diagnosed with breast, prostate, colorectal or gynaecological cancer, 23% responded that they didn't understand their risk of heart disease and 17% weren't sure about what they needed to do to look after their heart health (111). The importance of educating people with cancer regarding CVD risk is also communicated throughout the ESC guidelines on cardio-oncology (6). For example, the ESC recommends patients be educated regarding their own specific CVD risk profile, the role of a healthy lifestyle in managing

CVD risk and how to identify CVD signs and symptoms. Despite recommendations for the importance of education in cardio-oncology, an audit of Australian resources designed to provide information to people with cancer about CVD risk found only three online resources that solely focused on CVD risk in cancer (112). Resources had important limitations including poor readability and actionability and lacked cultural relevance to First nations people. Patient education relating to CVD risk in cancer should be tailored to individual needs and preferences to avoid challenges including informational overload which can cause the patient to feel overwhelmed and stressed (113).

2.2.2.6 CVD risk prediction tools

In healthcare, risk prediction tools are developed to identify an individual's risk for experiencing an unfavourable health event/outcome. Tools are underpinned by an algorithm/model that uses data (e.g., patient health data) to calculate risk which can be used to inform healthcare and improve outcomes (114). Multiple risk prediction tools exist to predict incident risk of cancer, e.g., a recent review identified 14 models developed to predict risk of oral cancer (115), and whilst Kim et al.'s 2021 review of breast cancer risk prediction models found eight (116). Risk prediction models for identifying risk of CVD in the general population are numerous and continue to be developed, e.g., Framingham (117), PREDICT (118), Systematic Coronary Risk Evaluation (SCORE) (119). However, many are not validated in people with cancer. In fact, studies evaluating the accuracy of cardiovascular risk prediction models in cancer populations have found they performed worse and underpredicted risk, particularly in haematological cancer populations and in the prediction of stroke in cancer patients (120, 121). These findings suggest that new risk prediction tools should be developed in order to predict CVD specifically in cancer populations. In addition, there is a call to include cancer history in new CVD risk prediction models to be applied to the general population (i.e. including people with cancer and people without), given the strong evidence that cancer increases CVD risk (122, 123). Our team developed and validated the first risk equation to predict cardiovascular outcomes in people with cancer (9, 10). This model involved five predictors of cardiometabolic risk of mortality in older cancer survivors: age, sex, history of cerebrovascular event, smoking and physical activity which together predict the cardiovascular-related mortality in older people with cancer (9, 10). The Heart Failure Association- International Cardio-Oncology Society (HFA-ICOS) (as proposed in the ESC guidelines) developed a risk prediction tool that is used to identify CVD risk in people diagnosed with cancer before they begin anti-cancer therapy. The HFA-ICOS tool integrates data from cardiac investigations such as echocardiography, cardiovascular history, patient-level CVD risk factors and cancer therapy. It categorises people as low, moderate or high/very high risk and makes recommendations for what care individuals in each category should receive (6). The Atherosclerosis Risk in Communities (ARIC) score was developed to predict risk of heart failure in the general population but has also been validated in cancer populations. It predicts 10-year risk of incident heart failure through assessing age, sex,

race, smoking, BMI, blood pressure, diabetes, CVD history, heart rate and left ventricular hypertrophy (124). Risk prediction equations have also been developed and validated to predict 5-year cardiovascular disease in cancer patients in New Zealand (125).More recently, Guha et al. used machine learning to develop and validate 'PREVENT", in which 10 factors were identified as the most predictive of 10-year CVD risk (for four separate cancer types: breast, colorectal, lung and prostate cancer) (126). The 10 most common predictors across cancer types; with age, total cholesterol and smoking being identified as the common (126).

Although there are some barriers to the use of risk prediction tools in healthcare, including perceived increased workload for clinicians and perceptions that clinician judgement should not be replaced by tools (127), the development and implementation of tools underpinned by risk prediction models for CVD in cancer can play an important role to reduce the impact of CVD in cancer. Furthermore, the rapid development and application of machine learning and artificial intelligence in healthcare presents an opportunity to develop sophisticated tools that can be smoothly integrated into routine care.

2.2.2.7 Summary of existing and potential approaches to CVD care in cancer

Multiple approaches have been identified as having the potential to reduce the impact of CVD in cancer. Existing approaches include cardio-oncology clinics, referral pathways and models of care; whilst lifestyle behaviour change, self-management, education and risk prediction tools have been identified as have the potential to contribute to the optimisation of CVD care in cancer. There is a diversity of strengths and limitations of all of the approaches and gaps in evidence regarding effectiveness, highlighting the complexity of developing and implementing CVD care in cancer that is effective and feasible.

2.3 Summary of the gaps in the literature and the research problem: CVD care in cancer is inadequate

CVD risk is an important issue for people who have been diagnosed with cancer, with many survivors experiencing significant cardiovascular-related morbidity and mortality as well as poorer cancer outcomes. Voluminous literature reports cardio-oncology research which has led to the development of guidelines, the most comprehensive of which is the ESC Guidelines on Cardio-oncology which provides evidence and expert consensus-informed recommendations to support clinicians to assess, monitor and manage CVD risk in cancer. Approaches to reducing the impact of CVD in cancer are developing, including cardio-oncology clinics and clinical pathways, but there are important barriers to their implementation and inadequate evidence that they are effective in reducing the impact of CVD in cancer. In addition, it is well-established that lifestyle behaviour optimisation, self-management, education and risk prediction tools can contribute to addressing the problem of CVD in cancer. However, despite evidence, guidelines and developing interventions in cardio-oncology, CVD risk remains a prevalent and significant issue facing the cancer population,

and there is a lack of understanding regarding the preferences of cancer care providers and people affected by cancer regarding CVD care. Finally, many approaches to reduce the impact of CVD in cancer are unimodal (e.g., development of clinical care pathway), may only target a specific aspect of the problem (e.g., risk prediction tools will only impact risk stratification), and often do not involve empowering people with cancer to be involved in reducing risk. Approaches may have more impact if they are flexible according to diverse needs and preferences, involve multiple techniques (e.g., education, self-management, lifestyle behaviour optimisation), and target multiple aspects of CVD in cancer (i.e., risk assessment, monitoring and management).

2.4 Aim

The aim of the research program is to develop understanding around the experiences and perspectives of cancer care clinicians and people with cancer with regard to CVD in cancer, and to use these experiences and perspectives to inform the codesign of a novel new approach to reduce the impact of CVD risk in people who have been diagnosed with cancer.

2.5 Research Questions

Seventeen research questions were developed to address the overall research aim, across four studies. The four studies are summarised below, followed by the research questions each study addressed.

Study 1: A systematic review of reviews conducted to summarise and synthesise evidence from randomised controlled trials which have examined the effectiveness of physical activity interventions in older people with cancer. Optimisation of lifestyle behaviour plays a key role in CVD risk management in cancer and effectiveness of physical activity interventions in cancer is well-established in adults. However, the evidence has not been synthesised with regard to effectiveness of physical activity in older people. Given cancer is an age-related disease, it was critical to establish if potential interventions in this group are likely to be effective. The research questions (1-3) addressed by Study 1 were:

1. What is the evidence supporting physical activity interventions improving patient outcomes (physical, e.g., fitness and strength; and psychological, e.g., fatigue and quality of life) in older people that have been diagnosed with cancer?
2. What is the effect of physical activity interventions on cancer outcomes (e.g., survival and mortality) in older people that have been diagnosed with cancer?
3. What is the effect of physical activity interventions on health service use outcomes (e.g., hospital length of stay) in older people that have been diagnosed with cancer?

Study 2: A qualitative study involving cancer care providers which explored their perceptions regarding CVD risk in cancer. Specifically, this study sought to achieve a deeper understanding of

the experiences and perspectives of cancer care providers related to CVD risk awareness, importance, needs, barriers and enablers to effective CVD care in cancer, and preferences for potential solutions to reduce the impact of CVD in cancer. The research questions (4-7) addressed by Study 2 were:

4. Are cancer care providers aware of CVD risk in cancer and do they think it is an important issue?
5. What are cancer care providers' perceptions regarding needs associated with the problem of CVD in cancer?
6. What are cancer care providers' perceptions regarding system-, staff- and patient-level barriers and enablers affecting effective provision of CVD care in cancer?
7. What are cancer care providers' preferences for potential solutions to improve CVD care in cancer?

Study 3: A qualitative study involving people who have been diagnosed with cancer which explored their perceptions regarding CVD risk in cancer. Specifically, this study sought to achieve a deeper understanding of the experiences and perspectives of people who have been diagnosed with cancer related to CVD risk awareness, importance, needs, barriers and enablers of engaging in CVD care, and preferences for potential solutions that aim to reduce the impact of CVD in cancer. The research questions (8-13) addressed by Study 3 were:

8. Are people with cancer aware of CVD risk in cancer and how much do they know about it?
9. Do people with cancer think CVD risk in cancer is an important issue?
10. What have been people with cancer's experiences with CVD risk management?
11. What are people with cancer's perceptions around needs associated with the problem of CVD in cancer?
12. What are people with cancer's perceptions around system-, staff- and patient-level barriers and enablers affecting their engagement in CVD risk management?
13. What are people with cancer's preferences for potential solutions to improve CVD care in cancer?

Study 4: A two-part study design (codesign followed by usability testing) involving cancer care providers, people affected by cancer and researchers was conducted to develop a website to provide information and support for people with cancer to self-manage aspects of their CVD risk, and to improve their outcomes. The new website was then tested for usability. The research questions (14-17) addressed Study 4 were:

14. What are the preferences of cancer care providers and people affected by cancer with regard to the content of the patient-facing website?

15. What are the preferences of cancer care providers and people affected by cancer with regard to the format, design and navigation of the patient-facing website?
16. What are the preferences of cancer care providers and people affected by cancer with regard to how the website can be engaging to users?
17. Is the website usable?

2.6 Research Plan

To address the aim of this doctoral research, a mixed methods program of research was conducted. All aspects of the research were guided by the principle of participatory research, specifically applying the framework: person-based approach to intervention development (PBAID). A participatory approach facilitates the equal involvement of end-users (cancer care providers and people diagnosed with cancer in this context) and researchers in the research process, so that the research output (website to optimise management of CVD risk in cancer) is a co-designed product that is likely to be acceptable and effective for its intended population. Participatory research is strongly aligned with critical realism (described in more detail in future sections), given it operationalises understanding stakeholders' experiences and perspectives – which are understood to inform reality according to the critical realist philosophy. Involving stakeholders also facilitates the aim of critical realism to acknowledge the need for understanding that leads to practical change. There are some challenges associated with a participatory approach which should be noted, including balancing the project objectives and resources available with preferences of users, and difficulties with ensuring authentic participation from all participants and accurate interpretation of contributions by researchers (128).

During the planning process, alternative methodologies were investigated, including approaches classified as user-centred, theory-driven or researcher-focused. Despite their strengths, it was the consistency between participatory approaches and critical realism that led to selection of these approaches. In order to better understand the congruence of mixed method participatory design and critical realism, it is useful to consider the inadequacies of other methodologies and study designs in seeking to understand the truth as understood by critical realists. For example, a researcher-focused quantitative approach would only be able to uncover data associated with the objective component of the phenomenon, but there would be no deeper exploration of how the subjective influence of agency shapes the truth, i.e. how does the social context and preconceptions and experiences of end-users influence what the truth is? Likewise, a researcher-focused qualitative approach could lead to an outcome that is not feasible, because end-users' perceptions and experiences have not been adequately understood and used to inform development.

In addition to this research program being underpinned by the broader approach of participatory research, this research was guided by the principles of the Person-Based Approach to Intervention Development (PBAID) (129). PBAID focuses on the importance of understanding and accommodating the experiences and perspectives of the people who the intervention targets (in this case, people who have been diagnosed with cancer) and the people involved in developing, implementing or supporting engagement in the intervention (cancer care providers and researchers). Other approaches to intervention development include theory-based and evidence-based processes. PBAID involves conducting research that is guided by the principle that all research and development must be person-centred so does not replace, but rather complements, the application of approaches that are theory- and evidence-based. PBAID is commonly used to guide the development of digital health-related behaviour-change interventions and involves a systematic approach that focuses on understanding and being influenced by users' perspectives about how an intervention is likely to influence behaviour-change. PBAID involves a comprehensive series of qualitative sessions to understand users' perspectives and preferences which are conducted throughout the intervention development process, with findings from each session informing the next stage of development. What differentiates PBAID from other approaches to intervention development is how it extends beyond simple codesign, usability and acceptability/feasibility evaluation, by considering how the characteristics of users impact their preferences, and focuses on understanding perspectives regarding the behavioural components of the intervention and how/if they are likely to lead to targeted changes (in this case, lifestyle behaviours including diet, physical activity, smoking cessation etc). Feedback is used to guide next steps to increase the likely relevance, satisfaction and effectiveness of the intervention based on the context in which it will be applied and the characteristics of the target users. Specific details about how PBAID informed each study in this research program are included in the study design and methods sections of chapters 3, 4, 5 and 6. However, a brief overview of how the approach is operationalised within the stages of the current research program is provided in Table 3.

Table 3 - Person-based Approach to Intervention Development – application to Research Program (129)

PBAID processes	**Research study (details)**
Identify and synthesise relevant existing literature involving user perspectives, to understand issues, needs and preferences informing the development of a new approach to reduce the impact of CVD in cancer	• Planning and conceptualisation of research program; • Systematic review of reviews; • Informal reviews informing development of qualitative studies (cancer care providers and people diagnosed with cancer) and codesign.
Understand the target user population's perspectives and experiences related to their needs and preferences to reduce the impact of CVD in cancer	• Qualitative study with cancer care providers; and • Qualitative study with people diagnosed with cancer.

Identify intervention design objectives (informed by issues, needs and barriers) and *specific aspects of the new approach* based on these needs, as well as user preferences (including behaviour change).	• Qualitative study with cancer care providers; • Qualitative study with people diagnosed with cancer; and • Codesign.
Seek and analyse user feedback based on interaction with website and *optimize subsequent iterations* of the website based on user perspectives.	• Codesign; and • Usability testing.

PBAID principles guide all stages of intervention development and evaluation, including implementation and effectiveness trials which are beyond the scope of this research program. It is anticipated that the new approach to reduce the impact of CVD in cancer developed in this PhD candidature will be tested for acceptability, feasibility and effectiveness in the future, and PBAID principles will inform these studies.

2.7 Philosophical underpinnings

In this project, I applied the concept of a research paradigm, which can be considered a framework for identifying researchers' ontological and epistemological beliefs, and in turn how these underpin study methodology and methods which are consistent with the researcher's inherent assumptions about knowledge and learning (130). Congruence between philosophical assumptions and methodology (and in turn methods) is necessary to ensure research authenticity and integrity.

1.8.1 Ontology, Epistemology and Meta-theory

Ontology is the theory or study of being; or in other words, what one believes to be real and true. Epistemology is the theory of knowledge, or the study of how we come to learn about reality and what is true. It also is the study of how we communicate this knowledge.

2.7.1.1 Critical realism

This research program was underpinned by critical realism. Critical realism has emerged as a worldview that aligns with aspects of positivism and interpretivism. Typically, positivism and interpretivism have been considered as being at either end of the philosophical spectrum. Positivist ontology, which is most commonly aligned with quantitative research methodologies, assumes that there is an objective truth which is independent of the subjects that come to know about it. The epistemological assumptions of positivist researchers are that they can find out this objective truth by making empirical observations using methodologies such as randomised controlled trials and objective data collection methods and statistical analysis to measure the phenomenon. In contrast, the ontology of interpretivism is relativist, i.e., there is no reality independent of, or influenced by, the thinking and reasoning of the people interpreting it, and knowledge is socially constructed and created by the mind. Interpretivist researchers commonly use qualitative methodologies to develop

a deeper and more meaningful understanding of the phenomenon, and this must occur through considering context, meanings and subjective experiences which all shape what can be known.

Critical realists believe that there is some objective reality that exists independently of our awareness, as per the realist ontology often described by positivists. However, they also argue that there can be multiple interpretations of that reality (as per interpretivism), asserting that reality can and is altered by interactions between objective and subjective forces (meaning that context and concepts impact the real). This can be better understood by considering critical realist ontology as stratified and consisting of three levels: the real, which refers to the independent and objective structures of reality and the causal capacity inherent to them; the actual, which is what occurs when, and if, the causal factors of the real are enacted (by, for example, factors in the social environment); and finally the empirical, which is also part of the actual and are the events that we can measure during investigation. Critical realism accepts that there can be multiple realities which are simply our own accounts of the truth, are fallible and are dependent on context. 'Judgemental rationality' is applied in order to judge which account of the same reality is more correct than the others.

2.7.2 Critical realism underpinning a mixed methods study design

This PhD program used a mixed methods study design, which involves collection and analysis of both quantitative and qualitative data in order to address the overall research aims to identify and manage CVD risk in people diagnosed with cancer. A mixed methods design was deemed appropriate because neither quantitative nor qualitative data alone could answer the research problem. It was decided that the integration of quantitative and qualitative data would lead to a more meaningful, rich and deep understanding of cardio-oncology leading to the development and testing of a new approach to improve assessment and management of CVD risk in people diagnosed with cancer. Specifically, an exploratory sequential mixed methods design was applied, where the findings of the review of quantitative studies examining the effectiveness of lifestyle interventions on outcomes in people diagnosed with cancer (study 1) and the findings of the qualitative research examining the perspectives of cancer care providers and people diagnosed with cancer (studies 2 and 3), together informed the codesign and usability testing of website to reduce the impact of CVD risk in cancer (study 4).

The application of the mixed methods approach in this research was underpinned and informed by the philosophical worldview of critical realism. Mixed methods and critical realism align to allow for the examination of both empirical (objective) and socially constructed (subjective) reality (131), leading to comprehensive understanding of CVD in cancer. Quantitative aspects of the program help to identify observable elements, whilst qualitative components allow for considering the context, nuances and social structures that also explain CVD in cancer. Using a mixed methods approach representing appreciation of reality as being both observable and socially constructed,

means the phenomena of focus are better understood, but also that these findings can be practically applied through the development of an approach to address the problems. Ultimately, the mixed methods approach, underpinned by critical realism represents a retroductive approach where observed reality is evaluated through quantitative research and qualitative research is utilised to understand the reasons behind the quantitative data (131).

2.8 Chapter summary

This chapter included a detailed synthesis of the existing literature relating to CVD risk in cancer, including prevalence and impact of CVD, cancer and co-existing disease; reasons for co-existence of CVD in cancer; risk factors; guidelines and recommendations and existing and potential solutions for reducing the impact of CVD in cancer. The synthesised data creates a strong rationale for the stated aim of this research program, i.e., to develop a novel new approach to reduce CVD risk in cancer. A detailed research plan is presented describing the appropriateness of a mixed methods approach, following principles of participatory research, specifically the PBAID approach. The chapter concludes with a detailed summary of the philosophical, epistemological and ontological foundations underpinning the research.

3 CHAPTER THREE: PHYSICAL ACTIVITY INTERVENTIONS IN OLDER PEOPLE WITH CANCER: A REVIEW OF SYSTEMATIC REVIEWS

3.1 Chapter Overview

This chapter reports the methods and findings of a review of systematic reviews examining the effectiveness of physical activity interventions in older people with cancer. This review was conducted in October 2021. Originally, the PhD candidate and supervisors planned to summarise and synthesise the review-level evidence for four types of lifestyle interventions in older people with cancer (physical activity, diet, smoking cessation and alcohol moderation). However, after discussions amongst the research team, it was determined that the review of systematic reviews would focus on physical activity, because of the lack of review-level evidence regarding diet, smoking cessation and alcohol moderation in older people with cancer.

This chapter begins with a summary of the existing literature in the area (background and context), justifying the need for this research and establishing what it will contribute to the broader evidence, and the aim of the review of systematic reviews. This also includes a summary of how this chapter contributes to the overall aims of the PhD research program. A statement of related publication is then provided describing that a version of the research reported in this chapter has been published (132). A detailed description of the Methods and Findings of the study is then provided. The discussion section of the chapter includes a summary of the findings in the context of the broader research including comparison to existing literature for the impact of physical activity interventions in younger people with cancer. There is also discussion about the limited evidence for diet, smoking cessation and alcohol moderation. Finally, there is a summary of the chapter, including how the findings informed the final studies conducted as part of the PhD research program (i.e., codesign and usability testing of a web-based resource to support self-management of cardiovascular disease risk in people with cancer).

3.2 Background and context

The 2022 European Society of Cardiology guidelines on cardio-oncology recommend assessment, monitoring and optimisation of lifestyle behaviours to prevent and manage CVD risk in people who have been diagnosed with cancer (6). In addition, multiple cancer guidelines and frameworks also guide people diagnosed with cancer to engage in adequate physical activity, eat a healthy diet, quit smoking, and moderate alcohol intake (90, 133-139).

In addition to preventing and managing CVD risk in cancer, there is voluminous literature describing other benefits of healthy lifestyle for people who have been diagnosed with cancer. Data suggests physical, psychological and social benefits of physical activity in cancer including

improved QoL, immune function, and experiences of social connectedness; and reduced fatigue and mortality rates (140). Healthy diet has also been associated with better outcomes for people with cancer, including improved QoL (141) and reduced mortality (142). Smoking after cancer diagnosis has been found to be associated with worse outcomes, including reduced treatment effectiveness and life expectancy (143). Finally, risky alcohol consumption habits in people diagnosed with cancer can lead to increased cancer recurrence rates, new cancers, and death (133, 142).

Given the well-established evidence for the importance of lifestyle in people with cancer, lifestyle interventions have been developed and assessed for their impact on outcomes in people with cancer. Majority of interventions target physical activity, which is reflected in the existence of multiple reviews of reviews, which have concluded physical activity interventions improve physical outcomes including function (144); psychological outcomes including better Quality Of Life (QOL) and reduced anxiety, depression and fatigue (144); and reduced mortality (145). No reviews of reviews have been conducted for diet, smoking cessation or alcohol moderation interventions in cancer. However, there is limited review-level evidence for mixed results for impact of diet interventions on QOL (146), treatment toxicity and complications (147, 148) and body weight (149). Reviews of smoking cessation interventions mostly report the effect in terms of quit rates (rather than other physical, psychological, health service use or cancer outcomes). Quit rates are diverse across the literature, ranging from 14.8% - 50.1% at 3 months in one review of people diagnosed with head and neck, breast or lung cancer (150), whilst another involving people diagnosed with urological cancer reported rates between 3.2% to 47.3% (151). Meanwhile, no reviews have reported the effect of interventions that solely focus on alcohol reduction in cancer. However, one review summarised data from primary papers reporting results of lifestyle interventions that *included* alcohol reduction, but also targeted for example, physical activity and diet. This review of seven papers reported that alcohol reduction was greater in the intervention group compared to the control group for only one study (152). The effect on alcohol interventions on outcomes other than alcohol consumption were not reported.

Although there is observational and experimental evidence for the importance of healthy lifestyle in cancer (with particularly high-level evidence for physical activity), the literature is much more limited when considering the impact of lifestyle behaviour and outcomes in older people with cancer. For example, there have been no reviews of reviews summarising the evidence for the impact of physical activity interventions in older people with cancer (compared to multiple reviews of reviews in younger people diagnosed with cancer, e.g., (11, 12, 153)). Similarly, there have been no reviews of reviews of diet interventions in older people with cancer, and only four reviews summarising data from a total of only 25 different primary studies. This is in contrast to multiple reviews in younger people with cancer, including a recent, large systematic review including 252 primary papers on diet interventions (154). No reviews have been conducted to summarise the

impact of smoking cessation interventions in older people with cancer, compared to at least three in younger people who have been diagnosed with cancer (150, 151, 155). No reviews have been conducted to synthesise data from older people with cancer regarding the impact of alcohol moderation interventions. The author is aware of the aforementioned review in younger people with cancer, which included seven primary studies.

It is critical to consider the impact of lifestyle interventions in older people with cancer for multiple reasons, including that cancer is an age-related disease, with the risk of majority cancer types increasing substantially with age. In addition, older people experience barriers and enablers to engaging in healthy lifestyle behaviours differently to younger people which could affect their participation. For example, older people with cancer are more likely to suffer from co-morbidities (including CVD, but also diabetes and arthritis) than younger people with cancer, which could limit their ability to tolerate exercise and present barriers to engagement related to physical limitations or competing medical priorities (156). There is also evidence that older people with cancer may not perceive physical activity to be important (157) and may be perceived by healthcare providers to be less willing to make changes to lifestyle behaviours (158), and are also less likely to attempt to quit smoking (159). Reduced social support, which is more common in older people, can also negatively affect healthcare accessibility disproportionately compared to younger people (160). In addition, older people with cancer can have different biological characteristics that could impact the effectiveness of lifestyle interventions. For example, older age is associated with changes in muscle structure and function, which in extreme cases includes sarcopenia (161) and mitochondrial dysfunction (162). Sarcopenia is a condition characterised by reduced muscle mass and physical function, associated with increased risk of frailty (163), hospitalisations and mortality (164). Sarcopenia is known to reduce older people with cancers' capacity to engage in exercise and may alter the physiological response to exercise (165).

Originally, the aim of the review reported in this chapter was to consider the effectiveness of physical activity, diet, smoking and alcohol interventions in older people with cancer. However, during the initial search it became apparent that the level and amount of evidence for each type of intervention varied substantially, making it difficult to conduct an appropriate type of review according to the data available across interventions pertaining to all four of these lifestyle behaviours. That is, there were multiple reviews of physical activity interventions in older people with cancer, meaning a review of reviews was warranted for this type of intervention, but there were only a small number of reviews of diet interventions and no smoking or alcohol interventions, suggesting that a review of primary evidence would be more appropriate. It was beyond the scope of this thesis to conduct multiple reviews, so the research team decided to conduct a review of systematic reviews that have summarised data from studies examining the effectiveness of physical activity interventions in older people with cancer. A review of reviews was justified for this area because there are already multiple systematic reviews examining physical activity in older

people with cancer, many of which include several of the same original papers showing that original data has been well-synthesised. In addition, a review of reviews will provide high-level understanding of the evidence and literature in the area which is appropriate to guide the development of interventions, as is the aim of the overall research program (166). It was determined 65 years and over would constitute 'older people' in this review. While the change in function associated with aging is impacted by many other factors other than chronological age including comorbidities, and for cancer survivors, type of cancer and its treatment, a cut off of 65 years is conventionally applied in the practice of geriatric oncology and geriatrics to identify the population of "older adults" and has been commonly applied to the research on this topic (e.g., (167, 168)). Our preliminary search of the literature identified only one review of PA in individuals where all study participants were 65 years or older (169), but multiple reviews where *majority* were 65 years or older.

As mentioned above, to date there have been three reviews of reviews synthesising evidence on physical activity in people with cancer, but no review of reviews that specifically focused on older adults with cancer (65 years or older). Fuller et al. (11) summarised findings from 65 papers involving 140 meta-analyses and of the 32 papers that reported participant age, 30 (94%) examined the impact of physical activity in people with cancer aged <65 years, Similarly, a review by Stout et al. (12) of 51 systematic reviews, 45 (88%) of the reviews reported a mean age <65 years. Finally, Posadzki et al. (153) summarised the findings of 17 reviews examining physical activity in people with cancer, and of 11 reviews to report age, 10 (91%) reported mean age of less than 65 years. None of these papers included a sub-analysis of physical activity in older people. Reviews of reviews are an important way of synthesising a large body of evidence where the evidence is mature and the presence of three such reviews for physical activity in cancer attests to the maturity of the field. Yet, despite the higher prevalence of most cancers with advancing age, coupled with a broad push for increased physical activity participation for cancer survivors, the lack of evidence synthesis on effectiveness of physical activity interventions specifically relevant to older adults is an important gap in need of further elucidation.

3.3 Aim

Therefore, the aim of this review was to summarise and synthesise the evidence for the impact of physical activity on patient outcomes (physical and psychological), health service use, and cancer outcomes (including progression and mortality) in reviews where majority of study participants were 65 years or older and diagnosed with any type of cancer.

3.4 Statement of related publication

A component of the research reported in this chapter was the focus of a paper, 'Physical activity interventions in older people with cancer: A review of systematic reviews', which was published in

the European Journal of Cancer Care (2022) (132). The original aim of this research was to conduct a systematic review of systematic reviews investigating the impact of lifestyle interventions (physical activity, diet, quitting smoking and alcohol moderation) on outcomes in older people diagnosed with cancer. A large majority of the included papers reported the impact of physical activity interventions (15 out of 17 reviews), with a small proportion examining the impact of dietary interventions (four of 17 reviews – some reviews synthesized evidence for both diet and physical activity). No interventions related to smoking or alcohol were identified. Although the original aim of this review of reviews was to summarise and synthesise review-level evidence for physical activity, diet, smoking and alcohol interventions, we decided to limit it to physical activity because of the availability of evidence appropriate for a review of reviews.

In regard to the paper published reporting the impact of physical activity interventions in people affected by cancer, Reegan Knowles (RK) is the primary/first author of the publication, with PhD primary supervisor Professor Bogda Koczwara as the senior/last author, and Dr Emma Kemp and Professor Michelle Miller as the second and third authors, respectively. Associate Professor Kade Davison (KD) is the fourth author and contributed his expertise as an Exercise professional. RK, MM, EK and BK conceptualized the research, with RK contributing 80% to the concept of the review. RK contributed 70% of the methodology of the research, with EK also significantly involved (particularly through screening). RK conducted 70% of the analysis of the data included, with all authors involved in reporting, interpreting and synthesizing the data from included reviews. RK wrote the first version of the paper, but all authors were involved in reviewing and editing the paper. RK conducted 80% of the writing and editing. All authors read and approved the final manuscript.

This chapter provides greater detail about the research that was reported in the peer-reviewed paper published in the European Journal of Cancer Care. Although there are differences in how the research is reported in this chapter compared to the paper, there is direct overlap of wording and content throughout. The published paper can be found at Appendix 1.

The last section of this chapter provides an overview of the review-level evidence identified in the original search used in this study, i.e., an analysis of the four reviews reporting impact of dietary interventions in older people in cancer. The lack of review-level evidence for smoking cessation and alcohol moderation is also discussed. The uneven representation of different lifestyle intervention types (i.e., several physical activity interventions compared to other intervention types) in the literature is discussed.

3.5 Methods

A review of systematic reviews was conducted given there were existing reviews examining the association between lifestyle interventions and health-related outcomes in older people with

cancer. In addition, many of these reviews did not specifically target research conducted in older people with cancer (i.e., the sample 'happened' to include people aged 65 or more); and results were not presented and interpreted with specific consideration of the population. Finally, we determined a need for the findings of these reviews to be synthesised and summarised to allow readers to appreciate the entire breadth of the topic. This review of systematic reviews was conducted and reported according to the PRISMA guidelines for systematic reviews (170) and the Joanna Briggs Institute (JBI) Manual for Evidence Synthesis (166). It was registered on PROSPERO (registration number: CRD42020156534).

3.5.1 Eligibility criteria

Only papers reporting systematic reviews were eligible for inclusion; all papers reporting original research of any study design and reviews that were not conducted systematically (e.g., scoping reviews and integrative reviews) were ineligible for inclusion. To be included, systematic reviews had to report randomised controlled trials (RCTs) or quasi-RCTs; reviews reporting only observational study designs were not included. Further, the RCTs synthesised in the review had to examine the impact of physical activity interventions on any health-related outcome (including physical, psychological, health service use or cancer outcomes). The interventions could only be targeting physical activity, i.e., review examining RCTs of mixed interventions such as those that target changes in multiple behaviours, e.g., physical activity and diet, were not included. To facilitate the focus on older people, we only included reviews if the majority of participants were 65 years or older. Review papers were included if either:

i. The mean age of all participants included in the review (i.e., the sum of participants from all included original studies) was 65 years or more; OR
ii. Where the mean age of all participants in the review was not reported, reviews were included if 50% or more of the original papers included participants with a mean age of 65 years or older.

If papers did not report mean age of all participants or the mean age of participants in each original paper, the original papers were sought. If mean age could still not be established, then the review was excluded. Participants could be anyone that was ever diagnosed with any type of cancer, except non-melanoma skin cancer. Participants did not need to have cancer at the time of the intervention, so long as they had been diagnosed at any time in their life – the intervention could have been delivered at any time after diagnosis (e.g., during or after treatment, or in people who did/would not receive anti-cancer treatment). Only papers published in English were included. The search was not limited by date.

3.5.2 Information sources

An experienced research librarian assisted in selecting the databases searched. Six databases were deemed appropriate: PubMed, Cumulated Index to Nursing and Allied Health Literature (CINAHL), Scopus, Web of Science, the Cochrane Database of Systematic Reviews and Embase.

3.5.3 Search

An experienced research librarian assisted in developing and implementing the search strategies in October 2021. Initially, the research librarian assisted in developing the search for PubMed and then translated the search for the other databases. Broadly, the search terms can be categorised into the following groups:

- Cancer;
- Physical activity interventions;
- Systematic reviews; and
- Older age.

3.5.4 Review selection

Search results from each database were imported into Covidence (Covidence, 2020). Duplicates were removed. Two researchers independently reviewed the titles and abstracts of all reviews, using the inclusion and exclusion criteria described above. Where researchers' decisions about inclusion of papers for full text review conflicted, the two researchers discussed and decided together about whether to include. For included titles, full texts were located and imported into Covidence. The same two researchers then reviewed the full text papers against the inclusion and exclusion criteria to determine whether they were included in the final review. Conflicts between the researchers in the full text screen were resolved through discussion between the two researchers, or by a third researcher.

3.5.5 Data extraction and organisation

Data extraction was conducted by two researchers independently, according to the JBI data extraction tool for Systematic Reviews and Research Syntheses (166). The JBI tool requires extraction of the following data from each of the included systematic reviews:

a) author/year;

b) objectives;

c) participants (number and characteristics);

d) intervention details (e.g., PA frequency, intensity, type, time, setting and context/mode; dietary behaviour/nutrient intervention);

e) sources searched;

f) range of years of included studies;

g) number of studies included;

h) types of studies included;

i) country of origin of review;

j) quality appraisal instrument used;

k) quality appraisal rating;

l) method of analysis;

m) outcomes assessed;

n) results/findings;

o) significance/direction; and

p) heterogeneity.

Outcome variables were then categorised into:

(1) patient outcomes – physical (including measures of physical activity, fitness and function, body composition and cardiovascular risk);

(2) patient outcomes – psychological (including, depression, anxiety, fatigue, QOL);

(3) health system outcomes (hospital length of stay [LOS] and complications); and

(4) cancer outcomes (disease progression and mortality).

Only the data relevant to the research aims and eligible for inclusion were extracted and analysed, including the analysis of overlap.

3.5.6 Quality appraisal

Two researchers independently appraised the methodological quality of included review papers using the JBI Critical Appraisal Checklist for Systematic Reviews and Research Syntheses (166). The tool assesses methodological quality against eleven criteria:

1. Is the review question clearly and explicitly stated?
2. Were the inclusion criteria appropriate for the review question?
3. Was the search strategy appropriate?
4. Were the sources and resources used to search for studies adequate?
5. Were the criteria for appraising studies appropriate?
6. Was critical appraisal conducted by two or more reviewers independently?
7. Were there methods to minimize errors in data extraction?
8. Were the methods used to combine studies appropriate?
9. Was the likelihood of publication bias assessed?
10. Were recommendations for policy and/or practice supported by the reported data?
11. Were the specific directives for new research appropriate?

The JBI Critical Appraisal Checklist requires users to select 'yes', 'no', 'unclear', or 'not applicable'. An overall score is not calculated as part of the appraisal process, rather the findings are reported qualitatively and provide a summary of whether papers met the criteria.

3.5.7 Assessing overlap across studies

The degree to which the same primary studies are included in multiple reviews across a review of reviews is defined as 'overlap'(171). Overlap is important because each time a primary paper is considered more than once, its results are over-represented in the findings of the overall review of reviews. The higher the overlap, the greater the adverse impact is on the precision of the conclusions that can be drawn from by the review (172). It is critical to report overlap to inform interpretation of results (166). In this review of reviews, we calculated the overlap (the degree of the same primary paper being included in multiple reviews) using the formula developed and reported by Pieper and colleagues (173):

'Corrected covered area' (CCA): (frequency of times a primary paper is included (after the first occasion); divided by, the number of different primary papers) x number of systematic reviews.

According to Pieper and colleagues (173), overlap can be categorised as:

- Slight = CCA is below 5%;
- Moderate/high = CCA is above 5% but below 15%; and
- Very high = CCA is above 15%.

3.6 Results

3.6.1 Review/Study selection

Figure 3 illustrates the flow of study selection. The search was conducted in October 2021. The original database searches located 5,497 papers, including 2,594 duplicates. Title and abstract screening of 2,903 deduplicated papers was conducted by two independent researchers. Two-thousand, six hundred and seventy-two were removed during title and abstract screening. Full texts were located for the remaining 231 papers and imported into Covidence for screening by the same reviewers. After conflict resolution, 216 were excluded because they did not meet the eligibility criteria. Specific reasons for exclusion were that:

1. The review reported research involving the incorrect patient population, e.g., participants had not been diagnosed with cancer, or the sample did not meet criteria for focus on older age (n=163);
2. The review did not synthesise research using the appropriate study design (i.e., had to be a systematic review of randomised controlled trials (RCTs) or pseudo-RCTs) (n=29);

3. The review did not include an analysis of primary papers examining the impact of physical activity (only) interventions (n=15);
4. The full text was not written in English (n=6); and
5. There were duplicates of articles not identified earlier in the review process (n=3).

Finally, 15 systematic reviews were included (149, 169, 174-185).

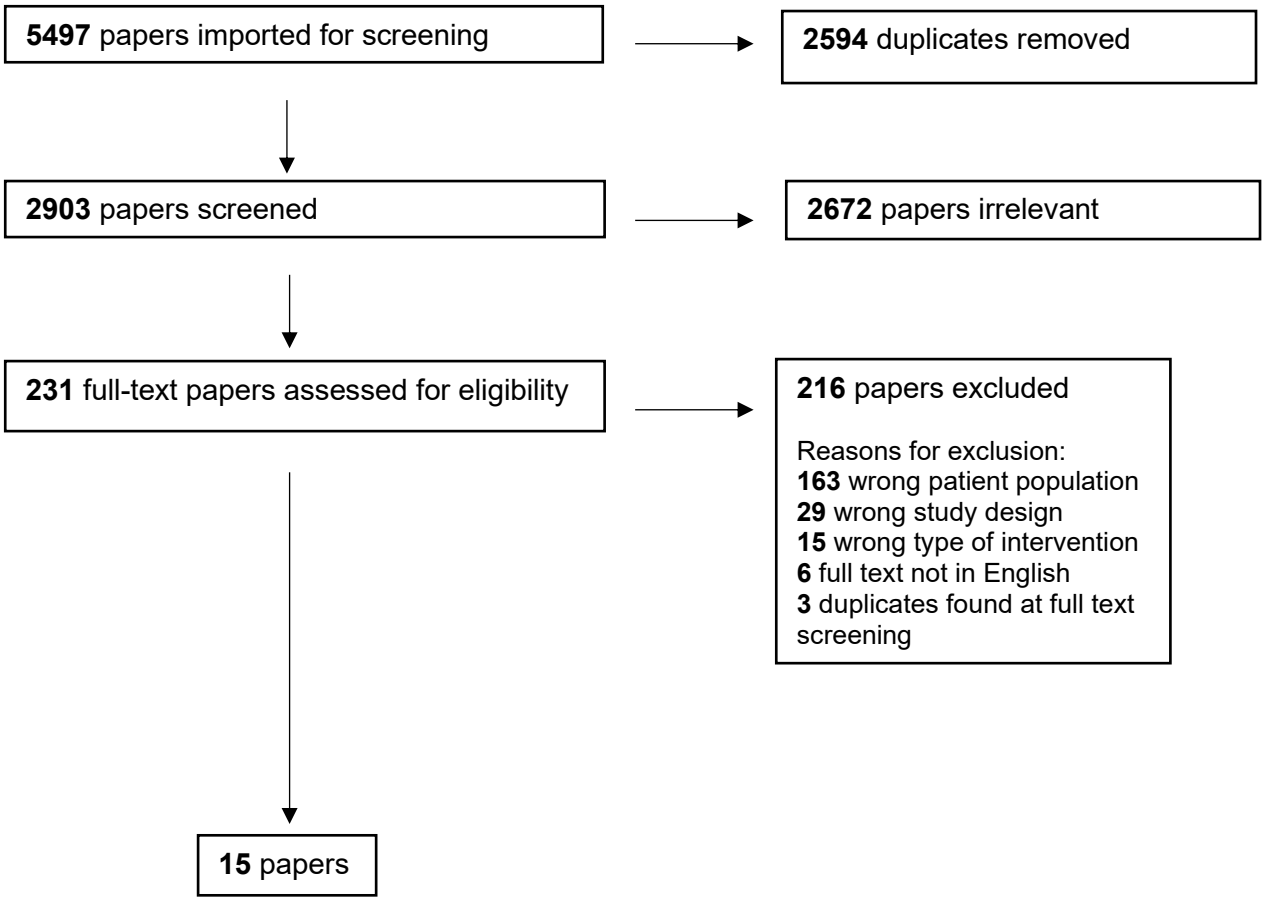


Figure 3 - PRISMA diagram representing study selection

3.6.2 Number and overlap of studies

When summing the number of primary papers reported in the analysis of physical activity interventions in each review, there were 156 primary papers including 10,652 people diagnosed with cancer. The number of primary papers included in each review ranged from four (169, 179) to 23 (184) (median = 10 primary papers). The number of participants included in each primary paper ranged from 167 (175) to 1,748 (184) (median = 628 participants). The degree of overlap of primary papers was calculated (i.e., determining how many primary papers are included in more than one review and therefore over-represented in a review of reviews if overlap is not accounted for) and found to be moderate (14%). After accounting for this overlap, 76 different primary papers involving 5,359 individuals with cancer remained.

3.6.3 Study characteristics

Tables 6 and 7 provide details of the 15 included reviews, including author, year published and country in which the review was conducted; research objective/aim/purpose (as presented by author in review paper); profile of sample (number of primary papers included in review, total participants, participant age (mean/median or mean/median range of age across primary papers), sex, cancer type/s; note cancer staging, and stage on the cancer care continuum was not included due to lack of reviews reporting this information); intervention details including physical activity frequency (how often the physical activity was performed, e.g., daily), intensity (i.e., how hard the participants 'worked' whilst engaging in the intervention, e.g., light, moderate, vigorous), time (how long each session lasted, and how long the entire interventions lasted) and type of physical activity (e.g., aerobic, resistance, sport, yoga etc.), intervention setting (e.g., home, hospital, community gymnasium), and intervention context/mode (e.g., whether physical activity sessions were conducted in a group or individually, or supervised (usually by a researcher or clinician such as an exercise professional) or unsupervised; outcomes and the method in which these outcomes were measured (e.g., questionnaire); effect size for meta-analyses reported in Table 6 or findings for narrative analyses in Table 7 including the number of primary papers that reported improvement, adverse effect, or no change to outcome being examined; and the quality appraisal tool used by each review and the corresponding score of the appraisal.

Figure 8 is an overview of the findings of all reviews synthesised by outcome. In the figure, the outcomes are categorised into 13 physical patient outcomes, six psychological patient outcomes, five health service use outcomes and one cancer outcome. Next to each outcome, the number of reviews in which the outcome was examined and the number of reviews which reported a beneficial effect is reported, and then the 'bar' for each outcome illustrates the proportion of reviews finding a beneficial effect, mixed findings (as reported by the included review author according to findings of primary papers), or no effect.

3.6.3.1 Years and country published

The search (conducted in October 2021) was not limited by date. The year of publication of the 15 included reviews are summarised in Figure 4, and ranged from 2012 to 2021, with seven of these published in 2020 (n = 3) and 2021 (n = 4). The country in which the reviews were conducted is summarised in Figure 5, with eight countries represented including Australia (n = 5), United Kingdom (n = 3), US (n = 2), and Austria, Denmark, Italy, Korea and Netherlands (n = 1 per country).

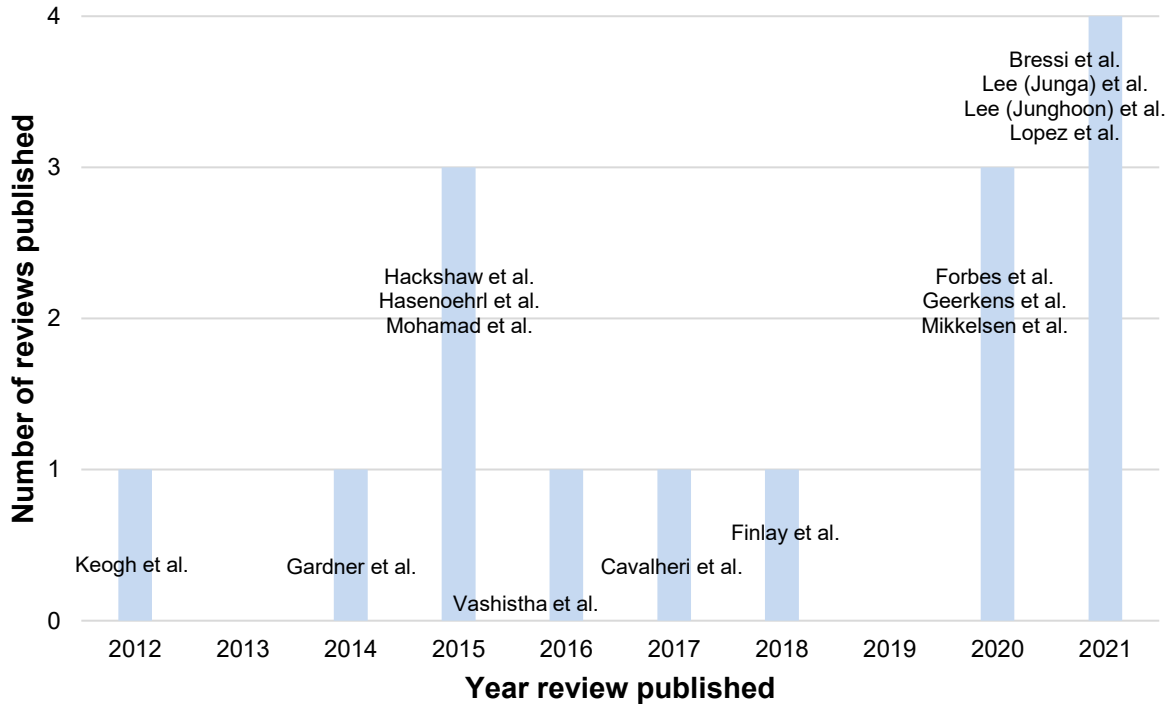


Figure 4 - Years of publication of included reviews

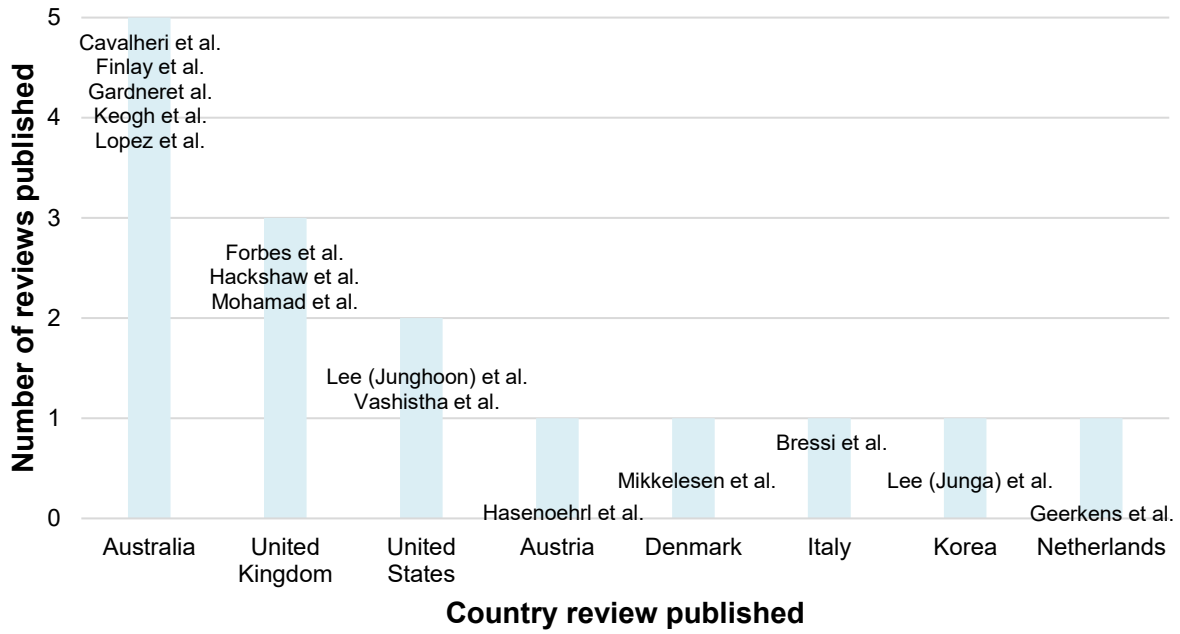


Figure 5 - Countries of publication of included reviews

3.6.3.2 Age

Tables 6 and 7 provide a summary of the age, sex and cancer type by study.

In Tables 6 and 7, age for each study is reported either a mean of all participants in the study (four reviews) (182-185), or as a range of the mean ages of participants in each primary paper (11 reviews). For the four studies reporting the mean age of all participants, mean age varied from 65 years (182) to 69.5 years (184). Of the remaining 11 reviews, mean ages of primary papers ranged from 54 years (175) to 77.5 years (178). As described previously, studies were included if at least 50% of the mean age of primary studies was 65 years or above, thus explaining some primary studies not reporting mean age 65 years or more.

3.6.3.3 Sex

The sex of participants was not reported in three reviews (169, 175, 176). Of the 12 studies that did report sex, ten reported that all participants were male (with prostate cancer) (149, 174, 177-181, 184-186). The two remaining reviews reported that the review sample were 66.5% male (183), and 61% male (182).

3.6.3.4 Cancer type

As shown in Tables 6 and 7, ten of the 15 reviews involved individuals with prostate cancer (149, 174, 177-181, 184-186). After accounting for overlap, these reviews analysed results from 50 different primary papers which involved 3,827 individuals with prostate cancer. This represents 71% of all individuals from which data was analysed in this review of reviews. Two reviews reported on people who had been diagnosed with lung cancer (175, 182), including 11 different

primary papers and 411 individuals (7.6% of all participants). The remaining three reviews included 26 different primary papers, involving 1,802 participants who had been diagnosed with one of the following cancers: multiple myeloma, leukaemia, lymphoma, endometrial, pancreas, ovary, biliary duct, lung oral, oesophagus, bladder, kidney, breast, lung, prostate or gastrointestinal (169, 176, 183). This represented 33.6% of all individuals in the review of reviews. These proportions do not add up to 100% because there was some overlap in primary studies included in both the reviews only including studies of people with prostate cancer, and the reviews including studies involving people with different cancer types.

3.6.3.5 Intervention details

Tables 6 and 7 summarise the details and types of interventions included in the studies.

For the studies examining the impact of physical activity on outcomes for people diagnosed with cancer, intervention details were reported according to the FITT principle (frequency, intensity, type, time), and also report the setting and context in which the interventions were conducted. The frequency of the interventions ranged from three times per day (175), to weekly (178). Intensity was reported in seven reviews and ranged between 50 and 85% of maximum intensity (heart rate or maximum repetitions). Resistance and aerobic exercise were the most common types of exercise, with all reviews reporting on the impact of resistance exercise, and eight reviews reporting on aerobic exercise. Interventions lasted between four and 104 weeks. Of the ten reviews to report the setting in which the intervention was implemented, nine reported on interventions that were conducted in more than one setting including home, hospital, clinic, gym or research centre. One review (185) included primary studies of interventions conducted at home only. Of the ten reviews that reported whether interventions were supervised or unsupervised, nine reported on both supervised and unsupervised interventions, and one included supervised interventions only (185).

3.6.3.6 Outcome measures

Outcome measures are listed in Tables 6 and 7. Across the 15 reviews the impact of interventions was assessed using multiple and diverse outcome measures. There was a total of 123 different outcome measures used to assess 25 different outcomes. As shown in Table 4, 12 reviews used objective measures to assess outcomes, 10 used self-report questionnaires.

Table 4 - Outcomes measures used in reviews of physical activity interventions

Review (author)	**Types of outcome measures**	
	Self-report questionnaires	**Objective**
Bressi et al.	✗	✓
Cavalheri et al.	✗	✓

Lee, Junga et al.	✓	✓
Lee, Junghoon et al.	NR	NR
Lopez et al.	✗	✓
Finlay et al.	✓	✓
Forbes et al.	✓	✗
Gardner et al.	✓	✓
Geerkens et al.	✓	✓
Hackshaw-McGeagh et al.	✗	✓
Hasenoerhrl et al.	✓	✓
Keogh et al.	✓	✓
Mikkelsen et al.	✓	✓
Mohamad et al.	✗	✓
Vashistha et al.	✓	✗

Note. NR, not reported.

3.6.3.7 Data analysis

In five reviews, meta-analysis was performed (175, 182-185) to analyse outcomes relevant to this review of systematic reviews. In each meta-analysis, a summary statistic was calculated for each primary study which describes the overall intervention effect (i.e., the difference between the outcome at baseline and after the intervention). Then a summary (pooled) intervention effect is produced by calculating the weight average of the intervention effects of the individual primary studies. These results are shown in Table 7. Heterogeneity was statistically assessed for all meta-analyses reported in the five included reviews to determine the variability between intervention effects of each study. Statistical heterogeneity was assessed using the Cochran Q test to calculate I^2. Heterogeneity was found to be low ($I^2 < 50\%$) (175) across all variables in the reviews by Cavalheri et al. (175) ($I^2 = 0\%$), and Lopez et al. (184) ($I^2 = 0\text{-}47\%$). For the review by Vashistha et al. (185), I^2 was below 50% for six outcomes assessed, but above 50% for four (QoL (physical) - $I^2 = 76\%$; QoL (general) - $I^2 = 77\%$; depression - $I^2 = 78\%$; and anxiety - $I^2 = 90\%$). The authors did not investigate the cause of heterogeneity further. For Lee (Junghoon) et al (183), two meta-analyses were conducted, with $I^2 = 0\%$ when examining muscle hypertrophy, but $I^2 = 85.2\%$ for muscular strength. Lee (Junga) et al. (182), reported that heterogeneity was high for aerobic capacity meta-analysis, but did not report the specific I^2 value, and did not report the measure of heterogeneity for other meta-analysis conducted. For 11 reviews, findings included in our analysis were reported narratively. Cavalheri et al. (175) conducted meta-analysis for some outcomes and narrative analysis for others.

3.6.3.8 Quality appraisal of primary papers as reported in included reviews

As shown in Tables 6 and 7, all reviews reported results of quality appraisal of primary papers. There were six different quality appraisal tools used, including Cochrane risk-of-bias (n = 9), PRISMA recommendations (n = 1), McMaster bias tool (n = 1), Downs and Black checklist of methodology (n = 1), Sackett evaluation of rigour (n = 1), and an unnamed appraisal tool (n = 2). Results of the quality appraisals varied substantially across the primary papers and reviews. The difference in tools used makes comparison across reviews difficult. However, for the nine reviews that appraised the quality of primary studies using the Cochrane risk-of-bias tool, six reported the range of scores for primary papers (out of seven criteria including random sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome data (attrition bias), incomplete outcome data (reporting bias), selective reporting (reporting bias) and other bias)). The range of scores reported in each review included 1-3/7 (175), 2-6/7 (149, 178), 3-5/7 (179), 3-6/7 (182), 4-6/7 (174). Three of the reviews that appraised quality using the Cochrane risk-of-bias tool did not report specific scores (i.e., out of 7), but Lopez et al. (184) reported that of the 15 primary papers reporting studies examining body composition, two reported some concern for risk of bias; and for those examining functional capacity, 10/13 studies reported concern for risk of bias. Mikkelsen et al. (169) used a revised version of the Cochrane risk-of-bias tool and reported that three of four included primary papers had some concerns of bias, and the remaining paper had a high risk of bias. One review did not report results of their appraisal using the Cochrane risk-of-bias tool (185). Of the remaining studies using tools other than the Cochrane risk-of-bias tool, Lee et al. (183) reported that 4/13 studies had a low risk of each type of bias measured using the PRISMA recommendations, Finlay et al. (186) reported majority of studies were appraised as moderate quality (plus one weak and one strong) using the McMaster Bias Tool, Gardner et al reported scores of 23-30/31 using the Downs and Black checklist of methodology, Keogh et al. (181) reported scores of 4-5/6 (Sackett evaluation of rigour) for the 12 included primary papers, Forbes et al. (176) stated that 4/10 primary papers reported studies with a high risk of bias and the remaining six with ‘some concerns’ using an unnamed tool to appraise quality whilst Hasenoehrl et al. (180) who also used an unnamed tool reported scores of 23-30/31.

3.6.4 Quality appraisal of included reviews

Table 5 summarises the results of conducting quality appraisal of the 15 reviews included in this review of systematic reviews using the JBI Critical Appraisal Checklist for Systematic Reviews and Research Syntheses. Eight reviews met 10 of the 11 quality criteria (169, 174-176, 178, 179, 184, 185), three reviews met nine criteria (149, 182, 186), and four met eight criteria (177, 180, 181, 183). Two reviews (149, 183) reported that only one researcher conducted quality appraisal, whereas for a further five reviews it was unclear how many researchers conducted quality appraisal (177, 180-182, 184). It was unclear in five reviews as to whether methods to minimise errors in data extraction were adequate (177, 180, 181, 183, 186), and 14 of 15 reviews did not

indicate whether publication bias was considered. Lopez and colleagues (184) were the only authors to consider publication bias.

Table 5 - Quality appraisal results for included review papers using the JBI Critical Appraisal Checklist for Systematic Reviews and Research Syntheses

	Review Q clearly stated	Appropriate inclusion criteria	Appropriate search strategy	Sources/resources adequate	Appraisal criteria adequate	Appraisal by two independent reviewers	Methods to minimise errors in data extraction adequate	Methods for combining studies appropriate	Publication bias considered	Policy/practice recommendations supported by data	Directives for new research appropriate
Bressi	Y	Y	Y	Y	Y	Y	Y	Y	U	Y	Y
Cavalheri	Y	Y	Y	Y	Y	Y	Y	Y	U	Y	Y
Finlay	Y	Y	Y	Y	Y	Y	U	Y	U	Y	Y
Forbes	Y	Y	Y	Y	Y	Y	Y	Y	U	Y	Y
Gardner	Y	Y	Y	Y	Y	U	U	Y	U	Y	Y
Geerkens	Y	Y	Y	Y	Y	Y	Y	Y	U	Y	Y
Hackshaw-McGeagh	Y	Y	Y	Y	Y	Y	Y	Y	U	Y	Y
Hasenoehrl	Y	Y	Y	Y	Y	U	U	Y	U	Y	Y
Keogh	Y	Y	Y	Y	Y	U	U	Y	U	Y	Y
Lee, Junga	Y	Y	Y	Y	Y	U	Y	Y	U	Y	Y
Lee, Junghoon	Y	Y	Y	Y	Y	N	U	Y	U	Y	Y
Lopez	Y	Y	Y	Y	Y	U	Y	Y	Y	Y	Y
Mikkelsen	Y	Y	Y	Y	Y	Y	Y	Y	U	Y	Y
Mohamad	Y	Y	Y	Y	Y	N	Y	Y	U	Y	Y
Vashistha	Y	Y	Y	Y	Y	Y	Y	Y	U	Y	Y

Legend

Yes	Y	No	N	Unclear	U

3.6.5 Effectiveness of interventions

3.6.5.1 Summary

Tables 6 and 7 summarise findings of the studies examining the impact of physical activity interventions in people diagnosed with cancer.

Figure 6 provides a visual summary of the outcomes of physical activity interventions showing improvements across multiple outcomes (including pain, lean muscle mass, functional performance and muscular strength), reduction in fatigue and improvement in multiple measures of health service use including post-operative complications. There was no evidence for reduction in anxiety or post-operative lung function. There were mixed findings for the impact of PA on quality of life and depression.

Findings are narratively described below in four categories: physical patient outcomes , psychological patient outcomes , health service utilisation outcomes, and cancer outcomes.

3.6.6 Patient outcomes – physical

Eleven reviews (149, 169, 174, 177, 178, 180-184, 186, 187) involving 64 different primary papers examined the impact of PA on 13 different physical outcome measures. Muscular strength was examined in seven reviews, and fitness and bone health were investigated in six reviews each. Functional performance was examined in five reviews, fat mass/adiposity in four reviews, and lean muscle mass and weight in three reviews each. Body composition was reported in two reviews, as were blood lipids, blood pressure, insulin resistance and PA levels. Pain was examined in one review. Tables 6 and 7 provide an overview of the outcomes measured and the findings of each of the 15 reviews included in this review of reviews.

Four of the six reviews examining muscular strength concluded that PA led to increased strength (177, 182-184), whilst Hasenoehrl et al. (180) and Keogh et al. (181) reported mixed findings; respectively, four of 11, and five of eight primary papers examining the impact of PA on strength concluded improved strength in the intervention group compared to control. Three of six reviews reported that PA increased fitness in older people with cancer (177, 181, 184) but two reported mixed findings and one meta-analysis found no statistically significant change (182) reported no change in fitness. Four of five reviews examining functional performance reported improvements with PA in older people with cancer (177, 180, 181, 184), but Mikkelsen et al. (169) reported mixed findings (two of four primary studies found a statistically significant increase in functional performance in the intervention group compared to the control group).

Bone health was examined in six reviews, with five reporting inconclusive evidence from primary papers (174, 177, 178, 180, 181). Mikkelsen et al. (169) reported that there was no evidence that PA improved bone health, although only one primary paper examined bone health in the review. The impact of PA on lean muscle mass was examined by three review papers, all of which reported increased lean muscle mass (177, 181, 184). Four reviews examined fat mass/adiposity, with only one concluding PA improves fat mass (184). The other three reviews did not find consistent evidence of reduced fat mass. One review reported that one of four primary papers found an improvement (177), another reported reduced adiposity in only one of nine included

primary papers (181), and two of four primary papers reported a significant reduction in fat mass in active people with cancer in a review by Mohamad et al. (149). No primary papers included in any of the four reviews reported increased fat mass. Physical activity was not associated with weight loss in one of three reviews (184), but Gardener and colleagues (177) and Mohamad and colleagues (149) reported mixed findings. That is, Gardner et al. (177) reported that one primary paper reported reduced BMI, one found increased BMI and three found no statistically significant change; whilst for Mohamad and colleagues (149), three primary studies reported reduced weight, one reported increased weight and four reported no statistically significant change. Body composition was not separated into components (i.e. fat, bone and muscle) in two reviews (178, 180), and both reported mixed findings.

Both reviews examining the impact of PA on blood lipids reported mixed findings (177, 180), whereas for blood pressure, one review reported no impact of PA (177) whilst another reported mixed findings, i.e. one of three primary studies reported improved blood pressure in the PA intervention group compared to the control group (178). Gardner et al. (177) also reported no change in insulin resistance in older people with cancer who engaged in physical activity, but Geerkens et al. (178) reported mixed findings. Pain was reduced in active older people with cancer (182).

3.6.7 Patient outcomes – psychological

Eight reviews (169, 176-178, 180-182, 185) examined at least one psychological outcome, summarising findings from a total of 53 different primary papers. Six psychological outcomes were assessed: all eight reviews examined the impact of PA on QOL, six assessed fatigue, three measured depression, two measured anxiety and one review each examined cognition and libido. Four of the six reviews examining the impact of physical activity on fatigue reported reduced fatigue, whilst two reported mixed findings (176, 178). Two of the eight reviews examining QOL which involved 19 primary papers concluded that physical activity improves QOL (180, 181), whilst the remaining six reviews reported that the evidence from included primary papers was conflicting, with some finding a positive association and others finding no association. Vashistha et al. (185) reported improved QOL in two of six meta-analyses. The data was derived from three different self-reported QOL questionnaires (the Functional Assessment of Cancer Therapy – General, the Functional Assessment of Cancer Therapy- Physical, and the Short Form 36) assessed at 12 weeks and 6 months after intervention. Likewise, Lee (Junga) and colleagues(183) reported statistically significant improvements in physical, social, functional and general wellbeing, but not for emotional, lung cancer-specific, and trial-specific wellbeing. Of the three reviews examining the impact of physical activity on depression, two concluded no association in men with prostate cancer (178, 185), whilst another review including meta-analysis reported reduced depression ($p<0.01$) in individuals with lung cancer (183). Both reviews examining the impact of physical activity on anxiety found no association (Vashistha et al., $p = 0.32$ (185); Lee (Junga) et al., $p=0.67$

(183)). Mikkelsen et al.'s (169) review involving four primary papers identified conflicting evidence for the role of physical activity in cognition in older people diagnosed with one of a range of cancer types. Finally, the one review examining the impact of PA on the libido and perceived sexual function of older men with prostate cancer, reported mixed results (178). Two of the primary papers included in the review reported no statistically significant changes in perceived sexual function, whilst one primary paper reported maintained sexual interest and activity. No reviews examining psychological outcomes reported that PA had an adverse effect on any outcome.

3.6.8 Health service use outcomes

One primary study examined health system use outcomes of PA, including hospital length-of-stay (LOS) post-operative complications and lung and exercise capacity (175). Pre-operative PA reduced length of hospital stay in people who had undergone lung resection to treat non-small cell lung cancer (NSCLC) ($p<0.0001$). Likewise, patients who had engaged in PA interventions before resection had lower rates of post-operative pulmonary complications ($p=0.004$) and post-operative duration of intercostal catheter ($p=0.001$), compared to those who were not active before surgery. Post-operative FVC and exercise capacity also increased with PA ($p<0.0001$), but lung function did not ($p<0.05$) (175).

3.6.9 Cancer outcomes

Four systematic reviews examined the impact of PA on measures of prostate cancer progression (177, 179, 180, 184). The three reviews which examined the impact of PA on testosterone levels (177, 179, 180) reported no change; as did the three reviews investigating the impact PA on prostate specific antigen (PSA) (177, 179, 184). Hasenoehrl et al. (180) reported immune-like growth factor-1 (IGF-1) increased with PA in the one primary study to examine this relationship but concluded that the evidence for the impact of PA on human growth hormone was unclear. No review examined the impact of PA on mortality.

Legend	No benefit of PA on health outcome Mixed evidence for impact of PA on health outcome PA benefits health outcome	The numbers (n/N) reported next to health outcome: n=reviews that reported a beneficial effect of PA on the health outcome; N=reviews reporting on that health outcome.

Figure 6 - Summary of the evidence for the impact of physical activity interventions on health outcomes in people with cancer aged >65 years

Table 6 - Summary of physical activity intervention studies involving meta-analysis

First author, Year, Country	Objective/Aim/Purpose	n included RCTs/quasi-RCTs (n participants) age – mean or range, sex, cancer type	Intervention: PA Frequency; PA Intensity; PA Time; PA Type; Setting; Context/Mode.	Outcomes (measures)	Effect size	Quality appraisal tool used (score)
Physical activity only interventions						
Cavalheri (175), 2017, Australia	The primary aims were to determine the effect of preoperative exercise training (compared to usual care) on postoperative outcomes, such as risk of developing a postoperative pulmonary complication, and postoperative duration of intercostal catheter use in adults scheduled to undergo lung resection for NSCLC. The secondary aims were to determine the effect of preoperative exercise training on length of hospital stay, fatigue, dyspnoea, exercise capacity, lung function, and postoperative mortality.	5 (n=167) Mean age range: 54-72.5y Sex NR Lung cancer (scheduled to undergo lung resection)	3xday–5xwk; intensity NR; aerobic, resistance, inspiratory training, stretching or combination; 1-4wk; setting NR; supervised or unsupervised or combination.	LOS (n days in hospital)	Z=7.02, p<0.00001	Cochrane risk-of-bias (ranged from 1-3/7)‡
				Complications (n days intercostal catheter	Z=7.02, p<0.00001	
				Complications (pulmonary)	Z=3.52, p=0.0004	
				Exercise capacity change (pre- vs post-operative change in 6MWD)	MD=18.23m, 95% CI 8.50, 27.96m, p<0.0001	
				FVC change (pre- vs post-operative)	MD 2.97%, 95% CI 1.78, 4.16%, p<0.0001	
				Lung function change (pre- vs post- operative change in $FEV_{1)}$	0/3	
Lee, Junga (183) 2021, Korea	The purpose of this meta-analysis is to investigate the effectiveness of exercise	6 (n=244) Mean age: 65y 61% male Lung cancer	Mean frequency: >5/wk; 50-80% maximum intensity; aerobic, resistance	Muscular strength (arm curl test)	d=1.39, p<0.01	Cochrane risk-of-bias (ranged from 3-6/7)‡
				Fitness (6MWT)	d=0.38, p=0.35	
				Pain (NR)	d=-0.68, p=0.03	

	interventions (compared to standard care) in patients with lung cancer (LC) during chemotherapy regarding physiological and psychological outcomes.		or combined; mean time 9.5wk; home or clinic/hospital; supervised or unsupervised.	QOL (FACT-P
				FACT-S;
				FACT-F;
				FACT-G;
				FACT-E;
				FACT-L;
				FACT-T;
				FACT-total)
					d=0.46, p<0.01;
					d=0.39, p<0.01;
					d=0.30, p=0.02;
					d=0.39, p=0.00;
					d = 0.07, p=0.61;
					d= − 0.12, p=0.84;
					d=0.21, p=0.58;
					d=0.39, p=0.73.	

				Depression (HADS)	d= − 0.55, p<0.01	
				Anxiety (HADS)	d = − 0.06, p=0.67	
Lee, Junghoon (182) 2021, US	The purpose of this study was to systematically review and quantify the effects of RT (comparator groups were not described) on muscular strength and hypertrophy in elderly cancer patients.	13 (n=717) Mean age 66y 66.5% male Prostate, breast, renal and gastrointestinal	2-3x/wk; 50-100% maximum intensity; resistance only; 8-48wk; research centres; supervised.	Muscular strength (NR)	Z= 0.87, p<0.001	PRISMA recommendations (4-13 studies had low risk of each type of bias assessed)[£]
Lopez (184), 2021, Australia	The aim of the present study is 1) to systematically review and analyse the resistance training effects on body composition measures, functional capacity tests, cardiorespiratory fitness, muscle strength, body mass index (BMI), and prostate-specific antigen (PSA) levels and 2) to verify the minimal dose regarding the prescribed exercise components (i.e., type, duration, volume, and intensity) and effects on these	23 (n=1748) Mean age 69.5y 100% male Prostate cancer	Mean frequency 2.4x/wk; 60-85% maximum intensity; resistance or aerobic and resistance; mean time 19.5wk; setting NR; context NR.	Fat mass/adiposity (% body fat; fat mass; trunk fat mass)	MD=-1%, p<0.001; MD=-0.6kg, p<0.001; MD=-0.3kg, p=0.025.	Cochrane risk-of-bias: (Studies examining body composition: 2 of 15 studies reported some concern for risk of bias; Studies examining functional capacity: 10/13 studies reported concern for risk of bias)[‡]
				Lean muscle mass (lean mass; appendicular lean mass)	MD=0.5kg, p<0.001; MD=0.4kg, p<0.001	
				Weight (BMI)	MD=0.0kg.m^2, p=0.736	
				Functional performance (30SS; 5xSS; 400m; 6m fast WT; 6m usual WT; TUG; SCT)	MD=2.8reps,p<0.001 MD=-1sec, p<0.001; MD=8.3sec, p<0.001 MD=-0.1sec, p=0.04; MD=-0.2 sec, p=0.225; MD=-0.3sec, p=0.261; MD=-0.2sec, p=0.008	
				Muscular strength (Chest press; Leg press;	MD=3.9kg, p<0.001; MD=23.5kg, p<0.001;	

	outcomes. Comparator groups were not described.			Leg extension; Seated row)	MD=8.8kg, p<0.001; MD=5.2kg, p<0.001	
				Fitness (VO_2 max)	MD=1.3ml.kg.min-1, p<0.001	
				Cancer progression (PSA)	MD=0.1ng.ml-1, p=0.583	
Vashistha (185), 2016, USA	To evaluate the effects of exercise interventions (compared to usual or standard care) on fatigue, QOL, depression, and anxiety in PCa patients.	13 (n=1,057) IG: 69.4y; CG: 69.3y 100% male Prostate cancer	Frequency NR; intensity NR; aerobic, resistance, combination or qigong; 4-24wk; home; supervised.	QOL (FACT-G 12 wk; FACT-G 6mo; FACT-P 12 wk; FACT-P 6mo; FACT-F 12wk; FACT-F 6mo)	Z=3.01, p=0.003; Z=2.78, p=0.005; ‘ Z=2.90, p=0.004; Z=1.97, p=0.05; Z=5.93, p<0.00001; Z=4.64, p<0.00001	Cochrane risk-of-bias (scores NR)‡
				Fatigue (FACT-F 12wk; FACT-F 6mo)	Z=5.93, p<0.00001; Z=4.64; p<0.00001	
				Depression (BSI)	Z=1.23, p=0.22	
				Anxiety (BSI)	Z=1.00, p=0.32	

£The PRISMA recommendations quality appraisal instrument assesses quality across six items: appropriate generation of random allocation sequence, allocation concealment, blinding of assessment and collection outcomes, participants lost follow-up, complete outcome data, and intention-to-treat. The scores were not reported for each original study, but the number of studies with low risk of each type of bias are reported.

Table Notes. DEXA, dual-energy x-ray absorptiometry; BMD, bone mass density; ADT, androgen deprivation therapy; NR, not reported; NSCLC, non-small cell lung cancer; n, number; FEV_2, forced expiratory volume; MD, mean difference; CI, confidence intervals; y, years; Z, effect size; GLTEQ, Godin leisure-time exercise questionnaire; BCM for PA, body cell mass for physical activity; CHAMPS, community health activities model program for seniors; AAS, Active Australia Survey; HRQoL, health-related quality of life; LWBC, living with and beyond cancer; FACT-G, Functional assessment of cancer therapy-general; FACT-P, FACT-physical; FACT-F, FACT-functional; FACT-B, FACT-breast; FACT-C, FACT-colorectal; FACT-E, FACT-emotional.

Table 7 - Summary of physical activity intervention studies using qualitative synthesis (not involving meta-analysis)

First author, Year, Country	**Objective/Aim/Purpose**	**n included RCTs/quasi-RCTs (n participants) age, sex, cancer type**	**Intervention: <u>For PA:</u> Frequency; Intensity; Time; Type; Setting; Context/Mode. <u>For Diet:</u> Nutrient/dietary behaviour targeted (approach; frequency; duration)**	**Outcomes (measures)**	**Findings: n primary studies that reported improvement, or adverse effect, on the outcome examined/n studies examining outcome**	**Quality appraisal tool used (score)**
Physical activity only interventions						
Bressi (174), 2021, Italy	This systematic review analyses the effectiveness of physical exercise (compared with standard care or placebo active control) in preventing accidental falls and fractures and reducing the loss of BMD in men with prostate cancer receiving ADT.	9 (n=625) Mean age range: 66-70.8y 100% male Prostate cancer in men receiving ADT	1xwk-5xwk; intensity 60-85%; time NR; aerobic, resistance, impact-loading exercise or football training; setting NR; supervised, unsupervised or combination.	Bone health (BMD - DEXA)	2/9 papers reported improvements, 7/9 reported no change.	Cochrane risk-of-bias (ranged from 4-6/7)[‡]

Cavalheri (175), 2017, Australia	The primary aims were to determine the effect of preoperative exercise training (compared to usual care) on postoperative outcomes, such as risk of developing a postoperative pulmonary complication, and postoperative duration of intercostal catheter use in adults scheduled to undergo lung resection for NSCLC. The secondary aims were to determine the effect of preoperative exercise training on length of hospital stay, fatigue, dyspnoea, exercise capacity, lung function, and postoperative mortality.	5 (n=167) Mean age range: 54-72.5y Sex NR Lung cancer (scheduled to undergo lung resection)	3xday–5xwk; 1-4wk; intensity NR; 1-4wk; aerobic, resistance, inspiratory training, stretching or combination; setting NR; supervised or unsupervised or combination.	Lung function change (pre- vs post- operative change in $FEV_{1)}$	0/3 papers reported improvements, 3/3 reported no change.	Cochrane risk-of-bias (ranged from 1-3/7)[‡]
Finla y(186), 2018, Australia	This review aims to provide a summary of physical activity behaviour change trials targeting prostate cancer survivors, assess the feasibility of these interventions and, if possible, identify intervention and study characteristics associated with significant intervention effects. Comparator groups received usual care or were waitlist controls.	6 (n=867) Mean age range 65.2-74.9y 100% male Prostate cancer	frequency NR; intensity NR; 4wk-6mo; aerobic, resistance, Wii Fit, or stretching; gym, home or clinic; supervised or unsupervised, education, telephone, peer-support, counselling.	Physical activity (7-day PA recall GLTEQ, BCM for PA, pedometer counts, accelerometer counts, CHAMPS, AAS, Sedentary 5-item questionnaire)	8/12 reported improvement, 4/12 reported no change.	McMaster Bias Tool (10 studies moderate, one study strong, one weak)[ᴖ]
Forbes (176), 2020, UK	The aim of this review was to summarize the current literature for the effectiveness of activity	10 (n=741) Mean age range 66-73y Sex NR	Frequency NR; intensity NR; aerobic, resistance, or balance; 1-52wk;	QOL (FACT-G, FACT-P, FACT-B, EORTC, QLQ-C30, SF-36, GSEB, CSI)	6/10 reported improvement or diminished decline, 4/10	Unnamed appraisal tool (4/10 papers overall high risk of bias, 6/10 some concerns)

	and nutritional based interventions (compared to usual care, active control or wait-list control), on health-related quality of life (HRQoL) in older adults living with and beyond cancer (LWBC).	Prostate, breast, lung, mixed (specific type NR), bladder	home, hospital or community; supervised or unsupervised.		reported no change.	
				Fatigue (FACT-F)	2/4 reported improvement, 2/4 reported no change.	
Gardner (177), 2014, Australia	The aim of this systematic review was to provide a comprehensive and up-to-date summary of the effects of exercise (compared to usual care or active control) on treatment-related adverse effects for patients with PCa (prostate cancer) receiving ADT.	10 (n = 564) Mean age range 63 – 72y 100% male Prostate cancer	Daily-2x/wk; 55-85% maximum intensity; aerobic, resistance or combination; 12-24wk; setting NR; supervised or unsupervised.	Bone health (BMD - DEXA)	0/1 reported improvement, 1/1 reported no change.	Downs and Black checklist of methodology (23-30/31)
				Fat mass/adiposity (fat mass, body fat %age)	1/4 reported reduced fat mass/adiposity, 3/4 reported no change.	
				Lean muscle mass (total and regional lean body mass, thigh volume)	4/4 reported improvement.	
				Weight (kg weight loss, neck and waist circumference, BMI)	1/5 reported reduced weight/BMI, 1/5 reported increased BMI, 3/5 reported no change.	
				Functional performance (6m walk, 6m backward walk, sit-to-stand, 6m fast walk, stair-climb, TUG)	4/5 reported improvement, 1/5 reported no change.	
				Muscular strength (upper- & lower-limb strength muscular endurance, grip strength)	8/9 reported improvement, 1/9 reported no change.	
				Fitness (400m walk, 6MWT)	7/9 reported improvement,	

					2/9 reported no change.	
				BP (arterial systolic and diastolic pressure)	0/1 reported improvement.	
				Blood lipids	1/1 reported mixed findings.	
				Insulin resistance (Fasting plasma glucose)	0/1 reported improvement, 1/1 reported no change.	
				Fatigue (NR)	4/7 reported improvement, 3/7 reported no change.	
				QOL (NR)	6/9 reported improvement, 3/9 reported no change.	
				Disease progression (PSA, testosterone serum levels)	0/6 reported improvement, 6/6 reported no change.	
Geerkens (178), 2020, Netherlands	The aim of this review is to systematically review randomized controlled trials on lifestyle interventions (comparator groups were not reported) on PCa patients undergoing androgen deprivation therapy.	20 (n=1217) Mean age range: 64 – 77.5yr 100% male Prostate cancer	Daily-1x/wk; intensity NR; aerobic, resistance, stretching, Wii Fit, football; 6-52wk; setting NR; supervised or unsupervised.	Bone health (BMC & BMC – DEXA; serum biomarkers: alkaline phosphatase, P1NP, N-telopeptide, N-telopeptide/creatinine ratio, vitamin D, osteocalcin, CTX, NTX, GBS-ASP)	1/5 reported improvement, 4/5 reported no change.	Cochrane risk-of-bias (ranged from 2-6/7)‡
				Body composition* (BMI, W:H ratio, waist girth, neck girth, EXCAP; specific measure NR to assess: mitochondrial protein measure, muscle cellular stress, total muscle fibres, myonuclei)	11/18 reported improvement in at least one measure, 7/18 reported no change.	

				Fitness (VO_2 max, 6MWT, 400m WT, respiratory gas analysis, 4MWT, HR)	4/8 reported improvement in at least measure, 4/8 reported no change.	
				BP (arterial diastolic and systolic)	1/3 reported improvement, 2/3 reported no change.	
				Insulin resistance (OGTT, fasting glucose, fasting insulin, glucose AUC, insulin AUC, IGF-1, IFGBP-1, IGFBG-3, HBA1c)	0/1 reported improvement, 1/1 reported no change.	
				QOL (STAI, SF-36, EORTC-QLQ-C30, QLQ-PR25, PSS, FACT-G, LFDI, FACT-P, PORPUS, EPIC)	4/14 reported improvement, 10/14 reported no change.	
				Fatigue (FACT-F, FSS, QLQ-C30, SF-36, SFS BMI, FACIT-Fatigue, WORTC-QLQ-C30, SPPB, BFI)	5/10 reported improvement, 5/10 reported no change.	
				Depression (CES-D, BSI-18)	0/4 reported improvement, 4/4 reported no change.	
				Libido/sexual function (QLQ-PR25)	2/3 reported improvement in at least one outcome, 1/3 reported no change.	
Hackshaw-McGeagh (179), 2015, UK	We conducted a systematic review of dietary, nutritional, and physical activity	4 (n=439) Mean age range: 65.3-71.9y	Frequency NR; intensity NR; aerobic or resistance; 13-	Disease progression (PSA)	0/4 reported improvement, 4/4 reported no change.	Cochrane risk-of-bias (ranged from 3-5/7)[‡]

	interventions (compared to usual care, waiting list or education booklet) aimed at modifying prostate cancer progression and mortality in men with prostate cancer.	100% male Prostate cancer	104wk; setting NR; context NR.			
Hasenoehrl (180), 2015, Austria	The aim of this systematic review was to focus on specific effects of resistance exercise (RE) in the adjuvant therapy and rehabilitation of PCa patients receiving or having received androgen deprivation therapy (ADT). Some studies did not involve a control group, and others compared to a usual care group.	13 (n=867) Mean age range 66.3-73.1y 100% male Prostate cancer	Daily-2x/wk; 55-80% maximum intensity; resistance; 12-52wk; home or fitness centre; individual or group; supervised or unsupervised.	Bone health (BMD - DEXA; serum osteocalcium, urinary deoxypyrodinoline cross-links)	1/3 reported improvement, 2/3 reported no change.	Unnamed risk-of-bias checklist (23-30/31)♂
				Body composition* (BMI, appendicular and whole body lean mass, visceral adipose tissue, whole-, lower-and upper-body muscle mass, subcutaneous & intermuscular mass, chest skinfold thickness, waist circumference)	7/12 reported improvement, 5/12 reported no change.	
				Blood lipids (serum total, HDL & LDL cholesterol and triglycerides)	1/3 reported improvement, 2/3 reported no change.	
				Functional performance (STST, fast 6MWT, usual 6MWT, TUG, 6m walk, 6m backward walk, stair climb, 5 chair stands, balance – neurocon smart balance master)	2/2 reported improvement.	
				Muscular strength (leg extension, chest press, grip strength, standard load test)	4/11 reported improvement, 7/11 reported no change.	

				Fitness (aerobic exercise tolerance, 400m walk)	4/9 reported improvement, 5/9 reported no change.	
				QOL (FACT-P, FACT-G, FACT-E, FACT-S, SF-36, PORPUS)	6/9 reported improvement, 3 reported no change.	
				Fatigue (FACT-F, MFSI-SF, RE, AE)	7/9, reported improvement, 2/9 reported no change.	
				Disease progression (PSA, testosterone, IGF-1, IGFBP-3, hGH)	3/8 reported improvement, 5/8 reported no change.	
Keogh (181), 2012, Australia	This systematic review of the literature evaluates whether exercise could reduce symptoms and improve quality of life for prostate cancer patients. Comparator groups were not described.	12 (n=359) Mean age range: 66-72y 100% male Prostate cancer	2-3x/wk; intensity NR; aerobic or resistance; 12-24wk; home or community; group or individual, counselling.	Bone health (DEXA)	1/2 reported improvement, 1/2 reported no change.	Sackett evaluation of rigour (4-5/6)ℑ
				Fat mass/adiposity (CTS, DEXA)	1/9 reported improvement, 8/9 reported no change.	
				Lean muscle mass (quadricep thickness, MRI, DEXA)	5/6 reported improvement, 1/6 reported no change.	
				Functional performance (SOT, TUG, 5STS)	3/5 reported improvement, 2/5 reported no change.	
				Muscular strength (isometric knee extension)	5/8 reported improvement, 3/8 reported no change.	
				Fitness (400m walk, 6MWT, VO_2 max, METS treadmill, shuttle walk test)	7/11 reported improvement, 4/11 reported no change.	

				QOL (FACT-P, QLQ-C30, SF-36)	5/12 reported improvement, 7/12 reported no change.	
				Fatigue (FSS, FACT-F, PFS, BFI)	3/10 reported improvement, 7/10 reported no change.	
				Fatigue (PMS, FACT-F, FACIT-F, BFI)	8/9 reported improvement, 1/9 reported no change.	
Mikkelsen (169), 2020, Denmark	The aim of this systematic review was to investigate the effect of exercise therapy (compared to usual care or active static stretching) during medical antineoplastic treatment in older patients (≥ 65y) with cancer.	4 (n=412) Mean age range: 68-77y Cancers: breast, prostate, colorectal, esophagus, oral, kidney, bladder, lung, stomach, biliary ducts, ovary, hepato-cellular, lymphoma, womb, endometrium, pancreas	1-5xwk; intensity NR; aerobic, resistance, Wii-fit, speed-feedback therapy; 4wk-12mo; home or clinic; supervised or unsupervised.	Bone health (DEXA)	0/1 reported improvement, 1/1 reported no change	Revised Cochrane risk-of-bias tool (3/4 studies some concerns of bias, 1/4 high risk bias)∞
				Functional performance (SPPB, GPCS, 6MWT, ADL, IADL, S&R, TUG)	2/4 reported improvement, 2/4 reported no change.	
				Muscular strength (CST, arm curl test, leg press, grip strength, chest press)	1/2 reported improvement, 1/2 reported no change.	
				Physical activity (EXCAP, self-reported PA)	1/3 reported improvement, 2/3 reported no change.	
				QOL (FACT-G)	0/1 reported improvement, 1/1 no change.	
				Cognition (FAB)	1/2 reported improvement, 1/2 reported no change	
Mohamad (149), 2015, UK	This systematic review looked at the effect of diet and exercise interventions (compared to normal/usual	8 (n=628) Mean age range: 66.3-76.9y	2-3xweekly; intensity ranged from 50-80% maximum; aerobic, resistance, or	Fat mass/adiposity	2/4 reported improvement, 2/4 reported no change.	Cochrane risk-of-bias (ranged from 2-6/7)ǂ

	care or active control) on body weight among men treated for prostate cancer.	100% male Prostate cancer	stretching; 4wk-6mo; home or clinic; supervised or unsupervised, education, group or individual.	Weight	4/8 reported reduced weight, 1/8 reported increased weight, 3/8 reported no change.	

*Body composition measure in Geerkens did not separate according to specific measure, so are reported in this table as one outcome measure.
‡ Cochrane risk-of-bias tool assesses six types of bias using seven criteria (random sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome data (attrition bias), selective reporting (reporting bias) and other bias). The range of scores of the included original studies is reported, with the higher the score out of seven meaning less risk of bias.
∞Revised Cochrane risk-of-bias tool assesses 5 types of bias risk due to randomisation process, deviations from intended intervention, missing outcome data, outcome measurement and selection of reported results. An overall risk of bias is reported based on the scores for each type of bias and the report is categorised as being at high risk of bias, as having some concerns of bias or as being low risk. The number of studies within each category are reported.
¥Queen's Joanna Briggs Collaboration forms for critical appraisal of experimental studies assessed the quality of 10 aspects of methodology: randomization, treatment allocation concealment, similar baseline characteristics, eligibility criteria specified, outcome assessors blinded to treatment allocation, care provider blinded, patient blinded, point estimates and measure of variability reported for primary outcomes, and intention-to-treat analysis (scores not reported).
^McMaster bias tool assesses the quality of 8 aspects of the studies methodology: selection bias, design, confounders, blinding, methods, withdrawals and dropouts, intervention integrity and data analysis and studies given overall assessment of strong, moderate or weak.
ℑ Sackett evaluation of rigour assessed six aspects: inclusion and exclusion criteria described, intervention adequately described, reliable outcomes measures, valid outcome measures, blind assessment, all allocated participants accounted for. The range of scores of the included original studies is reported.

Table Notes. DEXA, dual-energy x-ray absorptiometry; BMD, bone mass density; ADT, androgen deprivation therapy; NR, not reported; NSCLC, non-small cell lung cancer; n, number; FEV_2, forced expiratory volume; MD, mean difference; CI, confidence intervals; y, years; Z, effect size; GLTEQ, Godin leisure-time exercise questionnaire; BCM for PA, body cell mass for physical activity; CHAMPS, community health activities model program for seniors; AAS, Active Australia Survey; HRQoL, health-related quality of life; LWBC, living with and beyond cancer; FACT-G, Functional assessment of cancer therapy-general; FACT-P, FACT-physical; FACT-F, FACT-functional; FACT-B, FACT-breast; FACT-C, FACT-colorectal; FACT-E, FACT-emotional; EORTC, European organisation for research and treatment of cancer; SF-36, 36-item short form survey; CSI, cancer symptom inventory; QLQ-C30, quality of life questionnaire; MFSI-SF, multi-dimensional fatigue syndrome inventory-short form; RE, resistance exercise; AE, adverse events; MRI, magnetic resonance imaging; FSS, fatigue severity scale; PFS, piper fatigue scale; BFI, brief fatigue inventory; HADS, hospital anxiety and depression scale; S&R, sit-and-reach; IADL, instrumental activities of daily living; ADL, activities of daily living; FAB, Fullerton advanced balance; BP, blood pressure; kg, kilogram; PSA, prostate-specific antigen; BMC, bone mineral content; EXCAP, exercise for breast cancer patients; WT, walk test; BMI, body mass index; IG, intervention group; CG, control group; QOL, quality of life; LOS, length of stay; mo, months; wk, weeks; PA, physical activity; FVC: forced volume capacity; NR, not reported; GPCS, Global Physical Capacity Score; RT, Resistance Training; PCa, prostate cancer; MD, Mean Difference; 6MWD, 6 minute walk distance; 30SS 30 second sit-to-stand; TUG, timed up and go test; HR, heart rate; OGTT, oral glucose tolerance test; AUC, area under the curve: IGF, insulin growth factor; IFGBP-1, insulin-like growth factor binding protein; IFG, impaired fasting glycaemia; HbA1c, glycosylated haemoglobin; W:H ratio, waist-to-hip ratio; CTX, c-terminal telopeptide; NTX, n-terminal telopeptide; GBS, group b streptococcus; P1NP, procollagen-1 N-terminal peptide; STAI, state-trait anxiety inventory; PSS, perceived stress scale; LLFDI, late-life function and disability instrument; FACIT-Fatigue, functional assessment of chronic illness therapy; SFS, social family support; CES-D, center for epidemiological studies depression scale; QLQ-PR25, quality of life - prostate; PORPUS, patient-oriented prostate utility scale; SPPB, short physical performance battery; EPIC, European prospective investigation into cancer; HDL, high-density lipoproteins; LDL, low-density lipoproteins; ml.kg.min-1, millilitres per kilogram per minute; ng.ml-1, nanograms per millilitre; sec, seconds; $kg.m^2$, kilograms per metre squared; METS, metabolic equivalents; WC, waist circumference.

3.7 Summary and Discussion

This review synthesised review level evidence on the effectiveness of lifestyle interventions in people diagnosed with cancer, and where majority of study participants were aged 65 years or older. This review showed there is review-level evidence that physical activity interventions show improvements across multiple outcomes (including pain, lean muscle mass, functional performance and muscular strength), reduction in fatigue, and improvement in multiple measures of health service use including post-operative complications. There was no evidence for reduction in anxiety or post-operative lung function. There were mixed findings for the impact of physical activity on quality of life and depression.

The review showed that in this population physical activity was associated with multiple benefits but there were important differences in outcomes when compared to data from younger adults with cancer. Physical activity improved lean muscle mass, muscular strength, functional performance, and reduced fatigue, consistent with findings from younger adults (11, 12) but, in contrast to younger adults, physical activity did not impact anxiety, and the data on QOL and depression is mixed (11, 12).

It is proposed that differences in some outcomes of physical activity between older and younger adults may reflect the fact that older adults are more likely to suffer from co-morbid conditions that may increase the severity of anxiety, depression (188), and QOL (189) making these outcomes less responsive to physical activity. Studies comparing baseline characteristics of older and younger participants could shed light on this possibility. It is also possible that the mechanisms by which PA exerts its beneficial effect differ according to age, highlighting the importance of mechanistic studies in different populations.

The present review synthesised data from multiple reviews including over 5,400 individuals, majority of whom were aged 65 years or older. The data was heavily weighted towards men with prostate cancer (71% of all subjects) limiting somewhat generalisability of findings to other cancers. Based on the findings of this review, clinicians can be confident to recommend PA for older adults with cancer, especially those with prostate cancer, where the goal is to improve wellbeing and physical fitness. There was however no data on participants with unique geriatric conditions such as frailty and sarcopenia which are characterised by biological differences (165, 190) that could impact PA effectiveness. In addition, some outcomes were not studied, e.g. no review of older adults with cancer examined the impact of PA on mortality or cardiac outcomes which impacts the ability to make recommendations for PA in this population for these outcomes.

3.7.1 Strengths and limitations

This is the first review of reviews to synthesise the evidence for PA interventions in reviews where majority people were aged 65 years or older, highlighting multiple benefits of PA in older

individuals with cancer and the unique differences in outcomes as compared to younger adults (such as inconclusive findings for QOL and anxiety and depression). The review also highlights some notable gaps in evidence, including lower representation of cancers other than prostate and patients with comorbidities and sarcopenia that should be prioritised in future research.

There are also important limitations to this research. Only reviews written in English were included, meaning potentially eligible reviews published in other languages were not included in our analysis. It is possible that people from non-English speaking countries may have different experiences related to physical activity interventions (e.g., access to physical activity), the findings of this research cannot be assumed to be able to be extrapolated to non-English speaking populations. The study participants included a minority of younger individuals which might have affected the study findings. For some health outcomes, e.g. depression and health service use outcomes, findings are derived from a small number of primary papers and a limited number of reviews. Interventions that targeted more than one behaviour were not included (i.e., physical activity in addition to another lifestyle behaviour such as diet). The findings also may be limited by the study design used (review of reviews) because the findings of primary research that has not yet been reviewed would not be represented in the analysis. The majority of systematic reviews included in this review of reviews did not discuss the impact of publication bias on the findings. Thus, there is a lack of transparency which does not allow understanding of whether findings may have been overestimated/distorted because studies in which favourable results have been found were more likely to be published (191). In addition, there were some reviews that did not report whether multiple reviewers were involved with screening of original papers, which means that there is no checking of interpretation of whether original papers should be included. This may affect overall findings (192). Finally, the exclusion of reviews of data from multimodal interventions (i.e., interventions in which more than one lifestyle behaviour change was targeted) does not allow the review to add understanding about how different behaviours may interact to induce changes in outcomes, and reduces the applicability of the findings in the real-world settings where individuals may attempt to make multiple changes concurrently.

3.7.2 Impact of other types of interventions in older people diagnosed with cancer

Initial discussions between the candidate and supervisors led to the development of a research question to examine the review-level evidence for the effectiveness of physical activity, diet, smoking cessation and alcohol moderation interventions on CVD risk in older people who had been diagnosed with cancer. The findings of this initial research problem would inform decisions about the role of lifestyle behaviour advice and support in future approaches to reduce the impact of cardiovascular disease in cancer. The focus on older people was critical given existing evidence focuses on younger people with cancer, despite cancer and CVD being most common in older people. However, as is often the case in research, the research question developed and altered according to the availability of evidence and further discussions to ensure the meaningfulness of

findings. Specifically, there were a lack of studies examining the impact of lifestyle interventions on CVD risk outcomes in people affected by cancer and review-level evidence for lifestyle interventions apart from physical activity was scarce/non-existent (small number of reviews regarding diet interventions, and none for smoking and alcohol). It was deemed that the favourable impact of lifestyle interventions on cardiovascular outcomes (in people without cancer) was well-established and therefore it was more appropriate to consider the evidence for outcomes in cancer. Although there were primary-level papers reporting the impact of smoking and alcohol cessation interventions in cancer, a review of primary papers across all lifestyle interventions would be inappropriate (and beyond the scope of this candidature), given the many existing reviews of physical activity interventions, and a number of existing diet intervention reviews.

The findings of this review are an important contribution to the literature and support the role of physical activity in older people with cancer where the aim is to improve specific outcomes including wellbeing and physical fitness. There is a need for data to confirm the impact of physical activity on cardiac outcomes in older people with cancer. Although it was necessary to narrow the scope for the purpose of a meaningful and achievable review, it is important to summarise the data which does exist for other lifestyle interventions to consider their potential role in a future approach to optimise cardio-oncology outcomes, and to allow for a broad 'picture' to emerge regarding the impact of lifestyle in older people affected by cancer. Therefore, in the following sections, the limited review-level evidence for diet interventions in older people with cancer is summarised and discussed, followed by the primary level evidence for smoking cessation and alcohol moderation interventions in older people who have been diagnosed with cancer.

3.7.2.1 Effectiveness of diet interventions in older people affected by cancer

In initial searches (before the narrowing of focus on physical activity), four reviews were found that examined the impact of diet interventions on people aged 65 years or more and diagnosed with cancer (147-149, 178). Overlap of reviews was calculated and found to be 'slight' (0.3%) (calculated and interpreted according to Pieper et al. (173)), there were 26 different primary papers reviewed in the four reviews (i.e., only two primary papers were included in more than one of the reviews), involving 2,389 people diagnosed with cancer, with mean age range of primary paper samples being 55-78 years. Two reviews included examined the effectiveness of diet interventions in men with prostate cancer (149, 178), one in people with colorectal cancer (148), and one in people diagnosed with one of either colorectal, gastrointestinal, head and neck, pancreas, lung, or unspecified cancer (147). Of note is that two of these reviews were included in the physical activity review of reviews (149, 178), as they reported separate analyses of physical activity interventions and diet interventions. For the diet intervention studies, there were diverse types of interventions examined. Geerkens et al. (178) included two studies investigating the impact of a daily supplementation of 20 grams of soy protein in men diagnosed with prostate cancer undergoing androgen deprivation therapy. Looijaard et al. (148) synthesised data from three primary papers

assessing the impact of pre-operative oral supplementation in people diagnosed with colorectal cancer. These included two primary papers reporting interventions involving daily protein and calorie supplementation (one paper involved 24 grams protein and 602 calories; the other 40 grams protein and 600 calories). The third primary paper examined the impact of carbohydrate supplementation (200Kj) 2 hours before surgery (compared to post-operative supplementation, and pre- and post-operative supplementation). Mohamad at al. (149) synthesis of the impact of dietary interventions in men diagnosed with prostate cancer involved several different dietary interventions. Five of the six primary studies included dietary counselling or advice (weekly or bi-weekly), but recommendations varied across studies from low-fat diet with optional vitamin E and selenium supplementation, low-fat and low glycaemic index diet, low-fat and high fibre diet, calorie restricted diet, and plant-based with fish diet. The sixth study did not include dietary counselling/advice and involved participants replacing usual bread choice with rye bread to increase lignan intake. Hamaker et al. (147) study synthesised evidence from 18 primary papers, which included assessment of dietary counselling, oral nutritional supplementation/support, and parenteral nutrition. No detail was provided about the focus of counselling/advice or type of supplementation, or frequency of intervention. Intervention length varied across reviews, including 1-38 days (148), 12 weeks (178), and 4-48 months (149). One review did not report length of interventions (147). Outcome measures included self-report measures/questionnaires (e.g., QoL and fatigue) and observations of health information (e.g., length of hospital stay and complications/toxicity).

Synthesis of the data from the four reviews showed improvements across multiple outcomes including reduced treatment toxicity and complications, body weight; whilst there was mixed primary-level evidence for the impact on QoL and hot flushes. There was no impact on fatigue, libido, length of hospital-stay or mortality.

Two dietary intervention reviews reported physical outcomes. Mohamad et al. (149) reported the impact of diet interventions on healthy body weight and reported a positive impact (i.e., five of six primary papers reported a positive body weight change), whilst one primary paper reported an increase in body fat percentage. Geerkens et al. (178) reported mixed findings for the impact of diet on hot flushes (one of two primary papers found a reduction in the severity of hot flushes), and no impact on libido/sexual function (measured in one primary paper).

Two reviews reported the impact of diet interventions on four psychological outcomes for people diagnosed with cancer; QoL, fatigue, depression and anxiety. Both reviews examined the impact on QoL, with mixed findings. Geerkens et al. (178) included two primary studies which examined the impact of diet on QoL, and reported that one indicated improved QoL, whilst the other showed no change. Of the 14 primary studies reviewed in the study by Hamaker et al. (147) that reported the impact of diet on QoL, seven reported improved QoL and seven reported no change. The

impact of diet interventions on fatigue was assessed in one study (178) involving men with prostate cancer, with no change reported (one primary study). No change was reported in one primary study investigating depression, whilst there were mixed findings regarding the impact of diet on anxiety in men with prostate cancer (one primary paper reported reduced anxiety, another reported no change) (178).

Two studies reported the impact of diet interventions on four health service use outcomes. Both reviews reported on the toxicity/complications. Hamaker et al. (147) included four primary papers examining healthcare consumption and reported that only one reported reduced healthcare consumption, whereas three did not. Three primary papers investigated impact on hospital length of stay and there were no changes reported from any intervention (148).

Seven out of ten primary papers reported reduced toxicity/complications in people diagnosed with a range of different cancers who participated in a diet intervention (including dietary counselling, nutritional support or parenteral feeding) (147), whilst there was improved outcomes reported in one of three primary papers involving pre-operative protein and energy supplementation interventions in people undergoing colorectal cancer surgery (148).

Two diet reviews examined mortality and survival (147, 148). The impact of diet interventions (dietary counselling, nutritional support or parenteral nutrition) on survival was reviewed by Hamaker et al. (147), with seven of eight primary papers reporting no change. Mortality was also found to be unchanged after pre-operative supplementation in colorectal cancer patients in two primary papers included in the review by Looijaard et al. (148).

In comparing the review-of-review level evidence of the effectiveness of diet interventions on outcomes in older people with cancer to younger people with cancer, no reviews of reviews were found in the literature. However, a recent, large systematic review involving 252 randomised controlled trials (RCTs) of people diagnosed with cancer with a median age of 61 years, and which focused on cancer outcomes (154). This review highlighted that the review-level evidence for the impact of diet on cancer outcomes is very limited, because of inadequately powered trials and most primary papers reporting impact on non-clinical outcomes, although there were some quality RCTs and these results aligned with the current study, indicating no favourable outcomes for mortality/survival. However, various papers have reported the mechanisms by which diet can impact cancer growth by impacting energy metabolism, proliferation and apoptosis through reducing IGF-1 which upregulates these cancer processes (193). However, the dietary interventions impacting IGF-1 include intermittent fasting, ketogenic diets and caloric restriction (193). None of the reviews of diet interventions in older people with cancer included primary papers investigating the outcomes of these types of interventions, which could explain why some report no impact on these outcomes. However, Ilerhunmwuwa et al. (154) did include some these types of interventions and still reported no impact. The reviews of dietary interventions in older people with

cancer reported improvements in body weight and fat mass, which is consistent with findings in reviews in which age was not reported (e.g., (13, 14). However, the findings for older people regarding QoL were mixed, which was in contrast to McHugh et al. (14) who concluded favourable impacts on QoL. Given the limited (and often conflicting) evidence for the impact of diet interventions in people (of any age) that have been diagnosed with cancer, it is more difficult to postulate if real differences exist, and if so, why. Based on the limited evidence available, there was a difference in impact on QoL between younger (favourable) and older people (mixed), which could also be explained by the co-morbid conditions mean QoL is less responsive to interventions. However, the evidence for mechanisms by which diet can impact cancer progression and growth makes future research studying the impact of specific types of dietary interventions imperative.

3.7.2.2 Effectiveness of smoking cessation interventions in older people affected by cancer

There is strong evidence that quitting smoking has significant favourable health outcomes in people who have been diagnosed with cancer, including reduced depression (194), anxiety and stress (195); improved QoL (196), improved response to therapy (196), and improved survival (197). In addition, older people who quit smoking experience reduce risk of death from heart attack, stroke and cancer and have improved cognition (198). Older people are more likely to experience tobacco morbidity and mortality than younger people but are less likely to try to quit smoking. Despite this, there is inadequate representation of older people in the literature around smoking cessation (159).

At the time of conducting the review of systematic reviews reported in this chapter, there were no reviews examining the effectiveness of smoking cessation interventions in older people diagnosed with cancer. Furthermore, the author is unaware of any reviews of smoking cessation in older people with cancer that have been published since conducting the search. There have been no primary papers reporting interventions specifically targeted at older people with cancer, nor any that happen to include a sample that has a mean age 65 years or older.

Reviews have been conducted in younger people diagnosed with cancer (150, 151, 155). Of the reviews identified, majority of included primary papers only reported the impact of smoking cessation on the likelihood of quitting smoking (i.e., majority did not report impact on other outcomes such as physical, psychological factors other than quitting/abstinence, health service use, or cancer outcomes). Smoking cessation interventions included in these reviews included pharmacotherapy, counselling/support, referral to smoking cessation professionals, and information provision. Information and support were provided in-person, online, via printed materials, telephone or through electronic tools/apps (150, 151, 155). The findings regarding the impact of smoking cessation on quit rates were diverse. Frazer et al.'s (150) review which included 23 primary papers involving individuals diagnosed with either lung, head and neck, or breast cancer, reported quitting rates ranging from 14.8% to 50.1% at 3 months. They also reported that a

primary paper using a pharmacotherapy intervention (varenicline) found no significant differences in quitting between intervention and control groups; and differences in quitting rates according to demographic and medical factors (e.g., married people were more likely to quit than non-married, but people experiencing depression, pain, having another addiction and experiencing mucositis were less likely to quit than those not experiencing these afflictions). One primary paper reported no increase in depressive moods during quitting interventions and improved cognitive function during smoking abstinence. Zhao et al. (151) also reported varying quit rates ranging from 3.2% to 47.3% in their review of four primary papers examining smoking cessation intervention effectiveness in individuals diagnosed with urological cancer. In their review of 39 primary papers involving people diagnosed with any type of cancer, Scholten et al. (155) reported that combined interventions were more effective than uni-modal interventions. They also reported that pharmacotherapy interventions did not show a significant smoking cessation effect, but that behavioural interventions did.

There is a diversity in effectiveness of smoking cessation interventions reported in the literature, and that which is reported suggests that quitting rates are low in people diagnosed with cancer. In addition, there is a lack of quality evidence for the impact of quitting interventions on outcomes apart from quit rates, and there is no review-level evidence for the impact of quitting interventions in older people with cancer. Given the significant favourable outcomes for people with cancer who quit smoking, it is necessary to co-develop, with people affected by cancer, new pathways for effective smoking cessation that are tailored to individual needs/circumstances (150), including for older people. It has been reported that older people are less likely to try to quit smoking and to achieve smoking cessation (159, 167), and they are affected by smoking cessation predictors differently to young people (e.g., older people are less nicotine-independent, less motivated to quit, and less likely to have tried quitting) (159), so more research is needed to tailor interventions to this population. Such research needs to examine older peoples' specific needs, preferences and barriers to quitting smoking, to understand which interventions might be effective.

3.7.2.3 Effectiveness of alcohol moderation interventions in older people affected by cancer

There is evidence that excessive alcohol consumption is common in people diagnosed with cancer (199), and has negative health effects in people who have been diagnosed with cancer (compared to people not consuming alcohol, or consuming alcohol at lower levels), including increased risk of recurrence of cancer (200), increased risk of hospital admission (201), higher healthcare costs (201) and increased mortality (142).

At the time of conducting the review of systematic reviews reported in this chapter, there were no reviews examining the effectiveness of alcohol moderation interventions in older people diagnosed with cancer. Furthermore, no reviews have been published up until this thesis was submitted. However, there have been a small number of primary papers reporting on the impact of alcohol

moderation interventions in people with cancer, in which the sample had a mean age of 65 years or more (e.g., (202, 203)). However, these were also broad interventions targeting multiple health behaviours, and none focused only on alcohol moderation. For example, Hawkes et al. (202) reported the impact of a tele-based lifestyle intervention of health coaching including support to reduce alcohol consumption (as well as improve diet, physical activity, weight management and smoking) on behaviour change (i.e., physical activity, diet, alcohol intake and smoking) and QoL, fatigue and body mass, in people diagnosed with colorectal cancer and aged between 64.9 (intervention) and 67.8 years (control). After 12 months, there were statistically significant improvements in the intervention group (compared to the control group) for increased moderate physical activity, reduced body mass index, and fat and energy intake. There were no other significant changes in the other outcomes measured, including alcohol intake, QoL or fatigue. Grimmett et al. (203) also examined the impact of a telephone-administered health behaviour intervention in people who had been diagnosed with colorectal cancer (mean age 65 years). There were significant improvements in increased physical activity, increased fruit and vegetable intake, reduced meat consumption and improved QoL. There were no statistically significant improvements in alcohol intake, fatigue or physical function after the 12-week intervention.

A systematic review of the impact of alcohol reduction interventions in people diagnosed with cancer (where the majority were not aged 65 years or more) was conducted in 2017 (204). This involved seven primary papers reporting interventions for people who have been diagnosed with cancer, in which alcohol reduction was targeted. Of note, no interventions specifically focused on reducing alcohol consumption, rather alcohol reduction was included as part of interventions which mainly focused on physical activity and diet change in people with cancer. Only one of the primary papers included reported that alcohol reduction was greater in the intervention group compared to a control group not receiving the intervention (152). This intervention involved the provision of advice about nutrition and physical activity and likely included guidance about alcohol consumption (although this was not specified in the description of the intervention in the primary paper) (152). Interestingly all seven included primary papers noted that alcohol consumption reduced in all study participants (but there were no statistically significant differences between intervention and control groups apart from Greenlee et al. (152)). These findings may support the role of a cancer diagnosis as a ‘teachable moment’ leading to behaviour change or alternatively could be due to feeling unwell due to cancer and anti-cancer treatment.

There is a lack of evidence for the effectiveness of alcohol interventions in people with cancer, even more so in older people with cancer. However, given the significant negative outcomes of alcohol consumption in people with cancer, high rates of alcohol consumption in people with cancer, and the promise of alcohol reduction interventions in other population groups which may participate in risky drinking (e.g., older people without cancer (205), adolescents (206), and people attending primary care centres (207)); it is important that interventions are co-designed and

developed to reduce alcohol consumption, with a focus on the needs, preferences and barriers affecting older people with cancer.

3.7.2.4 Disproportionate amounts of evidence for physical activity, diet, smoking cessation and alcohol moderation in people diagnosed with cancer

There is a disproportionate amount of review-level and primary research examining the impact of lifestyle interventions in older people with cancer, with data regarding physical activity predominating, with some review-level data for the effectiveness of diet interventions, and very little regarding smoking cessation and alcohol reduction interventions. It is likely that the amount of evidence varies across different types of interventions for a number of reasons. The large number of physical activity interventions identified in this research reflects the proliferation of physical activity and exercise research more generally. There a large number of benefits of physical activity including prevention and reduced risk of multiple non-communicable diseases and improved experiences of wellbeing and QoL, and it has been estimated that 1.4 billion people worldwide do not engage in enough physical activity (208). This suggests that targeting the optimisation of physical activity may have potent, wide-ranging and far-reaching impacts. In addition, physical inactivity has large economic costs, with physical inactivity estimated to cost public healthcare systems approximately $US300 billion between 2020 and 2030, but increasing exercise can be achieved using inexpensive methods (208). The role of diet in cancer survivorship is not as well defined due to a lack of high quality studies investigating the relationship between diet and aspects of survivorship, and the fact that existing data comes from very diverse studies (examining various aspects of diet) (209). Furthermore, diet interventions can be expensive, particularly those involving supplementation. These factors may limit the development and evaluation of diet interventions. Smoking, while in some ways similar to lack of physical inactivity (due to clear negative health impacts and consequent economic costs (210)), has been described as being particularly difficult to change because the dependence is affected by behaviour, physiology, social factors and cognition (211). Thus, despite being a very potent risk factor for poor outcomes in cancer, the difficulty of quitting may mean interventions are less likely to be developed, and therefore less likely to be evaluated, because of potential ineffectiveness. Likewise, risky alcohol behaviour is affected by many factors, including stress and physiological dependency, and can be used as a coping mechanism during difficult times (such as cancer). People may also be less likely to want to address their alcohol consumption due to perceived stigma, previous unfavourable experiences or expectations of quitting alcohol and not believing they have a problem with alcohol (212, 213). This makes the behaviour difficult to tackle and may mean that interventions are less likely to be initiated for fear of ineffectiveness.

3.7.2.5 Clustering and interaction of lifestyle behaviours

Although it is beyond the scope of the review conducted as part of this research program, it is important to acknowledge that there is some evidence that individual lifestyle behaviours may

cluster or interact, and that combining multiple lifestyles may lead to stronger impacts on CVD risk in cancer. For example, Li et al. conducted a systematic review and meta-analysis of studies that measured the impact of at least three lifestyle behaviours (together) on CVD incidence and concluded that those with a healthier overall lifestyle had a reduced risk of developing CVD (0.53 (0.46 – 0.63) compared to those with less healthy lifestyles(214). Similarly, a prospective cohort study of UK Biobank data from people with breast cancer showed that individuals who participated in 4-5 healthy lifestyle behaviours had a lower risk of incident CVD (HR: 0.5; 95%CI:0.37, 0.66) (215). Such evidence supports that people with cancer may have more favourable CVD outcomes where they optimise multiple lifestyle behaviours, rather than targeting individual behaviours in isolation.

3.7.3 Chapter summary and linking to studies reported in chapters 4, 5 and 6

Lifestyle behaviour change is important to reduce and manage CVD risk in people with cancer. Despite older people being more likely to experience both cancer and CVD than younger people and having different barriers and physiology that may affect their engagement and response to behaviour-change, there was a gap in the literature regarding the effectiveness of lifestyle behaviour change in people aged 65 years or more. Due to varying levels of evidence for the effectiveness of physical activity, diet, smoking cessation and alcohol moderation interventions in older people with cancer, the scope of the review of systematic reviews reported in this chapter was limited to the effectiveness of physical activity interventions in people with cancer aged 65 years or more. This chapter provided a detailed report of the methods and findings of the review of reviews and showed there is review-level evidence that in older people, physical activity interventions show improvements across multiple outcomes including pain, lean muscle mass, functional performance and muscular strength, reduction in fatigue and improvement in multiple measures of health service use including post-operative complications. The findings for QoL and depression were mixed, and there was no evidence that physical activity interventions are associated with reduction in anxiety or post-operative lung function. These findings suggest that clinicians can be confident to encourage older people to engage in safe physical activity but should be aware that impacts on some outcomes may differ to younger people with cancer. For example, there is evidence that physical activity improves lean muscle mass, muscular strength, functional performance, and reduces fatigue in both younger and older people with cancer; but in contrast to younger adults, physical activity did not impact anxiety, and the data on QOL and depression is mixed. Variation in biology between younger and older people with cancer may account for some differences in the response to physical activity, although more studies are needed to shed light on the mechanisms explaining differences.

This chapter also discusses the limited evidence for the impact of diet, smoking cessation and alcohol moderation interventions in older people with cancer, based on an informal review of the literature. There is review-level evidence that diet interventions may have favourable outcomes in

treatment toxicity and complications and body weight, but evidence was mixed for QoL and hot flushes. There was no evidence that diet interventions impact fatigue, libido, length of hospital-stay or mortality in older people with cancer. The author is unaware of any papers reporting smoking cessation interventions in older people with cancer, and none that solely targeted alcohol moderation (i.e., a small number reported broad interventions targeting multiple health behaviours, limiting interpretation.

The broader aim of the PhD research program is to improve the assessment and management of CVD risk in people affected by cancer. The findings of review reported in this chapter are critical to informing the development of a new approach to reduce the impact of CVD risk in cancer. Guidelines highlight the importance of encouraging healthy lifestyle in people diagnosed with cancer and at risk of CVD (and this is further examined in the research reported in chapters 4 and 5), and given cancer is an age-related disease and CVD risk also increases with age, any approach to reduce the impact of these diseases (and their co-occurrence) should specifically consider whether it is likely to be effective in older people.

This chapter provides a comprehensive overview of the evidence for the effectiveness of lifestyle interventions in older people with cancer. The results of the review of reviews of physical activity interventions supports that optimising physical activity in older people with cancer can lead to improved wellbeing and fitness. There is also review-level evidence that diet interventions have some favourable outcomes for older people with cancer, and many positive impacts in younger people with cancer. There is a paucity of literature for the impact of smoking cessation and alcohol moderation in older people with cancer. Although there is a lack of evidence for the role of lifestyle behaviour interventions in improving cardiac outcomes, some studies show positive impacts on CVD risk and there is data highlighting the mechanisms through which lifestyle behaviour may influence outcomes in cancer and CVD. Ultimately, the strength of evidence for the broad range of negative health outcomes associated with these behaviours, and the lack of evidence for any adverse outcomes associated with improved lifestyle, supports the inclusion of information and support to optimise lifestyle behaviour in a new approach to manage CVD risk in cancer.

4 CHAPTER FOUR: PERCEPTIONS OF CANCER CARE PROVIDERS REGARDING CARDIOVASCULAR DISEASE RISK IN CANCER: A QUALITATIVE STUDY

4.1 Chapter overview

This chapter reports the methods and findings of a qualitative study to understand the experiences, perceptions, ideas and preferences regarding CVD risk in cancer, of a sample of health care providers who spend a significant amount of their work time providing care to people who have been affected by cancer.

This chapter begins with a summary of the existing literature in the area (background and context). The contribution of this research to the broader literature is also described, followed by the aim of this qualitative study. A 'statement of related publication' is provided describing that a version of the research reported in this chapter has been published (216). A detailed description of the methods and findings of this study is then provided. The discussion section of the chapter includes a summary of the study findings in the context of the broader research in the area, including comparison to other research that has examined cancer care providers' perspectives regarding cardio-oncology and other aspects of cancer care. Finally, there is a summary of the chapter, including how the findings of the study reported in this chapter link to the studies reported in chapters 2 (review of reviews of physical activity interventions in older people affected by cancer), 4 (qualitative study to examine perspective of people affected by cancer regarding CVD risk), and 5 (codesign and usability testing of a web-based resource to reduce the impact of CVD risk in cancer) as part of the PhD research program.

4.2 Background and context

Multiple guidelines and frameworks recommend CVD risk factor assessment, monitoring and surveillance and risk management/reduction as best practice supportive/survivorship care of people who have been diagnosed with cancer. In particular, the European Society of Cardiology's guidelines on cardio-oncology (released in 2022) provide comprehensive evidence-based and expert-informed guidance on risk assessment, surveillance for cancer-therapy related cardiotoxicity (6), and Nekhlyudov and colleagues' "Quality of Cancer Survivorship Care Framework" (90) also recommends surveillance and management of non-cancer conditions. According to relevant guidelines and frameworks, assessment and monitoring should include regular assessment of CVD risk factors (e.g. physical activity and smoking) as well as hypertension and hypercholesterolaemia, and/or imaging or testing for determining whether CVD is present/persisting (e.g., electrocardiogram or magnetic resonance imaging). CVD risk management may include assistance to change lifestyle risk factors (e.g., increase physical activity or smoking cessation), or pharmaceutical therapies, such as anti-hypertensives. Assessment,

monitoring and management of CVD risk may require referral to other healthcare professionals, e.g., cardiologists or exercise physiologists, or may be able to be self-managed, or managed under the care of the patient's GP, nurse or cancer specialist (i.e., without referral).

There is evidence that older people with cancer, compared to their younger counterparts, are more likely to experience comorbidities, and have a higher all-cause mortality and CVD mortality rate. This could be due to poorer lifestyle behaviours in older people, i.e., older people are less active than younger people with cancer or could be due to older people being particularly vulnerable to the adverse effects of cardiotoxic anti-cancer treatments or having biological differences that increase CVD risk.

Despite the evidence for the importance of CVD care in cancer, many people with cancer do not undergo CVD risk assessment, surveillance or support to manage/reduce their risk (217). Further to this, older people with cancer may be even less likely to be assessed for CVD risk compared to younger people diagnosed with cancer, with preventive health services provision in general reducing with increasing age (218). Despite this, there is limited understanding of why CVD risk assessment, surveillance and management are not routinely undertaken in people with cancer, with clinicians being well-placed to contribute their perspectives about why cardio-oncology support is not well-integrated across the cancer care system. One study published in 2015 (219), involving 393 healthcare professionals (mostly cardiologists (47%) and oncologists (40%)), reported that 97% of respondents agreed that CVD is an important issue to people diagnosed with cancer, but only 36% of participants agreed with a well-accepted cardiotoxicity definition. Another paper reported the findings of an international survey of 160 healthcare providers from 22 countries (mostly cardiologists (53.8%) and oncologists (35.2%), with 13.7% being general internists, cardio-oncologists, cardiac rehabilitation therapists, nurse practitioners, researchers and pharmacists) (220). The paper concluded there was incomplete understanding of cardiotoxic effects of anti-cancer therapy and reported that just under half of cardiologists in the sample felt they had good understanding of complications related to cardiotoxic anti-cancer therapies and 41% felt confident in treating these issues if they developed. Only 8.2% of oncologists strongly agreed they were knowledgeable about cardiotoxic effects of treatment and 2.1% felt comfortable treating them. Only just over two thirds (66.9%) of respondents were aware of international guidelines for managing cardiotoxicity, and of the oncologists that participated, only 65.3% reported that they would use such guidelines when making clinical decisions. Cardiologists and oncologists differed in their perceptions regarding best-practice, and held varying beliefs on whether people with cancer should be monitored for cardiotoxicity if asymptomatic (55.8% of cardiologists believed in monitoring, but only 12% of oncologists did); and half of the oncologists thought cardiologists should only be involved in the care of people diagnosed with cancer if they have developed cardiotoxicity (whilst only 6.5% of the cardiologists agreed with this statement). Another survey study reported that 39% of participants (n = 106 cardiology experts (including Cardiology Fellowship Training Directors and

Cardiology Division Chiefs) did not feel confident in addressing cardiovascular issues in people who had been diagnosed with cancer, and 65% felt that clinicians specialising in cardio-oncology would better care for these patients. Forty-three percent of cardiology experts reported via the survey that the program they worked in had not received any formal training in cardio-oncology and 70% indicated that would use cardio-oncology educational materials if they were provided with them (221). Respondents perceived that cardio-oncology services were not established because of a lack of funding (44%), guidelines (44%), interest (38%), infrastructure (36%), and education (29%) were identified as barriers to cardio-oncology.

Although the survey findings described above contribute some understanding of the awareness, and perceived importance of cardiotoxicity, and limited data regarding barriers to and preferences for cardio-oncology services, a greater depth of understanding is needed. Current understanding is based on quantitative research, and qualitative data is needed because it provides rich, in-depth data on a phenomenon/problem (222) which can inform future approaches to reduce impact. Given the overall of the PhD program is to develop an improved approach to the assessment and management of CVD risk in people diagnosed with cancer, the perceptions of cancer care providers are critical. As cancer care providers are crucial in the effective and sustained establishment and implementation of any new program to reduce the impact of CVD in care, their perspectives, needs, ideas and preferences must inform the development of the new approach. Existing literature has focused on awareness, understanding, current practices and perceived barriers; but more data is needed to elicit ideas and preferences for how best to move forward. In summary, the problem of incomplete translation of cardio-oncology knowledge into practice is seemingly complex and nuanced, qualitative data is needed to better understand the problem and solutions from the perspective of cancer care providers.

4.3 Aim

This study aimed to examine health care providers' perceptions and experiences of the management and assessment of CVD risk in older people with cancer.

4.4 Statement of related publication

The research reported in this chapter was the focus of a paper ("Reducing the impact of cardiovascular disease in older people with cancer: a qualitative study of healthcare providers"), which was published in the Journal of Cancer Survivorship (2023) (216). Reegan Knowles (RK) was the primary/first author of the publication, with PhD primary supervisor Professor Bogda Koczwara as the senior/last author, and Dr Emma Kemp and Professor Michelle Miller as the second and third authors, respectively. All authors contributed to the study conception and design, with RK contributing approximately 70% to the study conception and 80% to the research design. Ninety-five per cent of data collection was conducted by RK (developed topic guide with

consultation with other authors and facilitated all focus groups and individual interviews, with assistance from EK for the first focus group). Eighty per cent of data analysis was conducted by RK, with all coding conducted by RK with a sub-set of transcripts also conducted by EK for cross-checking of coding. Theme development was conducted initially by RK, but themes were revised iteratively via a series of discussions with all authors until finalisation. The first draft of the manuscript was written by RK and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript. This chapter provides a more detailed description of the research that was reported in the peer-reviewed paper in the Journal of Cancer Survivorship. For example, more detail about the methodology and methods utilised to collect data is provided, and the results section contains more quotes from participants along with relevant synthesis. Although there are differences in how the research is reported in this chapter compared to the paper, there is direct overlap of wording and content throughout. The published paper can be found at Appendix 2.

4.5 METHODS

4.5.1 Study design

A qualitative reflexive thematic analysis (RTA) methodology, using focus groups and interviews was used to examine the perceptions and perspectives of healthcare providers involved in the care of people with cancer, about awareness and importance of, barriers to, and preferences for, CVD care in cancer. The conceptualisation, planning and implementation of this research study was guided by the principles of the person-based approach to intervention development (PBAID). As described in chapter 2, the key element of PBAID is that the development of a new approach (in this case, to reduce the impact of CVD in cancer) must be based on the experiences, perspectives, needs, barriers and preferences of those involved in its application in the real world.

It is worth discussing RTA in the context of study design/methodology, rather than just as a type of data analysis, because the RTA approach also influences how research is planned, how data is collected, and how findings are reported. In RTA, patterns and ideas (themes) in the collected data are identified and interpreted , but a key aspect of this approach that differentiates it from some other approaches is that it acknowledges that the researcher plays a key role in the construction of the findings (223). The findings of the research are a result of how the researcher collects, interprets and presents the data, and therefore it is critical that the researcher reflects on their own biases, experiences and views so they can understand how this impacts the findings (223, 224). RTA was used in this study because it is well-established as an appropriate approach when researchers want to better understand a concept that has not been well-researched previously (i.e., requires an exploratory approach). In addition, RTA is an approach deemed useful for research that would benefit from the researcher's expertise and perspective (225), which aligns with the current research where the PhD candidate (and the entire research team) is strongly

immersed in the topic of cardio-oncology. RTA is described as a flexible methodological approach (224) that can be applied in a way that aligns with various theoretical and philosophical frameworks including critical realism, which is the epistemological and ontological foundation of the PhD research. Critical realism is a worldview that acknowledges that objective reality exists but that understanding is also determined subjectively (through the experiences and perspectives of people), whilst RTA is an approach which highlights the role of the researcher in constructing findings (225). More detail about how RTA was applied in this research is described in the 'Data analysis' sub-section below. Focus groups and interviews were conducted in person, via telephone and online.

4.5.2 Participant eligibility criteria

To be eligible to participate in this research study, cancer care providers had to be aged 18 years or older, provide care to people affected by cancer as part of their employment, and be able to participate in either a focus group or individual interview. There were no exclusion criteria.

4.5.3 Recruitment and consent

The target sample size was approximately 20 cancer care providers. There is a lack of consensus in the literature regarding adequate sample sizes for qualitative research, but it is accepted that there should be enough participants to generate novel and in-depth understanding of the research topic, but that the sample should be small enough for deep analysis of the data collected (222). In addition, sample size should be informed by the philosophical underpinnings of the research and practical and pragmatic factors (226). It was determined that approximately 20 participants would align with the philosophical and methodological approach of this research (to gain an in-depth but broad understanding of perspectives of cancer care providers regarding CVD, acknowledging the impact of people in interpreting and constructing knowledge). The proposed sample size was also informed by pragmatic factors including that the study was limited by practicalities such as time and access to eligible cancer care providers. Finally, the researchers planned that recruitment would continue until the researchers perceived enough data to conduct rich and meaningful analysis and to develop a report that is interesting, and informative for future research and clinical practice. This approach aligns with the premise that "new" data can always be collected and ceasing data collection is a pragmatic decision based on the objectives of the research (227).

Cancer care providers were recruited through researchers' existing networks using a non-random, purposive sampling technique. BK introduced the project to potential participants via email or in-person, whilst RK followed up with emails or phone calls to check if those who had been approached were willing to be involved. Potential participants were informed of the project aims and study procedures (verbally by either BK or RK, and via the Participant Information and Consent Form [PICF]), and were able to take time to consider their involvement before notifying the PhD candidate whether or not they wanted to participate. They were informed that participation

was voluntary and that they could withdraw at any time without any impact on their employment. They were assured that data would be kept confidential, deidentified, and stored according to the requirements of the Southern Adelaide Human Research Ethics Committee. Willing participants indicated consent by signing the PICF and returning in person or by email. Participants could choose whether they participated via focus group or individual interview, and whether they participated in-person, online, or via telephone. The PhD candidate arranged focus group or interview sessions at a date, time and location according to each participant's preference.

4.5.4 Study procedures

Data were collected via focus group or individual interview. All interviews and focus groups were conducted by the same investigator (RK) with assistance from another (EK) for the focus group. In line with McGrath and colleagues' tips for conducting qualitative research (228), and guided by the principles of PBAID (129), all study procedures were conducted to establish and maintain rapport, comfort and mutual respect so as to collect rich and meaningful data that would address the research objectives. This involved thorough preparation for sessions, including the development of a topic guide (see Appendix 3) to facilitate the collection of participants' perspectives around the central phenomenon of CVD in people with cancer. In line with PBAID principles, the initial version of the topic guide was developed by the PhD candidate based on study aims and informed by existing literature (particularly gaps in understanding of stakeholders' perspectives and including prompts to discuss concepts of behaviour change such as barriers and enablers). The topic guide was then tested with supervisors with feedback incorporated. Prompts facilitated discussion that would elicit detailed and meaningful data. Culture and power dynamics were also considered, particularly with regard to the focus group in which multiple cancer care professionals participated (228). To attempt to create an environment where participants had an equal opportunity to contribute their perspectives irrespective of their profession, participants were introduced to one another, and the researchers purposefully asked specific participants their perspectives during the session in cases of uneven contribution across the group (228). The introduction of participants and encouraging participants to contribute their views also assisted in establishing rapport, respect and trust. In addition, the researcher contacted participants before the session to provide information about the study and to arrange and confirm the session, which also increases familiarity even before the sessions began. The researcher also established rapport and respect by reiterating before and throughout the sessions that they were eager to hear individuals' own specific experiences and perspectives, and how these were valuable to understanding CVD in cancer (228). The researcher engaged active listening and resisted the urge to talk too much, allowing for participants to contribute their ideas but also to reflect on what had been said. In the focus group, the facilitator ensured all participants had the opportunity to contribute their perspectives, especially those who had not spoken for some time, and to account for perceived power imbalances amongst the groups. The researcher also acknowledged their role in

constructing the findings of the research (as per the RTA approach and critical realist worldview) and therefore, where appropriate, used their own knowledge and experience to create engaging discussions (225, 228). Recruitment was ceased based on the concept of “information power”, which acknowledges that although original data may continue to emerge with subsequent interviews, recruitment should stop when the researcher judges that the data already collected will meaningfully address the research objectives and that further data would not change the presentation of findings (227).

4.5.5 Data analysis

The focus group and interviews were audio-recorded and transcribed verbatim. The NVivo computer software program for qualitative analysis (229) was used to assist with coding and theme development. Coding and theme development was conducted iteratively, with the research team involved in a series of discussions throughout the analysis process.

The RTA approach to data analysis was applied as described in Braun and Clarke (230), which involves six phases: data familiarisation, coding, initial theme development, review of themes, refinement, and reporting. The PhD candidate became familiar with the data through conducting each of the data collection sessions (focus group and individual interviews), listening to the audio-recordings for quality, checking transcriptions after audio-recordings were transcribed verbatim by an external source, and throughout importing data into NVivo ready for coding. Initial coding was conducted by the PhD candidate using an inductive approach. New codes were constructed as new ideas and concepts were identified in each focus group/interview transcript. Coding was predominantly semantic, in that the codes were developed based on what was explicitly communicated by the participants in focus groups and interviews. The research team met to discuss the initial codes. The purpose of this discussion was not to ‘check’ for accuracy of coding, given RTA is underpinned by the philosophy that the findings are constructed by the researcher and influenced by their views and biases. Therefore, it is not considered important whether multiple researchers identify the same codes (225). Rather, these sessions helped to guide the PhD researcher in the method of coding, and facilitated the PhD candidate reflecting on how their views and biases impacted the development of codes, which is a key aspect of the RTA approach (223). Initial theme development was conducted by the PhD researcher, and review and refinement occurred throughout a series of discussions with the research team. Although coding was conducted predominantly semantically to increase the depth and richness of analysis, we also employed a latent approach to the analysis of some themes, in which we further discussed and analysed data to uncover the underlying meaning of participants’ contributions. In summary, the theme development approach was iterative and recursive, as discussions and drafting of findings often led to new ideas and perspectives which required further discussion and analysis. An example of the flexible and iterative approach used during both data collection and analysis was that although the aim of the study was to encourage discussion about CVD and cancer with a

specific focus on older people, the research team identified that many responses did not include differentiation between older and younger people. This was unpredicted but it occurred organically through the research process and the researchers chose to allow flexibility and authenticity in the application of the research methodology. Likewise, although the research team initially felt that the focus of the sessions would be on developing a risk prediction tool, the topic of sessions was broadened to consider other approaches given respondents communicated unfavourable perspectives regarding the need for a tool.

Throughout data collection and analysis, the researcher ensured reflexivity through implementing three main processes, comparing coding, discussion among the project team, and self-questioning regarding interpretation of data. The PhD researcher conducted coding of all transcripts, but a second member of the research team (supervisor EK) also coded three transcripts. The researchers discussed the codes that were constructed and most aligned very closely. This allowed for reflecting on any biases that may impact how data is interpreted (231). Further discussion amongst the research team throughout theme development also provided the opportunity to consider the impact of the researchers' perspectives, beliefs, experiences and perspectives on the construction of findings. Finally, the PhD candidate continually engaged in self-questioning throughout all aspects of the research to check how their own worldviews affected any interpretations of data and presentation of findings (231). nd consider the impact of the researchers' perspectives, perceptions and beliefs on the construction of knowledge in our research.

4.5.6 Ethics

Ethics approval was granted by the Southern Adelaide Local Health Network Ethics Committee on 22 January 2020 (HREC/19/SAC/309).

4.6 RESULTS

A total of 21 cancer care providers participated, including eight medical oncologists, four clinical nurses, three general practitioners (GPs), two dietitians, one physiotherapist, one cardiologist, one haematologist, and one research nurse. Nine cancer care providers participated in one online focus group which lasted 59 minutes; and 12 cancer care providers participated in an individual interview (face-to-face n=9; telephone n=2; online n=1), ranging from 12 to 53 minutes duration (median = 36 minutes).

The analysis identified four themes and 11 subthemes (Figure 7).

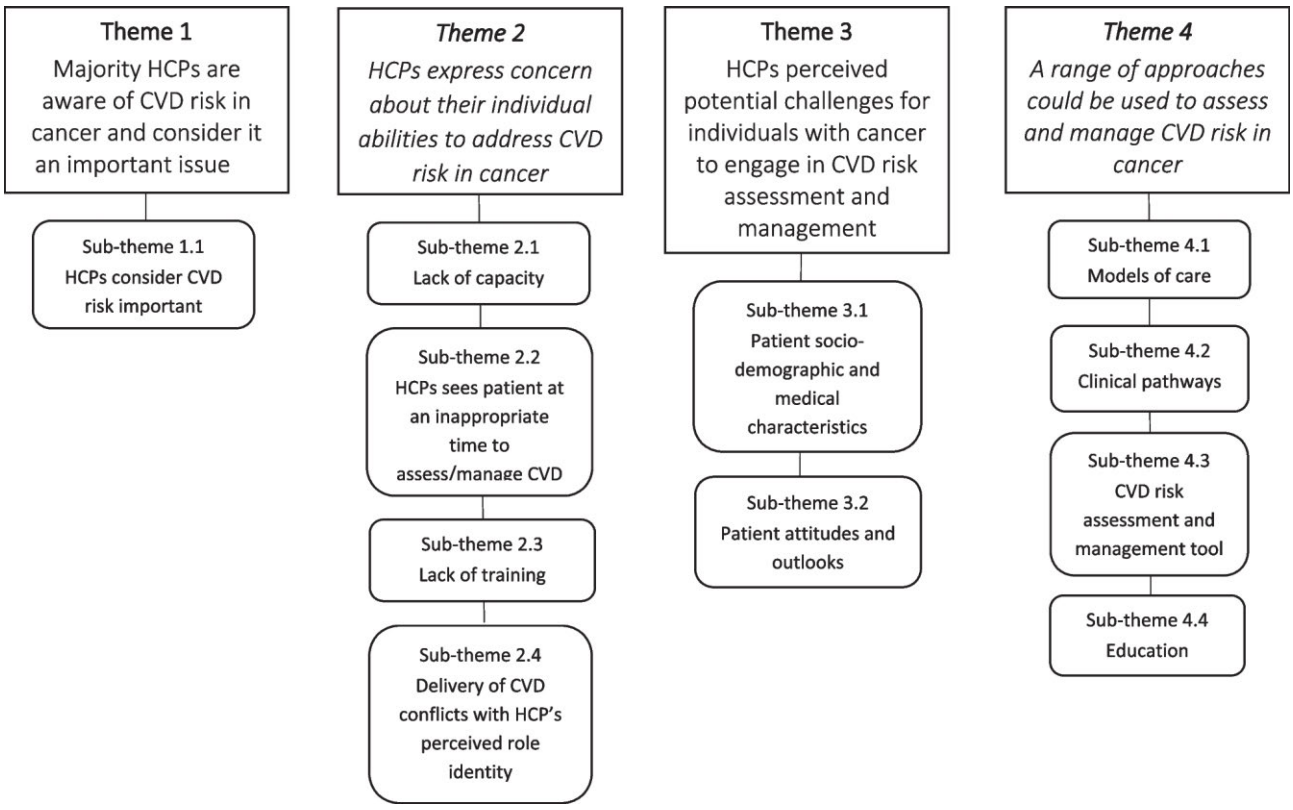


Figure 7 - Themes and sub-themes summarising cancer care provider's perceptions of CVD risk identification and management in older people with cancer

4.6.1 Theme 1: Majority of cancer care providers are aware of CVD risk in cancer and consider it an important issue to address

Majority of cancer care providers indicated that they were aware people with cancer had a higher CVD risk and summarised reasons for the co-existence of these diseases. For example:

> *"…toxicity of treatments we do for cancer, so for many of our chemotherapy or target treatments have a cardiovascular effect – that's one. Second is that some cancers have similar risk factors for development of the cancer as to cardiovascular disease, so its obesity, diet, smoking"* – Medical oncologist

Another participant mentioned they were aware of guidelines about cardiovascular disease in cancer:

> *"So, there are several guidelines...So, many of these [cardiovascular disease guidelines] at best have been used for a long time, so we are pretty much aware of cardiovascular risks and this screening which needs to be done."* – Medical oncologist

A nurse indicated she was aware of cardiotoxicity, but implied her knowledge was limited to discussing cardiotoxicity with patients.

> *"I think cardiac is definitely its own world and talking about cardiotoxicity very generally would be something I'm comfortable to do but I don't know how comfortable I would feel with doing screening."* - Nurse

One cancer care provider (GP) mentioned they were not aware of the impact of cancer diagnosis on CVD risk.

> *"I guess I'm not really well aware of that impact of increased risk [of CVD with history of cancer]…I don't think in my mind I factor in specifically as cancer survivors being at higher risk unless specifically their treatment has been flagged as being a potential risk factor."* – GP.

4.6.1.1 Sub-theme 1.1: Cancer care providers consider CVD risk important

Cancer care providers from a range of disciplines highlighted perceived importance of CVD risk in cancer. There was a strong focus on the perceived importance of weighing up the (cardiotoxic) risk and (anti-cancer) benefit of anti-cancer treatment.

> *"And if a patient has, for example, say, 20%, 30% risk of death just because of their cardiovascular risk it doesn't make sense to give them toxic treatments for 1% or 2% improvement."* – Oncologist

And similarly:

> *"…there's no point surviving your cancer treatment if you're going to go on and have a heart attack"* - Dietitian

Intervention to reduce CVD risk was identified as potentially improving patients' quality of life.

> *"…they've [typical lung cancer patient getting high dose radiotherapy] got a 20% chance of having a CV event in 2 years. Yet those patients are often not referred because you got people saying they've got such a poor prognosis there's no point. But if you could potentially prevent a cardiovascular event from a QOL perspective in the few years they've got remaining, why wouldn't you…?" – Cardiologist*

4.6.2 Theme 2: Cancer care providers expressed concern about their individual abilities to address CVD risk in cancer

Majority of participants expressed concerns about their ability to deliver CVD care to people with cancer because of a lack of capacity, training, inappropriate timing, or perception of CVD care as outside of their role identity.

4.6.2.1 Sub-theme 2.1: Lack of capacity

Lack of time was the most common barrier to delivery of CVD care. For example, dietitians discussed how time limitations precipitated the need for prioritisation of cancer-related needs over CVD, and the need for referral of patients with CVD-related issues to community dietetics services.

> *"I think it's all about priorities and so because everyone has limited time everyone aims at looking at the cancer."* – Dietitian

A lack of adequate resources and services and inadequate cohesion/coordination of tasks by different professions involved in cancer care, were identified as potential barriers to the provision of CVD care in cancer. A cardiologist commented that there was an inadequate number of cardiologists appropriately trained for providing cardio-oncology care and linked this to the absence of training programs.

> *"there's probably only about 30 cardiologists in the country that have got an interest, there's 2 that are certified with the ICS which is sort of the de facto forming international group interested, and there's about 2 or maybe 3 who have done international overseas fellowships. There's no training programs in Australia, no requirement for training, so we couldn't deal with all the work anyway."* – Cardiologist

A dietitian mentioned that hospital-based dietitians did not have the capacity to address CVD care in people with cancer, as their focus is on dealing with acute problems directly related to cancer.

> *"we're just trying to make sure that we meet nutritional requirements, there's a lot of issues with inability to eat so it's not often around food groups or what you focus on when you think about cardiovascular health, because we're just trying to help keep them alive really and then the patients we keep long-term it's often around trying to improve quality of life. So, our work is very acute."* – Dietitian.

Participants communicated their perception that many patients did not receive survivorship care/post-treatment care, with one participant suggesting that this would be where CVD risk management would best fit.

> *"…if the person comes out of the hospital with a clear survivorship plan, then there's a fair chance that it will be followed, but most people don't come out with a survivorship plan." – GP.*

A cardiologist identified that oncology and cardiology professions did not work together cohesively or communicate effectively, and this lack of connection between disciplines was perceived as a barrier to CVD care delivery.

"…there is a disconnect between oncology and cardiology because there are different journals… different language…different side effects, reporting algorithms, different conferences and we sit on two sides of a chasm. It's only in the more recent past that there's been more movement towards bringing those two sides together" – Cardiologist

Further from this, the same respondent addressed the need for systematisation of workflow, where the roles of patients and cancer care providers are defined, but this is limited by workforce capacity.

"We're looking at patient centric care, patients being more involved in their health care making decisions…and I think there needs to be a systematisation of the workflows, and that has to be balanced up against the workforce capacity to deliver the care and there is no way on the planet that there are enough cardiologists that are interested." - Cardiologist

4.6.2.2 Sub-theme 2.2: The time cancer care providers consult with patients is not the right time to raise CVD risk

Some participants expressed concern about *timing*, i.e., some felt the time at which they see their patient was not appropriate to introduce more information about another potential health problem. For example,

"…when you see somebody for the first time you have to talk to them for nearly an hour about what their disease means and the side effects of the treatment and all of that and that's without at all talking about vascular risk status and so, I guess, partly that's an issue for my time because it already runs over but it's also an issue for them because they're often frightened and overwhelmed and it's not really the time to be trying to pile on more information." - Haematologist.

"…people have to be ready to take information on board, I don't think during the peak time of treatment would be so cool [to provide CVD risk assessment/education]" – Dietitian

"At four weeks [after diagnosis], no, they're still usually so traumatised." – Dietitian

"I think it would be tricky to find the right window." - Dietitian

4.6.2.3 Sub-theme 2.3: Lack of training

Cancer care providers (including a GP, oncologist and cardiologist) perceived inadequate training/education to be a barrier to the delivery of CVD care in cancer.

"I don't feel like I have any guide, we know for example managing high BP, if you're a diabetic, your targets are much lower. If you've got a preexisting cancer, so am I aiming for a better target? What are the more important things to manage in terms of decreasing their

CV risk? I don't think it's beyond our scope, I just feel like we don't have the tools and the guidelines to direct those interventions precisely." – GP.

4.6.2.4 Sub-theme 2.4: Delivery of CVD conflicts with cancer care providers' perceived role identity

Many cancer care providers communicated their perception that delivering CVD care did not align with how they saw their professional role. Some cancer care providers explicitly described that they (or their discipline) were not appropriate to deliver CVD care. For example:

"I'm not up to date on the optimum level to diabetes or blood pressure and I'm not interested in acquiring that knowledge." – Haematologist.

"I don't see my role managing patients' cardiovascular health. I think what I can do is assess how much I'm going to cause damage and whether or not that treatment is worth doing. But whether or not they need their hypertension to be controlled better, the most I can do is write a letter to the GP." – Oncologist

Cancer care providers communicated that they perceived other professions as more appropriate for providing CVD assessment and management. For example,

"whether the head clinician likes it or not, they're still the gatekeeper for a lot of referrals" [as part of CVD care] - Dietitian.

" [patients could receive CVD care] if you had a nurse practitioner leading that program and the other nurse practitioners knew that…" – Dietitian.

Nurses identified GPs as being the most suitable for addressing CVD risk in patients because *"It's part of coordination and care and that's the GP, not like a snapshot of a nurse or a dietitian who has like one episode." – Nurse.*

A GP suggested that patients could play a role in the CVD care process through consultation with their healthcare team.

"Some of them [patients] I think are so motivated and very invested in their health…" GP

A haematologist stated that any of multiple professions could achieve this role.

"I wouldn't say that there's one person to initiate that conversation, I can see lots of people being good people to initiate that conversation and that ranges from the GP, the medical oncologist, the surgeon, of the surgeons referring for radiation therapy, you know, the rad oncs, other people that are involved, breast care nurses, you know the McGrath foundation

nurses, anybody that is involved in the care is in a good position to highlight the thought in the patient that they should think about it." – Haematologist.

One respondent agreed that their profession (dietetics) should play a role in cardiovascular care but stated that this should occur in the community setting, rather than the tertiary setting.

"So, cardiovascular stuff tends to be community-based…private dietitians, that's where it sits." – Dietitian.

4.6.3 Theme 3: Cancer care providers perceived potential challenges for individuals with cancer to engage in CVD risk assessment and management

Cancer care providers identified individual characteristics of patients with cancer that they perceived as barriers to engaging in CVD care. Some of these were demographic or medical factors, including level of disadvantage and prognosis. Other characteristics were related to patient attitudes and outlooks, such as low motivation and a fatalistic outlook.

4.6.3.1 Sub-theme 3.1: Sociodemographic and medical characteristics

One participant indicated that a patient's engagement in CVD assessment and management would be impacted by aspects associated with a patient's socioeconomic situation, e.g., financial barriers, health literacy and access to healthcare.

"it's so difficult to predict who's going to react [to CVD assessment/management] because it's just all about the person and their socio-economic situation…" – GP.

"So, I would imagine most of these things like this would be picked up by oncology…but possibly by…private specialists…unfortunately that will mean poor people won't necessarily be able to access the services." – GP.

A nurse working in cardio-oncology indicated their reluctance to refer to other cancer care providers for cardiovascular care due to perceptions that the patient may not be able to afford an extra cost.

"I don't want to subject them to more consultations and more costs." – Nurse.

Being isolated was also identified as reducing the likelihood that some patients would engage in CVD assessment/management.

"*Always having to reach the people [to provide them with CVD care] that have actually distanced themselves through it all [cancer treatment], they're the harder – the unreachables, so that's always the challenge."* – GP.

4.6.3.2 Sub-theme 3.2: Patient attitudes and outlooks

One nurse and one GP discussed their perceptions that aspects of a patient's outlook or mindset would reduce their engagement in CVD care, including: being in denial about their disease, having an "alternative" approach to healthcare, being unwilling/reluctant to make changes, being less demanding/entitled, and having a fatalistic outlook.

> *"But it's also denial. All these people with their inbuilt defence mechanisms, so that's [introducing CVD care] really, really difficult."* – GP.

> *"I've had one or two [patients] who are very alternative, so I guess the prospect of … starting any other medication is … revolting [to the patient]."* – Nurse.

> *"One or two [patients] are like 'I'm not quitting smoking, it's my only joy in life if I die of it then I'm ok.'"* – Nurse.

Being less demanding and having a fatalistic outlook were both specifically raised in the context of older people with cancer:

> *"…they [the older person with cancer] almost have a sense of being a bit fatalistic, like I'm getting older so why would I bother?'* – GP.

> *"…they [the older person with cancer] come into the doctor and they don't want to waste your time [asking questions about CVD risk], they're a bit more old school, they're not as entitled or as demanding…"* – GP.

Other participants noted that they perceived patients may interpret the offer of CVD care as overservicing or exploitation:

> *"…some of the things they [the patient] are worried about is that this is just a money-making thing for the business and that's why you're referring, that goes down very poorly."* – Cardiologist.

4.6.4 Theme 4: A range of approaches could be used to assess and manage CVD risk in cancer.

Cancer care providers discussed a diverse range of solutions and approaches which could improve delivery of CVD care in cancer, including new models of care, clinical pathways, tools, and education. In addition, participants discussed the specific components they perceived as important in approaches to CVD care in cancer, including automaticity, communication, and a patient-centred approach.

4.6.4.1 Sub-theme 4.1: Models of care

Cancer care providers discussed a range of models of care for the identification and management of CVD in individuals with cancer. These included cardio-oncology clinics; care models

led/coordinated by selected professions (i.e. GPs and nurses); and multi-disciplinary/teams-based models.

A range of cancer care providers from nursing, haematology and allied health discussed the potential for a cardio-oncology clinic. For example:

> *"I would prefer it if there were a kind of cardio-oncology clinic that could see people, even if it's once, and make an assessment and give them a package of advice."* – Haematologist

Cancer care providers (including a nurse) suggested a nurse-led model of care, such as that used in other areas of care, could also deliver CVD care:

> *"I think that if you look at it in cardiology, cardiac rehab has these nurse-led multi-D team…, there's heart failure, there's hypertension and there's AF [atrial fibrillation], this is just an extension of those models of care, in reality we're not reinventing the wheel, we're just stealing basically." – Nurse*

Nurses highlighted the role of the GP in coordination of care, implying that this role makes GPs most appropriate for coordinating a cardio-oncology model of care.

> *"GPs coordinate care. A lot of our referrals more than often are from GPs…that's where we get medical histories from…the GP is getting the letters from us, from oncology, …. the physio, …. lymphedema assessment from the radiotherapist… So, they're the linchpin."* - Nurse

Multi-disciplinary or teams-based approaches to care were discussed by a range of cancer care providers. Several asserted the success of multi-disciplinary teams in other areas of care and highlighted that by involving a range of professions in the model of care less responsibility is felt by individuals.

> *"Well, I guess, I think the ideal arrangement [is] … a multidisciplinary team with cardiologists and specialists and so on together with the dietician and educator what have you.* – Haematologist

> *"…you kind of build up a bit of a team and sort of a collaboration so people don't feel like they're always bothering the same person…"* – Physiotherapist.

4.6.4.2 Sub-theme 4.2: Clinical pathways

Cancer care providers discussed the potential for a clinical pathway to ensure coordinated CVD care in cancer.

> *"Well, ideally there would be a referral pathway."* – Dietitian

"Yeah. I think it should be referral and integration so that the messages are transferred over to GP practice as well so when they move to specialty care that you have a clinical pathway where you've got integrative care." - Nurse

"I think there needs to be a systematisation of the workflows, and that has to be balanced up against the workforce capacity to deliver the care." – Cardiologist.

Cancer care providers asserted the importance of protocols in providing care.

"that's how these things will work best, you have a protocol, a system that just gets followed based on the best available evidence." – Cardiologist

However, there was also discussion about how protocols are specific to the health service and are unlikely to be transferrable to other services.

"…the trouble [with developing a CVD risk reduction approach/intervention] is that every location, geographically, will have a slightly different solution in terms of the process because of the way pre-existing processes are there." – Cardiologist.

4.6.4.3 Sub-theme 4.3: CVD risk assessment and management tool

Several participants voiced their support for the development and integration of CVD risk assessment and management tools to improve CVD care in cancer, including treatment decision-aides, risk stratification and education tools.

Participants varied in their opinions regarding what would be the most useful purpose of a tool in the area of cardio-oncology, with some asserting the need for the tool to aid in treatment decisions whilst others indicated they would prefer the tool to stratify patients according to level of risk so that care provision can be triaged accordingly.

"a tool… that could provide me with some evidence in terms of that person's cardiovascular risk and particularly if it told me that they had a high risk of dying because of their heart problems, then that might actually influence the decision for the [anti-cancer] treatments that might be recommended for that patient" – Nurse Practitioner

Most cancer care providers preferred a digital tool, but some mentioned barriers to this indicating that some clinicians may be more likely to use a pen and paper version. Tablets (e.g., iPads), websites and smartphones were identified as potential delivery modes for a digital tool.

"[the tool has to be in the form of] either a phone app or it has to be online' – Nurse.

"I think probably online portal, like I could just have it as a bookmark and then when I was seeing patients just kind of flick to that." - Physiotherapist

Cancer care providers from a range of professions asserted the importance of specific aspects/components of a tool to deliver CVD care. Participants identified automaticity and embedding the tool into a current system (e.g limited need for cancer care providers to be involved in data collection/analysis) as being crucial.

> *"…I think if you could use something … that's running in the back of EMR [electronic medical records] and pulls all the information and spits you out a risk, I think that would be helpful because then you know who to target." – Dietitian.*

> *"I don't [want to] have to somehow input it [data about CVD assessment and management] back into the notes" – GP*

> *"A lot of these kinds of tools, they should be automated into our work" – Oncologist*

Participants indicated that a tool should also facilitate communication, particularly between cancer care providers involved in the patient's care.

> *"I just think there needs to be some sort of feedback to them [other cancer care providers], if you're doing some sort of screening that this has happened." - Oncologist*

Participants identified that not all patients would be appropriate for the administration of a tool, and tools should be flexible so they can be tailored to the individual needs of different patients.

> *"What I'm trying to actually say is that these tools are helpful, but we cannot actually use that on every patient, it just needs to be identify the situation where we can actually use it or individualise it for patients". – Oncologist*

4.6.4.4 Sub-theme 4.4: Education

Participants also identified education and awareness in both cancer care providers and patients as important in delivering CVD care to people with cancer. A GP communicated that they would feel more capable of delivering CVD care if they were educated appropriately.

> *"It's some guidelines or education [of GPs] that's kinda missing." – GP*

Education of patients was identfied by several participants as having a positive impact of integrating CVD care into cancer care. This could, for example, lead to patients initiating conversations with cancer care providers about their CVD risk profile, and being more involved in the management of of their own risk.

> *"I think it's education of providers, I think its education of patients, particularly where we're looking at patient-centric care, patients being more involved in their health care making decisions, I think patients need to be made more aware." – Cardiologist.*

4.7 DISCUSSION

This study presents a comprehensive qualitative analysis of the perceptions of cancer care providers regarding the identification and management of CVD. Cancer care providers were aware of CVD risk in cancer and perceived it to be important but had concerns about their own ability to deliver CVD care. In addition, there was a lack of consensus of cancer care providers' perceptions regarding the best way to reduce the impact of CVD in cancer.

Previous research specifically examining cancer care providers' perceptions regarding cardiotoxicity of anti-cancer treatment reported some providers were not aware of the increased risk and associated poor outcomes of CVD in cancer patients, and those that were aware did not perceive the relationship between CVD and cancer to be an important issue. For example, Koop and colleagues (232) reported that majority of participants (who were Dutch oncologists, n=12) were unaware of the incidence of cardiotoxicity and perceived cardiac surveillance as burdensome, and a recent survey (n=190 Dutch cancer and cardiac specialists) found only 33.2% were concerned about the cardiotoxic effects of anti-cancer treatment (233). However, in line with the findings of the current study, a survey of 106 cardiology specialists in the US found that >70% perceived potential CVD complications as an important consideration of anti-cancer treatment (221, 233). Many factors may influence awareness and perceptions of CVD risk in cancer. For example, training and education in CVD risk in cancer varies across institutions (221); and individual cancer care providers (and the institutions where they are employed) may have different preferences/interest in cardio-oncology (234). It is possible that our findings reflect a growing awareness of the field of cardio-oncology through recent publications of recommendations and guidelines in this area (235), in particular the European Society of Cardiology's guidelines on cardio-oncology (6).

A novel finding of the current qualitative study involving research was that cancer care providers were concerned about their (and their profession's) abilities to deliver CVD care in cancer alone. This finding has important implications for the development of future approaches to improve CVD care in cancer, where CVD care, like the rest of cancer care, is likely to require a teams-based approach. In addition, we are not aware of other research highlighting a perceived conflict between delivering CVD care and role identity in cancer care providers involved in cancer care. However, conflicting role identity was identified as a barrier in a systematic review of 43 papers examining staff-reported barriers to the implementation of hospital-based interventions such as the administration of screening tools and behaviour-change interventions, but this did not include any research specifically involving CVD care in cancer (236). Similarly, Collaco and colleagues' (237) review of 32 primary papers examining healthcare professionals' perceptions about the integration of primary and secondary cancer care services (especially for follow up of patients after treatment)

reported that primary care and oncology roles needed to be delineated clearly in terms of responsibility of specific tasks.

Lack of training and time were identified as barriers to implementing CVD care in cancer by the study participants. Although no other studies have reported perspectives in CVD and cancer, staff training and time have been identified as barriers to implementing other aspects of cancer care. For example, Collaco and colleagues' systematic review described previously identified a lack of training and guidelines as barriers to effective integration, as well as cancer care providers' high workload and consequent lack of time (237).

This research also identified cancer care providers' perceptions regarding patient-level barriers reducing engagement in CVD care, including socioeconomic disadvantage, lack of motivation, having a fatalistic outlook, and aversity to more intervention. Only one previous study was found that reported cancer care providers' perceptions regarding potential patient-level barriers (232), and this study also identified patient socio-economic disadvantage and having a fatalistic outlook as potential barriers to CVD care engagement (232). In addition, responses did not differentiate between older and younger people with cancer, which may suggest that there are no differences in perception of barriers (and preferences) related to age. Although our findings go some way to bridging the gap in evidence in this area, it highlighted the need to clarify patient-level barriers with people with cancer themselves. There is also a lack of literature reporting cancer patients' perspectives regarding barriers to engagement in CVD care. Hence, the next study in this research program (reported in chapter 5) examines people with cancers' perceptions concerning CVD care in cancer, including their perceptions of patient-level barriers.

An important and unexpected finding was that respondents were not supportive of the development of a risk prediction tool. As described earlier in this chapter, the research team initially planned to examine participants' perspectives regarding the development of risk prediction tool based on a risk prediction model developed and validated by members of the research team. Participants responded that they did not see a risk prediction tool was likely to be used in practice, nor have a meaningful impact on improving cardio-oncology care. This finding was in contrast to the European Society of Cardiology guidelines for cardio-oncology, which encouraged the role of risk prediction tools (6). This finding therefore highlights that despite evidence-based guidelines recommending specific approaches, it is critical to consider the relevance and appropriateness of approaches in different contexts. It cannot be assumed that guidelines will be applicable in every context, and this highlights the importance of engaging with cancer care professionals who are best-placed to provide guidance on potential implementation and effectiveness of approaches to improve cardio-oncology care. In addition, participants' preference for approaches other than risk prediction tools does not mean these tools wouldn't be valuable, but that other options would be preferable to be developed and implemented first, because they were perceived to have a greater

likely impact. The rejection of the risk prediction tool by participants interviewed early in the data collection process led to changes to the way in which subsequent interviews and focus groups were conducted. The semi-structured topic guide was broadened to encourage participants to consider and discuss any potential approach to improve CVD management people with cancer. It also informed the development of the topic for the next study which sought the perspectives and preferences of people with cancer regarding CVD management in cancer. It raised new possibilities for what the new approach to CVD management in cancer might look like when developing the approach as the final aspect of the overall research program.

By reducing the focus on a risk prediction tool, discussions broadened to consider preferences for other types of approaches to reduce the impact of CVD in cancer, including a new model of care, a clinical pathway, education, and a specialised cardio-oncology service/clinic. There was a lack of consensus amongst participants for which approach could best reduce the impact of CVD in cancer. This suggests that there is not necessarily one approach that is best placed to address the problem of CVD in cancer, and a suite of intervention types is most likely required. This may be achieved through a complex multi-component intervention, or a series of single component interventions that each contribute to addressing the overall objective of improving CVD care in cancer. In addition, the diversity of barriers identified in this research, and the differing preferences for the specific characteristics of individual interventions (e.g., who should implement the intervention and when)' supports the need for approaches that can be tailored to the individual patients' needs and the context in which care is delivered (i.e., taking into account differences in services and resources). Although interventions have already been developed previously to improve CVD care in cancer, it is critical that interventions for particular settings address/work to overcome barriers impacting that setting, including resources, funding, patient population and workforce. For example, a cardio-oncology clinic may not be an appropriate approach to reduce the impact of CVD in cancer given the significant funding requirements. Likewise, an individual clinical pathway may only be appropriate to one setting, because it relies on tasks being allocated to specific professionals that may or may not be available in certain services. It is ideal to develop an approach that would be applicable to multiple settings, and this may require flexibility to individualise to settings and resources as well as individual patient needs.

4.7.1 Strengths and limitations

4.7.2 The major strength of the research reported in this chapter is the comprehensive, reflexive and flexible approach employing the RTA methodology to increase understanding of cancer care providers' perceptions regarding CVD in cancer. There are also notable limitations of our research. Limited demographic data were collected, which makes it difficult to compare feedback between groups and to estimate the generalisability of findings. Majority of participants were employees of one hospital, all were English speaking, and although several professions participated in our research, there were small numbers from some disciplines

(e.g., one cardiologist). Given data were collected from a small sample of cancer care providers and from one health care setting, the study findings cannot be assumed to be representative of broader healthcare system experiences. However, of the limited similar data available for comparison, there were some similarities in perspectives provided by health care providers including staff and perceived patient level barriers to engagement in interventions (e.g., lack of training and patient socio-economic disadvantage).Chapter summary and linking to chapter 5: Perceptions of people with cancer regarding cardiovascular disease risk in cancer: a qualitative study

To gain a better understanding of all aspects of cardio-oncology, including current practice, barriers and enablers to CVD care in cancer and needs and preferences for how to optimise care, it is critical to elicit the perspectives of those at the 'coalface', i.e. cancer care providers (as reported in the current chapter) and the perspectives of people affected by cancer. It is well-established that patients are best-placed to provide feedback about, and contribute to the development of new, healthcare services (238). The current research involved cancer care providers communicating some perceptions around patient-level barriers and needs, but it is critical that patients themselves have the opportunity to contribute their own experiences and perspectives, i.e., understanding of patient factors must come predominantly from patients. Therefore, it is apt that the subsequent step in this research program was to conduct a study to understand the perspectives, experiences, needs, barriers, enablers and preferences of people affected by cancer regarding cardio-oncology. This study used the same research methodology and methods as reported in the current research, with small alterations according to the nuanced differences of the sample populations (discussed in chapter 5). The perspectives of both the cancer care providers (reported in this chapter) and people affected by cancer were then integrated in order to provide a detailed contribution to understanding of the cardio-oncology to inform the conceptualisation and development of a new approach to reduce the impact of CVD in cancer.

5 CHAPTER FIVE: PERCEPTIONS OF PEOPLE WITH CANCER REGARDING CARDIOVASCULAR DISEASE RISK IN CANCER: A QUALITATIVE STUDY

5.1 Chapter Overview

This chapter reports the methods and findings of a qualitative study to understand the experiences, understanding, perceptions, needs and preferences regarding CVD risk in cancer, of a sample of people who have been diagnosed with cancer. This research builds on the findings of the previous research reported in chapter 3, in which experiences and perspectives about CVD risk in cancer were examined in a sample of cancer care providers.

This chapter begins with a summary of the existing literature in the area (background and context), including the findings of chapter 4, and how they justify the need for the research reported in this chapter. The contribution of this research to the broader literature is also described, followed by the aim of this qualitative study. This also includes a summary of how understanding the perspectives of people affected by cancer regarding CVD risk contributes to the overall aims of the PhD research program. A 'statement of related publication' is provided describing that a version of the research reported in this chapter has been published (239). A detailed description of the methods and findings of this study is then provided. The discussion section of the chapter includes a summary of the study findings in the context of the broader research in the area, including comparison to other research that has examined patient perspectives regarding cardio-oncology and related topics. The discussion also integrates the findings of this chapter and the previous chapter (i.e., the perspectives of both cancer care providers and people affected by cancer regarding CVD risk in cancer). Finally, there is a summary of the chapter, including how the findings of the study reported in this chapter (and chapter 4) link to the review of reviews reported in chapter 3, and how they informed the final studies conducted as part of the PhD research program (i.e., codesign and usability testing of a web-based resource to support self-management of cardiovascular disease risk in people with cancer, reported in chapter 6).

5.2 Background and context

The perspectives of those involved providing care, as well as people who are affected by cancer is needed to better understand why CVD risk assessment and management is not routinely undertaken. It is well-established that understanding the perspectives of patients and involving them in all stages of research leading to health care change better identifies barriers and facilitators of healthcare engagement and management, leading to positive healthcare outcomes including effectiveness and satisfaction with care (240). In addition, it is important that people affected by cancer have the opportunity to communicate their own perspectives, because health care providers make assumptions about their patient's experiences and perspectives that may

sometimes be inaccurate including, for example, overestimating anxiety, stress and inability to cope, but underestimating negative effects of health conditions on QoL (241, 242). In the research reported in chapter 4 (cancer care providers perspectives of CVD care in cancer), participants reported patient-level factors that they *perceived* may impact patients' engagement in CVD care (including socioeconomic disadvantage, a fatalistic outlook and aversion to further medical intervention) (216), but it is critical to honour the voice of people affected by cancer so they can contribute their own experiences, understanding, perspectives about CVD care, and their preferences for how it can be improved in the future.

There is a dearth of literature reporting the perspectives of cancer survivors regarding CVD care. However, one recent quantitative study collected data from 502 people diagnosed with cancer residing in the community in the United States, via a survey about cardiovascular health in cancer (243). Although the focus of the survey was to understand the prevalence of CVD risk factors and disease, the authors also assessed (via a 7-point Likert scale) patient understanding of their CVD risk, CVD risk management, and preferences for communication with oncology providers. Seventy-seven percent of participants reported they understood their risk of heart disease, 83% indicated they knew what they needed to do to look after their heart health, 73% responded that it was important to talk to their cancer care providers about heart health, and 79% thought their oncology providers should speak to them about heart health (243).

In addition to the very limited quantitative literature reporting people affected by cancer's experiences, perspectives and preferences regarding CVD care, the PhD candidate is unaware of any published qualitative data that have focused on gaining in-depth, rich data to improve understanding of current and optimal CVD care in cancer from the perspectives of people affected by cancer.

5.3 Aim

The aim of the research reported in this chapter is to examine people with cancer's experiences, perspectives, and preferences regarding CVD care in cancer, including CVD risk factor awareness, assessment, and management.

5.4 Statement of related publication

The research reported in this chapter was the focus of a paper ("There could be something going wrong and I wouldn't even know": a qualitative study of perceptions of people with cancer about cardiovascular disease (CVD) risk and its management), which was published in the Journal of Cancer Survivorship (2023) (239). Reegan Knowles (RK) was the primary/first author of the publication, with PhD primary supervisor Professor Bogda Koczwara as the senior/last author, and Dr Emma Kemp and Professor Michelle Miller as the second and third authors, respectively. All

authors contributed to the study conception and design, with RK contributing approximately 80% to the study conception and 80% to the research design. Data collection was conducted by RK (although other authors contributed to the development of the topic guide, RK facilitated all focus groups and individual interviews). Eighty per cent of data analysis was conducted by RK, with all coding conducted by RK. Theme development was conducted initially by RK, but these were revised via a series of discussions with all authors until finalisation of the themes. The first draft of the manuscript was written by RK and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript. This chapter provides greater detail about the research that was reported in the peer-reviewed paper in the Journal of Cancer Survivorship. The findings of the research are also synthesised in the context of the overall doctoral research program. Although there are differences in how the research is reported in this chapter compared to the paper, there is direct overlap of wording and content throughout. The published paper can be found at Appendix 4.

5.5 METHODS

5.5.1 Study design

A qualitative study design, involving interviews conducted in person, via telephone and online, was employed to examine the experiences, perspectives and preferences regarding CVD in cancer, using a reflexive thematic analysis (RTA) approach, involving individual interviews with people with cancer. The conceptualisation, planning and implementation of this research study was guided by the principles of the person-based approach to intervention development (PBAID), in that approaches to optimise CVD care must be based on the experiences, perspectives, needs, barriers and preferences of intended users.

As described in chapter 4, RTA can be considered a methodology in addition to guidance for data analysis. RTA was an appropriate approach to address the aims of the research reported in this chapter, which required an exploratory approach given the lack of research focusing on patients' perspectives of CVD care. RTA is also appropriate for this study given the research team is immersed in the topic area of cardio-oncology and can benefit the research process which may lead to the construction of in-depth and meaningful data (225). RTA is a type of thematic analysis which determines and interprets patterns in data but differs from other methodologies in that it recognises and argues for the important role of researchers in constructing findings (reflexivity is conducted to consider how the researcher's biases and experiences impact findings) (223, 225). As described in chapter 4, the application of RTA in this research aligns with critical realist philosophy underpinning the entire research program reported in this thesis, in that both RTA and critical realism are based on the epistemological and ontological appreciation of the role of subjectivity in research, i.e., the researcher's role and influence on the entire research process is

highlighted as necessary and valuable (225). More detail about how RTA was applied in this research is described in the 'Data analysis' sub-section below.

5.5.2 Participant eligibility criteria

People were eligible to participate in this study if they:

1. were aged 18 years or older;
2. had been diagnosed with any type of cancer regardless of stage or prognosis, and at any stage on the cancer continuum (e.g., during treatment, post-treatment survivorship);
3. had sufficient English language ability to provide informed consent; and
4. were well enough to participate in a focus group or individual interview.

There were no exclusion criteria.

5.5.3 Recruitment and consent

The researcher's target sample size was approximately 20 participants. As discussed in chapter 4, there is a lack of consensus in the literature regarding adequate sample sizes for qualitative research, but that sample sizes should be informed by philosophical, practical and pragmatic factors of the study (226) and should facilitate the collection of 'enough' data to allow novel understanding of people affected by cancer's perspectives about CVD risk whilst being manageable for in-depth analysis. As for the research involving cancer care providers, it was determined that a sample size of approximately 20 people diagnosed with cancer aligns with the critical realist philosophical worldview, the RTA methodological approach and the practical constraints of the PhD research program, whilst being appropriate for addressing the research aim. It was also decided that recruitment would continue until the researchers perceived enough data to conduct rich and meaningful analysis and to develop a report that is interesting, informative, contributes to the literature and can inform future improvements in CVD care in cancer.

Participants were recruited via their treating clinician (oncologist or oncology nurse) at Flinders Medical Centre, a large metropolitan, tertiary referral centre in Southern Australia. Clinicians known through researchers' existing networks, were approached via email from the researcher to determine if they wanted to be involved in recruitment. Clinicians willing to be involved in the recruitment of patients were provided with a recruitment flyer and Participant Information and Consent Form (PICF) to facilitate the recruitment of potential participants during consultations. Patients who indicated a willingness to participate in the research consented to having their contact details provided to researchers. The PhD candidate contacted all such potential participants by telephone, provided them with more information about the research and facilitated the provision of informed consent. Given the dependent relationship between patient and clinician, potential participants were reassured by their clinician that they did not need to indicate willingness to be involved in the research, and they were again assured by the PhD candidate (and the PICF) that they could choose not to participate (or withdraw from participating at any time) without any

adverse consequences. They were assured that data would be kept confidential, deidentified, and stored according to the requirements of the Southern Adelaide Human Research Ethics Committee. Willing participants indicated consent by signing the PICF and returning this in person or by email. Participants could choose whether they participated via focus group or individual interview, and whether they participated in-person, online or via telephone. In addition, potential participants were encouraged to take as much time as they needed to decide if they would like to participate, and to discuss their participation with trusted family and and/or friend(s). Once informed consent was provided, a face-to-face or telephone interview was scheduled according to the preferences of the participants.

5.5.4 Study procedures

The PhD candidate conducted all semi-structured individual interviews. Guided by the person-based principles of PBAID and using techniques described by McGrath and colleagues (228), the candidate aimed to establish and maintain rapport, comfort and mutual respect in order to ensure the collection of meaningful and rich data regarding participants' experiences, perspectives and preferences regarding CVD risk in cancer. A topic guide was developed by the PhD candidate based on the research aims and relevant previous literature, piloted with the research team (see Appendix 3), with team suggestions for improvement then incorporated. In line with the key element of applying PBAID, discussion about behaviour change was prompted by the topic guide, to understand willingness to engage in behaviour change and challenges associated with this in the context of CVD in cancer. Culture and power dynamics were considered during recruitment and data collection. Given the dependent relationship of some participants to one member of the research team (Professor Koczwara is a cancer care provider working where participants are being treated for cancer), it was critical to take steps to encourage participants to feel comfortable, respected, and trusting. These steps included contacting participants before the session to provide information about the study and indicate availability to provide more detail; starting sessions with an introduction, reminding participants of the aims of the study and their options for withdrawing and only engaging in discussions they feel comfortable to engage in; starting sessions with definitions about the topic and starting with broader topics before moving to more specific topics; encouraging participants to contribute their views and ideas and prompting them to add greater detail if needed; and repeating/paraphrasing participants' contributions to confirm they had been interpreted accurately (228). The facilitator also listened actively and allowed the participant to speak as much as they wanted to and allowed them time to reflect on what they had previously said. Having said this, the researcher also acknowledged their role in constructing the findings of the research (as per the RTA approach and critical realist worldview) and therefore, where appropriate, used their own knowledge and experience to create engaging discussions (225, 228).

Participants were recruited until the researchers perceived adequate "information power" (227), that is, sufficient data to address the aims of the research, to provide a meaningful contribution to

the research literature and to inform future research and practice, particularly in the development of a new approach to CVD risk identification and management in people with cancer. Ceasing recruitment based on reaching adequate information power aligns with the principle that original data may continue to emerge with subsequent interviews; and the decision to cease recruitment is therefore pragmatic and based on reflexive researcher judgement that further data would not change the findings and that the data analysis has led to a convincing response to the research objectives (227).

5.5.5 Data analysis

Interviews were audio-recorded and transcribed verbatim. The NVivo (Version 1.3) computer software program for qualitative analysis (229) was used to assist in coding and theme development. The construction of themes and interpretation of findings occurred through a series of discussions between the research team.

Reflexive thematic analysis (RTA), underpinned by a critical realism, was used to analyse data. Our analysis, as per the RTA framework (230), involved six steps: data familiarisation, coding, initial theme development, review of themes, refinement and reporting. The PhD candidate became familiar with the data through conducting each of the interviews, checking audio-recordings and checking transcriptions which were performed by an external transcriber. In addition, the PhD candidate conducted coding in NVivo, which meant further familiarisation with the data. Coding was conducted using an inductive approach, where new codes were formed as new data were identified in transcripts. The majority of data analysis was semantic, meaning the construction of knowledge was based on the data explicitly communicated by participants in their interviews. However, latent analysis was also used to identify more complex meanings which were perceived to underlie participants' responses. The research team engaged in a series of discussions about the coding and theme development, in which their expertise aided in the construction of findings. The process of the construction of knowledge was iterative, recursive and flexible, where new data and ideas arose in subsequent interviews, through researcher discussions and drafting of results.

5.5.6 Given RTA is an approach that acknowledges the role of the researcher in the construction of knowledge derived from data collection, analysis and interpretation (230), the PhD candidate regularly practiced reflexivity through all stages of analysis, to understand how perceptions and experiences influenced the construction of knowledge derived from the analysis. In particular the researcher undertook self-questioning throughout data collection and analysis in which they checked and refined their interpretations and presentations of findings where they could identify their own biases and experiences impacted their analysis. The researcher was also aided in this active process of checking their own role in interpretation by regularly discussing coding, development of themes, and interpretation and

presentation of data, with their research team throughout all aspects of the research process (231). Ethics

Ethics approval was granted by the Southern Adelaide Local Health Network Ethics Committee on 22 January 2020 (HREC/19/SAC/309).

5.6 Results

A total of 15 people (n = 6 male) participated in the research. Thirteen interviews were conducted via telephone, and two were conducted in-person. Six participants had been diagnosed with breast cancer, one with oesophageal cancer, one with cervical cancer and one with rectal cancer. Six participants did not report the type of cancer they had been diagnosed with. The interviews lasted between 10 min, 33 seconds and 46 min, 21 seconds (median = 23 min, 1 second).

Inductive code development led to the construction of initial codes. A series of discussions were conducted amongst the research team, including how responses might be able to be grouped together into the same code, and discussions by the researchers regarding how responses could be interpreted to hold latent meanings. The researchers engaged in reflexive practices to identify how existing views and biases might impact code and theme development. For example, it was critical that the PhD candidate's previous experience in collecting and analysing cancer care providers' perspectives about CVD in cancer (reported in chapter 4), did not lead to inaccurate assumptions being made in the way in which data were collected (i.e., the types of prompts given) and how data were interpreted. However, given a strength of the RTA methodology is that the impact of researchers on the construction of findings is acknowledged and valued, existing knowledge and expertise of researchers informed data collection and analysis to ensure that rich findings were constructed, and in-depth understandings were achieved.

The analysis identified two themes, one of which had four subthemes (see Figure 8). Each of the themes and sub-themes are described in the paragraphs below.

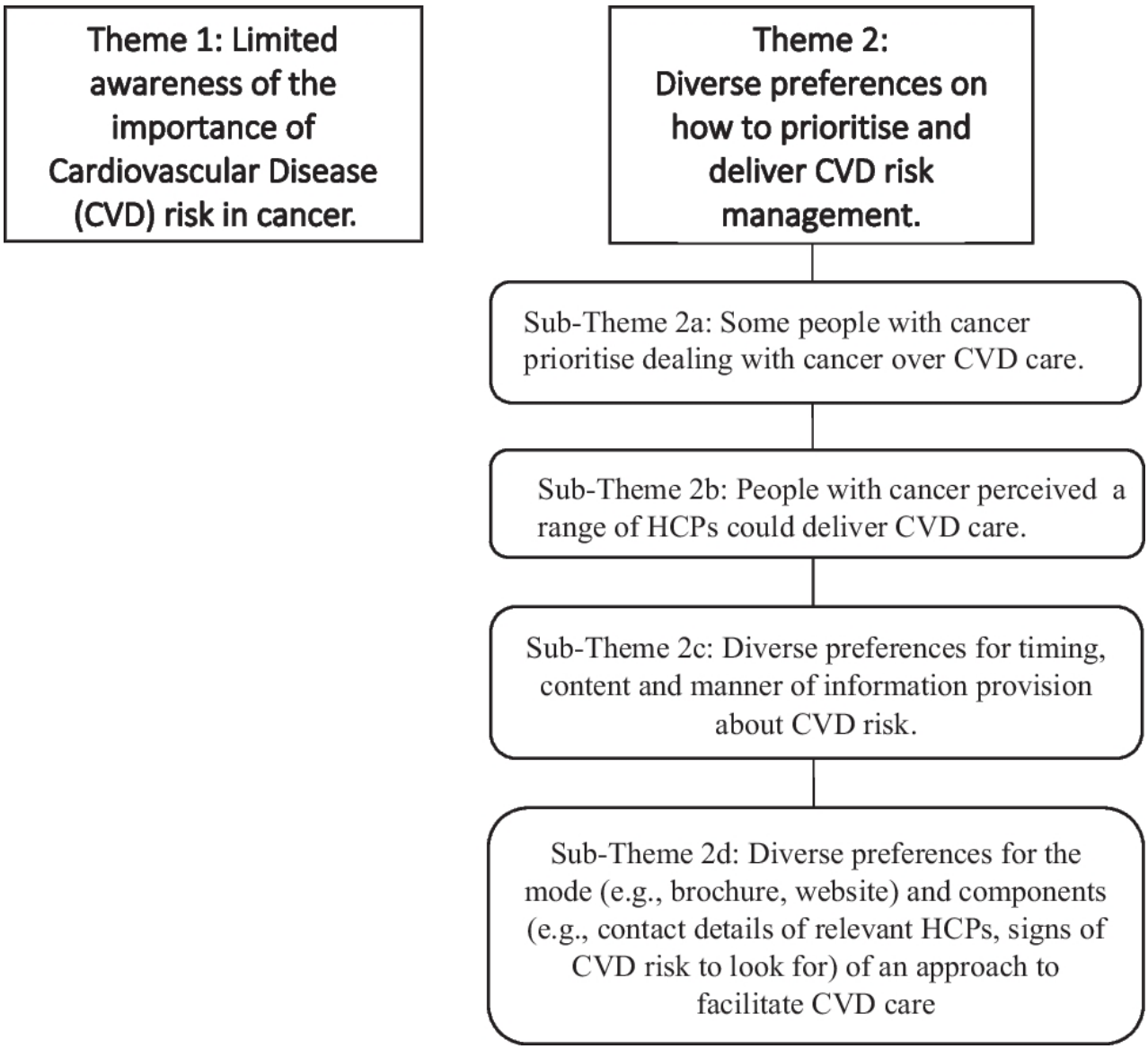


Figure 8 - Themes and sub-themes from qualitative interviews of people with cancer regarding cardiovascular disease in cancer

5.6.1 Theme 1: Limited awareness of the importance of CVD risk in cancer.

Majority of participants indicated that they did not know CVD risk was increased in cancer and had not been told about this by anyone in their cancer care team. For example, one participant stated, "I don't think I knew that it [cancer] really affected the heart."

Other participants indicated that they deduced there was an increased CVD risk associated with cancer (treatment), without having been explicitly informed by anyone in their cancer care team.

> "*He [my oncologist] mentioned the word toxic chemotherapy… I knew exactly what he meant… [the oncologist told me it was] just toxic. Yeah, nothing [specific] to do with the heart. I know, it's my understanding that that that kind of chemotherapy actually destroys the heart muscles, reduces the ejection fraction.*"

Some were unsure as to whether they had been informed of increased CVD risk, querying their own capacity to absorb information at the time it was provided.

> "*At the beginning I wasn't really aware of it [CVD risk] at all. It [CVD risk] may have been mentioned to me perhaps in passing earlier on, but because you're taking on board so many other things and you're so concentrated on what's happening to you with your cancer, I don't really remember even considering it or thinking that it could be a concern back then".*
>
> *"…I know it's silly, but they could have mentioned it [CVD risk], but the thing is I reckon for the first three months I didn't hear a word that they said."*

A minority of respondents were aware of increased CVD risk, most of whom had been informed of this by their oncologist.

> "*Yeah, especially after radiation that it [CVD risk] could definitely affect me."*

All respondents agreed increased CVD risk is an important issue and that it is important to be aware of it.

> "*Oh, look, I just like to know, that's all. There's no reason, I just want to know what's happening, you know? I don't want to be – I want the doctor to tell me the truth about stuff like that.*"

Some participants acknowledged that informing patients about increased CVD risk could elicit negative emotions, but all but one reported they wanted to be fully informed despite this. For example, one participant said:

> "*I want them to tell me [about CVD risk…irrespective of how devastating it would be…"*

Similarly, another respondent said:

> *"I need the information to be able to cope with it and process it and organise my family. And I don't care if [it's] bad information. I just want to know."* They went on to communicate their perception that knowledge can facilitate a better care experience: *"I want to know all the information. Yeah. Yeah, definitely. I think that you can't advocate for your health for yourself if you're not informed."*

Only one participant suggested they did not want to be told about CVD risk:

> "*And I just don't know that it's fruitful to be told of all the things that might go wrong because then you almost manifest that to happen."* They went on to explain that *"I think that people have a tendency to catastrophise with too much information."*

5.6.2 Theme 2: Diverse preferences on how to prioritise and deliver CVD risk management.

Participants provided diverse preferences regarding when and how CVD care should be delivered and who should be involved in CVD care.

5.6.2.1 Sub-theme 2a: Some people with cancer prioritise dealing with cancer over CVD care.

A small number of respondents discussed they prioritised dealing with cancer over CVD care. One participant explicitly mentioned this:

> "*I suppose the big picture's trying to sort the other – the cancer out* ".

Whereas other participants alluded to the prioritization of cancer over managing CVD risk when they are discussing other issues, such as when would be the best timing to provide CVD risk information. For example:

> *"*[if] *you sort of hear things are progressing well* [with the cancer]*, that's probably all I'm hearing at that point in time regardless of what my blood test results or my ECG results [assessing CVD risk] are being said, I'm really just focussed on the fact that are things going well or have I got something to worry about at that point in time* [related to the cancer]*."*

> *"After they got it [cancer] stabilised sort of thing, yes, it's good now, you need to talk about the next step and bring it [information about CVD risk] in as a gentle conversation and not on top of the person like a lead brick".*

5.6.2.2 Sub-theme 2b: People with cancer perceived a range of cancer care providers could deliver CVD care.

Participants identified a range of cancer care providers they perceived to be appropriate to assist them to self-manage their needs and provide CVD assessment and management, including nurses, oncologists and GPs. They provided reasons for why they had determined these cancer care providers suitable for this role. For example,

> "*Because you can get in to see the GP usually a lot easier than you can the oncologist and if the GP's doing ECGs and he's checking your blood pressure and all the other general medication and issues, I think the GPs the one that actually know about it and do something about it for you.*"

> "*…he's [the GP] supposed to be the guy that takes care of me and the oncologist is the guy who looks after the cancer itself. So, this heart disease, it's not part of the oncology treatment, it's a separate issue. So, therefore, your GP should be the guy that's says, alright, cancer – we can start expecting heart disease as well.*"

"*these guys [nurses] see everyone every day constantly and they don't back down, they come up again and try and help support you.*"

The oncologist was also identified as being an appropriate person to provide CVD care:

"I think, yeah, I think it's your oncologist. Yeah. Not necessarily [only] oncologist, but I think that that person should be like, at your checkups and stuff would be okay. Like, this is your information for dealing with life after cancer?"

"I reckon the GP things get lost as well, like if the oncologist is looking after you, like in the one consult or something, I don't know…Probably easier [for the oncologist to provide CVD care] yeah and keeping track of – because even related to cancer and all this stuff it's probably easier to be dealt with one person."

"My trust is in [my oncologist] and I talk to different nurses and different faces about different things – there isn't a unified response about different things and it's much easier with the person that you have built a level of trust with."

One participant mentioned that it could either be the oncologist or GP:

"Yeah, I think if they're joined together [cancer and CVD] that people should be informed that there is a potential – if the oncologist doesn't do it, go and see a good GP and get it monitored and tested and checked regularly."

Nurses were also identified as cancer care providers that could provide CVD care:

"Straight back to when I was first diagnosed and I go and see that nurse … where they tell you about your hair falling out and I think probably at that stage there because that was quite a harsh conversation to have now that my hair's going to fall out, so I'd probably get all that stuff out the way to begin with."

One participant communicated that a range of cancer care providers could effectively guide them to manage aspects of their CVD care.

"*Everyone seems to be fairly knowledgeable [about everything health-related]… so I really wouldn't mind who [guided me].*"

Another expressed that the person who provides CVD care should be based on who is providing care to the patient at the time when it is appropriate that the care be provided, e.g., the cancer care provider who is conducting discharge from treatment:

"So, I think whoever, whether it's the oncologist or the radiotherapist, or whoever is that last point of call, when you think, you know, discharged in remission, which I'm not up to, so I

don't know the whole process yet. But I would say probably, then is a good time to be able to process the information [about CVD risk].”

5.6.2.3 Sub-theme 2c: Diverse preferences for timing, amount and manner of information provision about CVD risk

Some respondents felt the timing of CVD risk assessment and management was important and could impact their engagement with CVD care. Respondents had specific ideas about *when* would be appropriate, and this varied from participant to participant. For example, some participants would prefer to engage in CVD risk management after treatment:

> “*[At the end of treatment] I would have a capacity to think okay, now I'm getting back into the swing of life… I think I would have the mental capacity to process the information…”*

In contrast, another participant expressed a preference for information to be provided earlier in the cancer continuum:

> “*I’d rather know all of it [cancer and associated risks including CVD risk] in one go, or like spaced out so I kind of absorb it and then I know the next bit and the next bit, but I want it all relatively soon*.”

There were also diverse preferences for *how much* information should be provided, suggesting that flexible and tailored information provision approaches are needed. For example,

> “*I’m the sort of person that needs to know basically what’s going on, I don’t need to get into the really nitty gritty, but I like to know and then I try and process it and then I try and get on with it…*”

> “*Sometimes you can get bombarded with stuff you don’t need to know.*”

> *“I think all the way through I tried to take the minimum anyway, but for some people want to have more information which I didn’t do…Like, I didn’t want to know.”*

Other participants reported a preference for being provided with a comprehensive amount of information about CVD risk. For example,

> “*I’d rather have all the information and then I can read back through it if I need to, if I feel like I need to…”*

> “*I want to know all the information. Yeah. Yeah, definitely. I think that you can't advocate for your health for yourself if you're not informed.”*

Others indicated that would prefer to be provided with information when they requested it (or when they perceived they needed it):

"Sometimes I am curious, and I can ask [for more information about aspects of health], but yeah."

"…there's a lot of information, it can feel very overwhelming and at times it can be like, well, I'll worry about it when I need to worry about it when I detect certain symptoms that have been flagged as things to look out for. And then if I don't experience those symptoms, I suppose, I don't ignore the risks, but I'm probably not as alert to the risks as what I would have been when they were first explained."

Although respondents reported they want to be informed of CVD risk in cancer, several communicated that the *way in which information is provided* should be carefully considered. For example:

"Definitely [CVD risk information should be] presented in a way that doesn't scare you more because you're already so scared."

"People want information about CVD risk to be communicated to them gently and in a non-judgmental manner."

"Bring it in as a gentle conversation and not on top of the person like a lead brick."

Two patients mentioned how the delivery, and type, of the information can help the patient exert control over how much, and when information is received:

"So, I think in a very non-threatening manner, the basics should be gone over the medical facts. Yeah. Yeah. And leave it, somewhat leave it, to the patient to decide whether it applies to them. Yes. Yeah. provide all the help that you can, should they decide to do something about it? Yes. Yeah. We are here to help. Yes. Okay. Not to criticise. This is what we want to cover. Yeah. This is what we want to offer. And then it's up to the patient to say, yea or nay."

"Give the option of the information and to say that it doesn't necessarily mean it will happen to you, but we're keeping you informed."

To illustrate the importance of the manner of communication, one participant gave an example of a negative experience of how they received care previously when they were admitted into hospital (after being diagnosed with COVID-19):

"*One or two doctors need to get some bedside manner... but I probably would have if they had taken it differently – and it might sound a bit precious, but I do think if you can just do it a different way, just you're not as severe, do you want to be resuscitated or what?"*

5.6.2.4 Sub-theme 2d: Diverse preferences for the mode (e.g., brochure, website) and components (e.g., contact details of relevant cancer care providers, signs of CVD risk to look for) of an approach to facilitate CVD care.

A range of suggestions were provided by respondents regarding how CVD risk information could be provided and how people with cancer can be supported to undergo CVD risk assessment and management. A brochure and website for providing CVD risk information and guidance were suggested and discussed favourably.

> "*Website is pretty good too. You can go on that website and go and read what to expect."*
>
> *"Paper probably to begin with just so I've got a hard copy of what I needed, but if I didn't have a paper copy of it then Internet would be fine because I could print it off if I needed to or I just had to go onto it if I'm worried about something, I can just check the website, so."*
>
> *"I wouldn't go looking for it* [website about managing CVD risk] *…[But] if someone gave me a link in an appointment, I would [access a website about CVD risk].*

Another participant discussed their preference for support groups in which participants discuss and assist each other to navigate aspects of cancer (including CVD risk).

> "*So, I'd like to be able to have a resource or the opportunity to regularly check in with others going through similar treatments and processes and I suppose there's a warmth attached to that, talking to people that are going through similar experiences, but there's also a real knowledge base asking really targeted individual questions in the hope that, yeah, okay, someone else has had that same experience and this is what was advised to me, so it can either then build your confidence that everything's probably okay."*

Other respondents indicated they would prefer they were informed about CVD risk and supported to manage their risk through direct interactions with cancer care providers. For example,

> *"I personally prefer talking to someone [about my health]."*
>
> *"And if it's verbally said, I think it carries a little bit more weight than a piece of paper given to you and the piece of paper is probably a little bit of reinforcement if you care to read it, but if it's spoken to you, look, you've got cancer, it's great, it's under control, however, you should have your heart checked and ECG and blood pressure monitored regularly and organise it with your GP and go in every month or whatever and get it checked and tested or what not."*
>
> *"I much prefer, personally, I prefer to go and see my doctor and have a chat with my doctor and he can say, right, we can do some bloods and we're going to check on this level, we're going to get you an ECG done, you know?"*

Participants indicated that combining methods to provide CVD education and care could be helpful, e.g., written information and a discussion with a cancer care provider.

> *"I think both [talking to a HCP or a brochure] would be good, but someone just clarifying – you kind of get a better feel for the likelihood and the significance of it – is it really significant or is it something that I don't really need to think about too much if someone talks about it and then start to where to sort of place it in the risk priorities, you know?"*

> "*Speaking to somebody [about CVD risk] really, but also reading, definitely where you can ask questions."*

Participants also discussed specific components of an optimal approach to reduce the impact of CVD in cancer including:

(a) Provision of information about CVD risk in cancer:

> "*I want to know all the information. Yeah. Yeah, definitely. I think that you can't advocate for your health for yourself if you're not informed".*

(b) List of CVD risk-related symptoms/signs the person with cancer should be aware of:

> "*I mean, there could be something going wrong and I wouldn't even know. Sometimes I'm hopping around and think oh, okay, fine, you know? So, you just don't know what level of damage has happened or is happening and so, I don't know, if there is some sort of a measure…"*

> *"Yeah, I think it's probably more of a case of what to look [signs of CVD risk] for or a feeling, this could be happening, where to go to get advice if you feel you need to go to the next stage."*

(c) List of cancer care providers/services that could be contacted to assist with CVD issues:

> "*I think it's…where to go to get advice if you feel you need to..."*

(d) Self-management support:

> "*In the end, my health is my responsibility. I'm the one that needs to study up on these things and to understand how my body's going to respond to the cancer and I'm the one who needs to [deal with it]*."

(e) Guidance/support for CVD risk assessment and management (including behaviour change):

"If [I was advised that] a specific type of training will reduce your risk of heart damage…, I'd try and put them into my training…"

"I think my experience as a cancer patient is I'll do whatever I'm told to do provided I have enough detail and enough logic to understand what those benefits for me then are. I suppose there's always going to benefits, although it's not mentioned, they're talking me through a little bit of a program and, well, what does that actually look like for me and my particular cancer experience as opposed to just a generic here's a few things that you can do differently."

Despite our topic guide including discussion prompts about barriers and enablers of optimal CVD care in cancer, participants did not discuss in great detail factors they perceived to impact existing CVD care (which could inform a new approach to reduce the impact of CVD in cancer). Given, several respondents were unaware, or only somewhat aware of CVD risk in cancer, they may have not been in a position to make these suggestions. The small number of identified barriers included financial barriers:

"…you've started that eight weeks in the gym, at the physiotherapy [free service provided to patient during his care], then you're out because you know, it's not funded… it would probably be a great idea if you could ease the way for people moving out of the aid with physiotherapy into getting themselves into a gym…I look, I suppose I could have found the money?"

The same participant also mentioned the importance of psychological factors in influencing likeliness of patients to engage in CVD care:

"But a serious, convincing discussion to motivate the patient to do it. Yeah. Yeah. As opposed to, you know, I'm suffering from depression…What's the one we can't go out? agoraphobia? Yeah. Yep. sort of help with people in that position, which is pretty much where I was. Yeah…the motivation around to continue and why it was important or how important…this is psychological state where you've stopped taking care of yourself…. I don't run around being depressed. I'm not agoraphobic. But there is that hole that people can fall into."

5.7 Discussion

This study of perceptions of people diagnosed with cancer regarding the CVD risk assessment and management shows that majority of respondents were unaware or only somewhat aware of the issue of CVD risk in cancer. However, for those who were aware (and those who became aware as part of this study), they perceived it to be an important issue. The participants had diverse preferences on how to prioritise and deliver CVD risk management (including preferences related

to who should deliver care, and what and when information and support should be provided), and different ideas about what would be important aspects to address as part of any approach to reduce the impact of CVD in cancer.

The majority of participants in this study were relatively unaware of increased CVD risk in cancer, which is concerning given the existence of multiple guidelines which highlight the importance of CVD risk identification, monitoring and management in cancer (6, 36). In addition, majority of participants want to be provided with CVD care, which aligns with evidence that providing patients with health care information can improve a patient's feelings of control, decrease anxiety and even improve clinical outcomes (244). In contrast, some respondents expressed they may have been told about CVD risk but had not "absorbed" the information due to "information overload" and/or prioritisation of coping with their cancer diagnosis and treatment. This aligns with concerns of cancer care providers that people with cancer may be burdened by receiving information about CVD risk whilst dealing with cancer (216). The findings of this study provide an example of the concept termed by Jensen et al. "cancer information overload" (CIO), where up to three quarters of people with cancer have reported being overwhelmed by information (245). Given CIO can induce fatalistic thinking and reduced engagement in positive health behaviour (245), it is important to consider how to meet the expressed needs of patients to be health-informed, whilst also reducing the risk of CIO. Thoughtful consideration of how, how much and when information provision occurs may be able to achieve the balance between these opposing concepts.

This study reported diverse priorities and preferences for CVD risk identification and management in cancer. This is unsurprising given the lack of awareness of CVD risk of majority of participants, which may be due to limited (previous) consideration of the possibility and practicality of potential solutions. It is also important to acknowledge that diversity of health care preferences likely reflects differences in people (e.g., demographics, attitude/outlook and personalities) and their disease (e.g., cancer type and stage in continuum). Diverse preferences highlight that the development of any new approach to reduce the impact of CVD in cancer should be holistic, multi-pronged, flexible and tailored to individual needs and preferences. Furthermore, it is critical that conceptualisation and development of a new approach must be guided by meaningful and authentic consumer engagement (246), e.g., using codesign methodology.

Examining perceptions of people affected by cancer regarding CVD risk in cancer facilitates comparison with the research involving cancer care providers reported in chapter 4 (216). An important difference between the perceptions of people with cancer and those who provide cancer care were the perceived barriers to CVD. Cancer care providers identified multiple barriers to the provision of CVD care, including perceived conflicts with role identity and lack of time and training. In addition, they communicated what they perceived may be barriers affecting the engagement of patients in CVD risk assessment and management. These included sociodemographic

disadvantage or financial stress, social isolation, perceived denial about their disease, and perceptions that the patient may be unwilling/reluctant to make changes. Respondents also spoke of perceived barriers specific to older people with cancer, including being less demanding of health services and having a fatalistic outlook. In contrast, in the current study involving people who have been diagnosed with cancer, very few barriers to engaging in CVD care were identified (financial and psychological barriers were mentioned briefly). This may reflect patients' lack of awareness of CVD risk in cancer, meaning they likely had not considered potential barriers, and may perhaps also reflect health care consumers' trust in the Australian health care system. Meanwhile, cancer care providers were aware of CVD risk and that care is not always adequate, so they are more likely to have considered potential reasons for this. The contrast in findings regarding barriers identified by cancer care providers compared to people diagnosed with cancer highlights the importance of meaningful and authentic patient engagement in all stages of the research process, so that needs and barriers are accurately identified, and solutions are informed and shaped by this information. Unlike the differences in perceived barriers, cancer care providers and people diagnosed with cancer both contributed diverse ideas for solutions to optimise CVD care. Again, this highlights that future approaches to CVD care in cancer must be flexible and individualisable and must be conceptualised and developed involving a broad range of stakeholders including people diagnosed with cancer, cancer care providers and researchers.

This research makes a novel contribution to the limited existing literature on perspectives of people diagnosed with cancer regarding CVD risk. It is critical that the increased understanding of both patients and cancer care providers' needs, barriers and preferences for CVD care informs a new approach that can reduce the significant adverse impact of CVD in cancer. Given the diversity of perspectives contributed by participants in this research, no individual intervention/approach would align with all preferences. However, it is proposed that a patient-facing website providing information and support for the self-management of CVD in cancer could address many of the needs and preferences of the stakeholders and could take into account majority of the barriers identified by study participants. First, information provision is critical to increase awareness of CVD risk in people who have been diagnosed with cancer, and patient education was identified by cancer care providers as a potential approach to reducing the impact of CVD in cancer. Many participants in the current study expressed support for the provision of information and support via a website. Second, a website can provide the specific types of information and support discussed by people diagnosed with cancer in the current study, including what they should look out for regarding their cardiovascular health, resources and services available for support, and behaviour changes they can make to reduce risk. A website can support patients to self-manage aspects of their health and disease, which was identified as important for some people involved in our research. Third, a website can cater for diverse preferences regarding the amount and detail of information provided, where information can be present in a general and simple way but with

options to navigate to greater detail for those who prefer it. The use of videos, pictures, text and interactive activities can also create an individualised experience catering to user's different needs and preferences. Finally, a website may circumvent some barriers to providing CVD care identified by cancer care professionals, including that they do not have the time or training to provide adequate CVD care, and that they feel their profession cannot provide CVD care alone.

5.7.1 Strengths and limitations

This is the first study to examine people with cancer's perceptions and experiences of CVD in cancer. The use of RTA methodology was a key strength of this research and led to the construction of new and in-depth knowledge that serves as a novel contribution to the limited literature in this area. There were important limitations of this research. All participants were recruited from one health care setting.There were important limitations of this research. Data were collected from a small sample of people affected by cancer and most participants were recruited from one health care setting. Given cardio-oncology care is likely impacted by the setting in which it is provided due to differing resources and funding, the applicability of findings to other settings may be limited and therefore the sample cannot be assumed to be representative of broader healthcare system experiences.Participants were not specifically recruited to achieve diversity in socioeconomic or educational backgrounds and given the impact of these factors in shaping patient experiences and perspectives, the data may not be representative of disadvantaged populations. Limited demographic and medical data were collected, including cancer stage or phase on the cancer continuum (e.g. during active treatment, survivorship), nor the presence of existing CVD or CVD risk factors, meaning comparisons of perspectives according to demographics was not possible.

5.7.2 Chapter summary and linking to chapter 6: codesign and usability testing of a web-based resource to support self-management of cardiovascular disease risk in people with cancer

This chapter reported the methods and findings of a qualitative research examining the perspectives of people diagnosed with cancer regarding CVD care in cancer. Findings included that people affected by cancer were unaware or only somewhat aware of increased CVD risk in cancer, but that they perceived it to be an important issue. Participants identified a diverse range of ideas for how CVD care in cancer could be improved, including through information provision and self-management support. They felt that many cancer care providers could deliver CVD care effectively and had diverse preferences related to the amount and type of information and support provided and the mode by which it was provided (e.g., delivered in person vs website). This chapter provided a comparison of the perspectives from cancer care providers (reported in chapter 4) and people affected by cancer. This chapter proposes that a patient-facing providing information and self-management support can address the needs and preferences of cancer care providers

and people affected by cancer. The codesign and usability testing of this approach is described in chapter 6.

6 CHAPTER SIX: CODESIGN AND USABILITY TESTING OF A WEB-BASED RESOURCE TO SUPPORT SELF-MANAGEMENT OF CARDIOVASCULAR DISEASE RISK IN PEOPLE WITH CANCER

6.1 Chapter Overview

This chapter reports the methods and findings of a study to codesign and test the usability of a web-based resource (website) to support self-management of CVD risk in people with cancer.

This chapter begins with a summary of the existing literature in the area (background and context). The contribution of this research to the broader literature is also described, followed by the aim of the study. A 'statement of related publication' is provided describing that a version of the research reported in this chapter has been submitted for publication. A detailed description of the methods and findings of this study is then provided. The discussion section of the chapter includes a summary of the study findings in the context of the broader research in the area, including how aspects of the website align with existing evidence for the provision of effective CVD care. Strengths and limitations of the study are reported, as are implications for practice and recommendations for future research.

A paper has been produced reporting the findings of this research study (see Appendix 5), but it has been rejected by the Journal of Cancer Survivorship. The authors are currently preparing to submit the paper to another appropriate journal.

6.2 Background and context

Earlier studies in this program of research (reported in chapters 4 and 5) found that people who had been diagnosed with cancer were unaware, or only somewhat aware of their increased CVD risk; yet, once made aware of this risk, they perceived it to be an important issue. Cancer care providers were aware of CVD risk but identified several barriers to the provision of CVD care including lack of time and perceived role conflict, where they didn't believe their professional role could (or should) deliver CVD care alone (216). Both people affected by cancer and cancer care providers communicated diverse solutions to optimise CVD care. Cancer care providers identified education and clinical pathways as potential approaches to improve CVD care, whilst people who had been diagnosed with cancer noted the importance of information provision (i.e., general information about CVD risk in cancer), including information on signs and symptoms of CVD that they should look out for, and support to access services and resources relevant to CVD risk management. Self-management was identified by both cancer care providers and people diagnosed with cancer as necessary in effective CVD risk management. Self-management "is the

individual's ability to manage the symptoms, treatment, physical and psychosocial consequences and lifestyle changes inherent in living with a chronic disease" (101), and in cancer involves managing (risk of) comorbid conditions through risk factor management (247). Self-management is increasingly expected of people with chronic diseases (102), given it is associated with improved health outcomes and patient experiences and reduced use of other healthcare resources (248). Although people with cancer discussed the importance of being involved in their own care, they also contributed views regarding which health care providers would be best placed to provide/coordinate CVD care to them (i.e., suggestions included nurses, GPs and/or oncologists). They also had diverse views regarding the amount and level of detail of information they would like to receive (e.g., simplified, general and limited information vs detailed and specific), and the timing of CVD care provision, with some suggesting they would like to receive the information as soon as possible following diagnosis whilst others expressed concern about being overwhelmed close to diagnosis. Websites, brochures, support groups and education by their own healthcare team were suggested as potential ways to provide information and support.

Informed by the findings reported in chapters 4 and 5, together with existing literature (particularly the ESC guidelines for cardio-oncology (6)), it was determined that a patient-facing web-based (website) resource to support the self-management of CVD risk in people diagnosed with cancer would be an optimal way to meet the needs identified. It was deemed important that the website should provide information and support to all people affected by cancer who are at risk of CVD, whether that be due to cardiotoxicity of anti-cancer treatment or through the presence of other CVD risk factors including physical inactivity, overweight and smoking. The research team argues that a website can address several of the needs identified by people affected by cancer (e.g., increased awareness and understanding of the problem) and can overcome barriers affecting cancer care providers, including role conflict and lack of time and training. A website can facilitate information provision, education regarding signs of CVD risk to look out for, self-management support, and support to access resources and services. A website also caters for differences in individual needs and preferences, e.g., general simplified information can be presented but with options for users to navigate to more detailed information and is a resource that can be accessed at a time the individual feels ready for it.

There are a lack of quality resources and support for self-management of CVD risk factor management in cancer (112). For example, we are not aware of any websites for people affected by cancer that focus on CVD and cancer, with limited advice provided in other websites with a broader scope such the Alfred Health and Australian Cancer Survivorship Centre websites (112, 249, 250). This is despite findings that web-based interventions have been shown to be an effective approach to improving health outcomes for people affected by cancer (251, 252), including improving self-efficacy(253), indicating potential for a web-based intervention to improve self-management of CVD risk in people affected by cancer.

6.3 Aim

The aim of this study was to codesign and test the usability of a web-based resource (website) for people affected by cancer, to improve assessment and management of CVD risk in cancer.

6.4 Statement of related publication

The research reported in this chapter is the focus of a draft manuscript to be submitted to an appropriate academic journal (Codesign and usability testing of a cardiovascular disease risk management website for cancer survivors) . Reegan Knowles (RK) was the primary/first author of the publication, with PhD primary supervisor Professor Bogda Koczwara as the senior/last author, and Dr Emma Kemp and Professor Michelle Miller as the second and third authors, respectively. All authors contributed to the study conception and design, with RK contributing approximately 70% to the study conception and 80% to the research design. Eighty per cent of data collection was conducted by RK (developed topic guide with consultation with other authors and facilitated all focus groups and individual interviews). Eighty per cent of data analysis was conducted by RK, with all coding conducted by RK (qualitative descriptive analysis was conducted of data collected in Codesign Round 2 and Usability testing). Topic development was conducted initially by RK, as was the identification of changes to be made to iteration of the prototypes and website, but these were considered and informed via a series of discussions with all authors until website finalisation. The first draft of the manuscript was written by RK and all authors commented on versions of the manuscript. All authors read and approved the final manuscript. This chapter provides a more detailed description of the research reported in the draft manuscript. For example, more detail about the methodology and methods utilised to collect data is provided, and the results section contains more quotes from participants along with relevant synthesis. More details are also provided about the changes made to iterations of the prototype and website. Although there are differences in how the research is reported in this chapter compared to the paper, there is direct overlap of wording and content throughout.

6.5 METHODS

6.5.1 Study Design

To develop the website, a qualitative two-round codesign methodology involving focus groups and individual interviews was conducted, with web development supported by an external website developer (Stage 1). Qualitative methodology using the ‘Think Aloud’ approach (254) was then employed to examine the usability of the codesigned website (Stage 2). These study designs were selected as they align with the person-based approach to intervention development (PBAID) (129), in which the key principle is to ensure the systematic and authentic engagement of stakeholders (people diagnosed with cancer and cancer care providers) in all aspects of intervention development with a particular focus on understanding how psychosocial characteristics of users

affect their preferences. More detail about how the PBAID principles informed the codesign and usability testing in the current study are reported in the methods section below. As per the entire research program, codesign and usability testing study design align with the PhD candidate's epistemological and ontological foundation in critical realism. Developing the website with people affected by cancer and cancer care providers is consistent with the worldview that knowledge is constructed based on an objective reality and shaped by subjective influences (i.e., people's experiences and perspectives).

6.5.2 Participant eligibility criteria

Stage 1: Codesign

Participant group 1: People affected by cancer

People were eligible to participate if they:

1. were aged 18 years or older;
2. had been diagnosed with any type of cancer regardless of stage or prognosis, and at any stage on the cancer continuum (e.g., during treatment, survivorship) OR were a friend or family member providing informal support to a person diagnosed with cancer;
3. had sufficient English language ability to provide informed consent; and
4. were well enough to participate in a codesign session.

There were no exclusion criteria.

Participant group 2: Health care providers providing cancer to people affected by cancer

People were eligible to participate if they:

1. were aged 18 years or older; and
2. were employed as a health care provider who spent at least 10% of their work time providing care to people affected by cancer.

There were no exclusion criteria.

A website developer was engaged to develop the website ready for Usability testing.

Stage 2: Usability testing

Participant group 3: People affected by cancer

People were eligible to participate if they:

1. were aged 18 years or older;
2. had been diagnosed with any type of cancer regardless of stage or prognosis, and at any stage on the cancer continuum (e.g., during treatment, survivorship) OR were a friend or family member providing informal support to a person diagnosed with cancer;
3. had sufficient English language ability to provide informed consent; and
4. were well enough, and available to participate in an in-person usability testing session; and

The only exclusion criterion was if the person affected by cancer had participated in Stage 1

(codesign).

6.5.3 Recruitment and consent

The target sample size for Stage 1 (codesign) was a total of at least 12 participants. Qualitative codesign sampling should be based on meeting two main purposes, to ensure adequate representation and meaningful participation of relevant stakeholders (i.e., in this case, people affected by cancer and healthcare providers) and to increase to the likelihood that the product developed will be scalable to a broader population (255). Despite a lack of consensus regarding specific sample size targets, 10-12 participants has been recommended as appropriate for participatory methodologies in co-creation of health interventions, but the focus should be on achieving the abovementioned purposes of sampling (255).

Potential participants for Stages 1 and 2 (all three participant groups) were identified through the existing networks of researchers. Sampling was non-random and purposive in an attempt to achieve diversity in cancer types and sex of people affected by cancer (Stages 1 and 2), and health care provider group (i.e., type of profession). People who had participated in Stage 1 were not approached to participate in Stage 2. This was to facilitate a broader range of feedback regarding the website, which is key tenet of the person-based approach to intervention development (129). An introductory email was sent to eligible participants to provide a brief description of the study as well as a link to a participant information sheet and online consent. Potential participants were encouraged to discuss participation with trusted family or friends and could take as long as required to decide about participating. They were also informed that they could decline to participate or withdraw consent at any time without any adverse consequences. Those who provided informed consent were contacted to schedule an individual interview or participation in a focus group (Stage 1, with stage 2 scheduled subsequent to stage 1 participation), or usability session (Stage 3).

6.5.4 Study procedures

Figure 9 provides an illustrative summary of study flow of co-design rounds and usability testing aspects of the study, with further details provided in the sub-sections below.

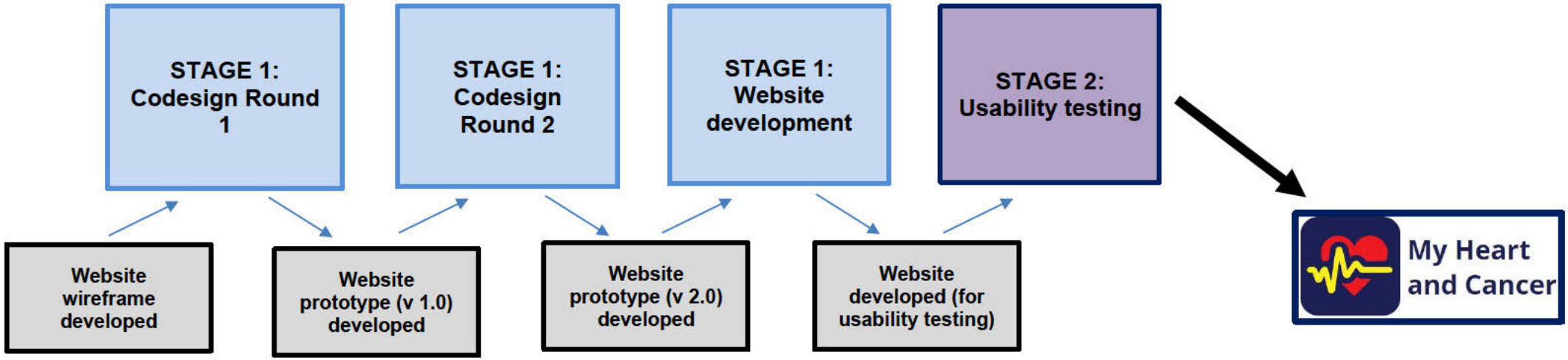


Figure 3 - Summary of study flow

6.5.4.1 Stage 1: Codesign

The codesign stage involved two rounds of codesign sessions, conducted as either focus groups or individual interviews, either online or in-person and facilitated by the PhD candidate. For focus groups, participant groups were separated from one another (i.e., people affected by cancer were not involved in the same session as healthcare professionals).

Developing a wireframe for Codesign Round 1

The PhD candidate developed a basic wireframe which was reviewed by supervisors, then incorporated into a PowerPoint file, to facilitate participant discussion regarding preferences for the structure, format and content of the web-based resource. Figure 10 (A-J) shows the pages of the wireframe. The structure of the web-based resource was informed by existing literature, including our group's qualitative research examining people affected by cancer and healthcare professionals' awareness of CVD risk in cancer, current practice in addressing CVD risk, and preferences for how to reduce the impact of CVD in cancer. Based on this literature, we determined the web-based resource should consist of six main sections: 1) provision of information about CVD and cancer, 2) assessment of CVD risk, 3) signs and symptoms of CVD, 4) self-management of CVD risk, 5) healthcare professionals' role in CVD risk management, and 6) accessing services and resources for CVD risk information and support. Other than these suggested sections, all other aspects, format and specific content of the web-based resource was not pre-determined, as the wireframe was developed to prompt codesign participants to contribute their ideas and preferences.

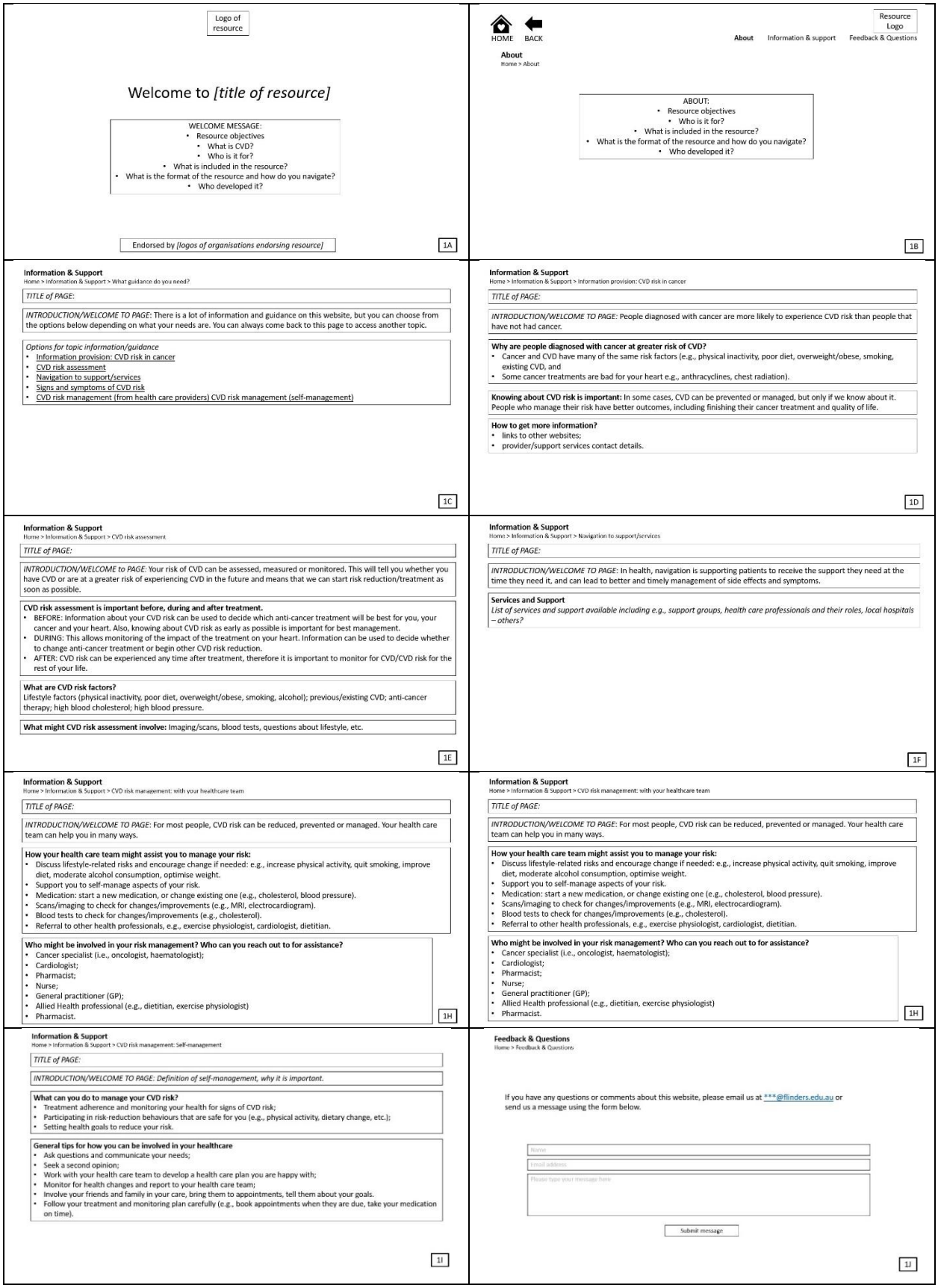


Figure 4 (A-J) - Wireframe of web-based resource to reduce the impact of cardiovascular disease in cancer for Codesign Round 1

Codesign Round 1

All Codesign Round 1 sessions were facilitated by the PhD candidate. Sessions were focus groups of 3 or 4 participants, or individual interviews. Sessions were conducted face-to-face or online according to participants' preferences. Only participants of the same type (i.e., either persons affected by cancer or healthcare professionals) participated in the same session.

As for the entire research program, all study procedures were informed by the principles of person-based approach to intervention development (PBAID) (129). As per the qualitative studies reported in chapters 4 and 5, all focus groups and interviews were conducted so as to ensure rapport, trust, comfortand respect were built. Participants felt comfortable and confident to contribute which led to the collection of rich and meaningful data. Each session began with the facilitator describing the purpose of the web-based resource and how previous research justified the need for this research to ensure participants understood the research objectives and would put individuals at ease about what would be discussed(228).The participants were also encouraged to speak at any time throughout the sessions, about specific aspects of the wireframe as well as to contribute general comments, ideas and preferences about the resource more broadly. In focus groups, people who had contributed less to the session were prompted to answer specific questions to ensure their perspectives were represented. A topic guide (see Appendix 6) was used, along with the wireframe and prompts (Appendix 7).

In particular, participants were encouraged to discuss/indicate their preferences for:

- Website structure (i.e., whether the main sections of the website meet the needs of intended users);
- Website navigation (i.e., participants' ideas and preferences for how users should be able to navigate from page to page within the website);
- Content (i.e., what information should be included on the website); and
- Preferences for how to increase user engagement and interaction with the website (e.g., videos, pictures and activities).

Each slide of the PowerPoint wireframe represented one 'page' of the web-based resource. The facilitator displayed each section of the wireframe (i.e., PowerPoint slide) sequentially, on a large monitor for face-to-face sessions or on the screen for online sessions. All participants had the opportunity to provide feedback (or not) about any part of the wireframe, and to contribute general comments and feedback about the overall resource at the end of the session. To facilitate discussion in the codesign sessions, multiple questions were incorporated to appear one-by-one in each page of the PowerPoint presentation to encourage participants to discuss their preferences for each of these aspects of the page. Figure 11 illustrates an example of this procedure, providing a wireframe of the landing page of the website. The questions shown in this figure were developed

to elicit participant discussion, feedback and preferences regarding the title of the website, the logo, whether the website should include endorsements by relevant organisations, what information should be included and general information about the presentation and format of the page.

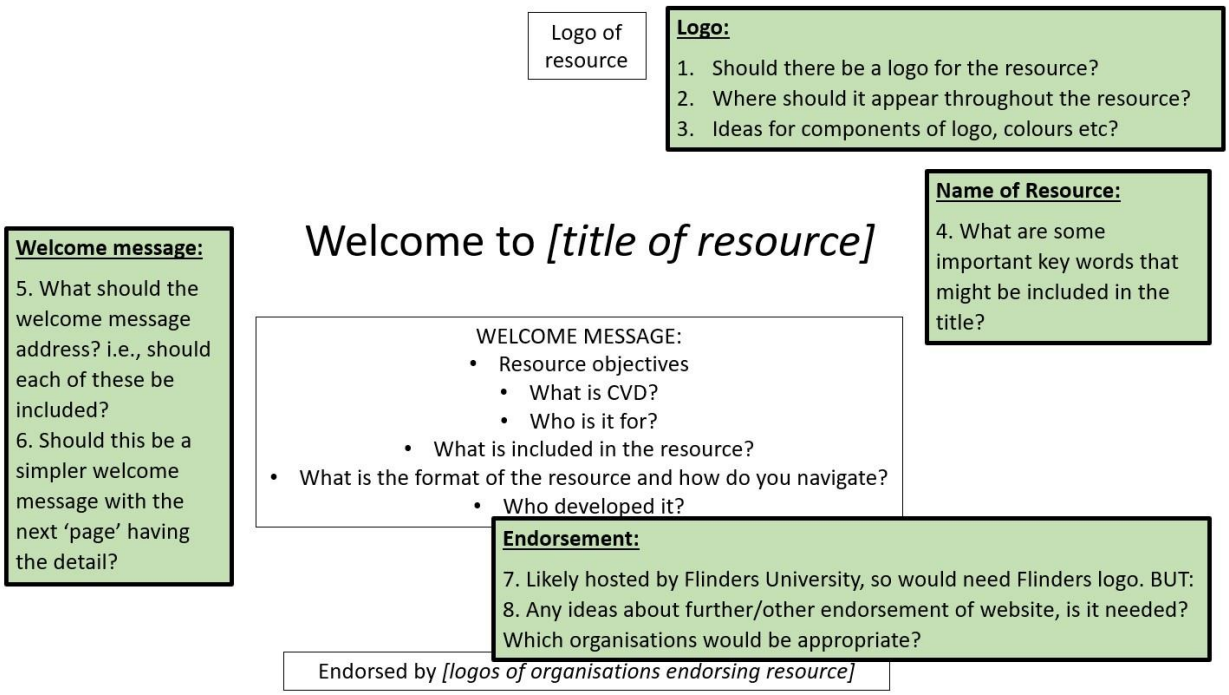


Figure 5 - Example of wireframe with questions to prompt participant discussion and feedback

All sessions were audio-recorded, and the facilitator took written notes throughout. The perspectives of the participants in Round 1 were discussed by researchers in a series of face-to-face and email discussions to identify how preferences for website structure, navigation, content and user engagement enhancement would be represented in the prototype ready for Codesign Round 2. This was an iterative process in which the PhD candidate developed aspects of the prototype (based on Round 1 data and research literature), which were circulated to the wider research team for feedback. The PhD candidate made revisions based on this feedback. Where there were differences in opinions between researchers, consensus was reached through discussion. This process continued until an initial prototype (prototype version 1.0, named “My Heart & Cancer” was finalised ready for Codesign Round 2. The prototype was developed using Qualtrics, a software program used to develop surveys and websites. Developing the prototype using Qualtrics was appropriate to ensure that in the Codesign Round 2 participants were exposed to a website format and could provide informed feedback about content, navigation and formatting.

Codesign Round 2

All Codesign Round 2 sessions were conducted as individual interviews (face-to-face or online), by the same researcher (RK). In these sessions, participants were exposed to all sections of the “My Heart & Cancer” Qualtrics prototype on a laptop. Participants were encouraged and prompted to provide feedback about each of the prototype sections with regard to website structure, navigation, content and user engagement and interaction. The researcher prompted participants to express their views about what they liked/disliked about website prototype, and how it may be able to be improved.

All sessions were audio-recorded, and the facilitator took written notes throughout. Audio-recordings were transcribed verbatim, and data was analysed using qualitative descriptive analysis (QDA). QDA was determined to be an appropriate choice to analyse data collected via codesign and usability testing for this study because it is a simple, straightforward approach which allows understanding and summarising of participants’ experiences and perspectives. The findings remain closely aligned with the contributions of the participants and these can be applied easily in the iterative development and refinement of the web-based resource (256). Using NVivo computer software program, similar sentences and concepts were grouped into ‘codes’ which were labelled to describe the data contained (e.g., content is written at an understandable level, more pictures needed on website, use dot points (to reduce text) etc.). Next, codes were grouped into broader ‘topics’ and ‘sub-topics’ addressing similar aspects/components of the website.

Through a series of emails and meetings, researchers discussed the findings of the analysis to determine how they would inform revisions to the resource. The content of the prototype was transferred into a Microsoft Word document, with comments describing preferences for website

navigation and other operations (e.g., how user activities should work, how users can use 'buttons' to access more information). A Microsoft Word document was the preferred format of the website developer. The researcher that conducted the interviews developed the Word version of the prototype and circulated to the other researchers for feedback, with multiple iterations of this process occurring until all researchers were satisfied with the Microsoft Word prototype (prototype version 2.0).

Website development

The researchers engaged the services of an external website developer who used the Microsoft Word prototype developed in Round 2 to create the 'My Heart and Cancer' website. The researchers and website developer participated in a series of discussions via telephone/email throughout which the website evolved to its final version ready for usability testing.

6.5.4.2 Stage 2: Usability testing and website finalisation

All individual usability sessions were conducted in-person by the PhD candidate, using the 'Think Aloud' approach. In 'Think Aloud' procedures, whilst participants engage in the intervention being tested, they are prompted to verbalise their thoughts and attitudes about all aspects of the intervention (254). The specific 'Think Aloud' procedure we implemented was based on the procedure reported by Beatty and colleagues (257) in assessing the usability of the Finding My Way-Advanced a web-based self-guided psychosocial program for women with metastatic breast cancer, and Wu and colleagues' (258) testing of a smartphone application targeting smoking cessation in pregnant women. First, the researcher provided a brief overview of how and why the 'My Heart and Cancer" web-based resource was developed and explained the 'Think Aloud' procedure with an example of how the participant might verbalise their perspectives of any aspect of the resource, whether these be positive or negative comments. Throughout the usability sessions, the researcher occasionally provided explanations or descriptions if clarification was needed. If required, the researcher prompted the participant to continue to voice their perspectives, e.g., 'What do you think about this section?".

All sessions were audio-recorded, and the PhD researcher took notes throughout. Audio-recordings were transcribed verbatim. Data was analysed by the PhD Candidate using qualitative descriptive analysis, as per Round 2 codesign. However, in contrast to the Round 2 Codesign data analysis approach, after descriptive analysis we conducted an additional quantitative analysis to calculate the frequency of references within each topic (as per Beatty and colleagues (257)). This involved counting the number of participants that provided feedback relevant to each topic, and the number of references per topic. These quantitative findings provide additional insight into the frequency and thus the potential significance of the issues raised, aiding decisions about whether/how these issues should inform changes to the website. Specifically, counting codes, themes, and the number of participants contributing to each theme provides an overview of the

findings and illustrates how frequently ideas emerged which supports transparency and helps readers understand whether a theme was raised by one or multiple participants, while ensuring that rich narrative data remains central to addressing the research objectives (259). Qualitative and quantitative data emerging from the usability sessions informed the refinement of the “My Heart and Cancer” web-based resource. Where decisions for website changes based on findings were simple and clearcut (e.g., fixing typographic errors, specific changes where multiple participants have expressed the same preference for change), the PhD Candidate facilitated the website change with the help of the website developer as required. For complex findings (e.g., when participants’ perspectives were varied or contradictory), the PhD Candidate made recommendations for how findings should inform website revision, and the research team engaged in email and face-to-face discussions until consensus was reached. All website changes were facilitated by the PhD candidate with the assistance of the website developer where required.

6.6 Results

6.6.1 Stage 1: Codesign and website development

Codesign Round 1

Between November and December 2023 16 individuals (seven patient advocates and nine healthcare providers) participated in Codesign Round 1. Participant demographics are summarized in Table 8. Of the 12 sessions conducted, two were focus groups (one with 4 patient advocates and one with 2 patient advocates) and 10 were individual interviews. All participants only participated in one Round 1 session. One focus group was conducted online, and the other was face-to-face. Seven individual interviews were conducted online (1 patient advocate, 6 healthcare providers) and three were conducted face-to-face. One focus group lasted 53 minutes, 45 seconds, whereas the other lasted 69 minutes, 31 seconds. Interviews lasted between 25 minutes, 53 seconds and 75 minutes, 52 seconds.

Table 8 - Participant demographics

Demographics	Codesign		Usability testing (n = 5)
	Round 1 (n = 16)	Round 2 (n = 11)	
Sex			
Male	5	4	2
Female	11	7	3
Participant type			
Patient advocate	7	5	5
Healthcare provider	9	6	
Cancer type (patient advocate only)			
Breast	3	2	1
Head & neck	1	0	1
Lymphoma	0	0	1
Prostate	1	1	0
Carer	1	1	1
Unknown	1	1	1
Profession (healthcare provider only)			
Nursing professional	3	1	
Cardiologist	1	0	
Dietitian	1	1	
Exercise physiologist	1	1	
General practitioner	1	1	
Medical oncologist	1	1	
Physiotherapist	1	1	

Feedback was provided throughout the Codesign Round 1 session as participants responded to question prompts presented with each of the 12 'pages' of the wireframe (see Figures 10 and 11). Participants expressed a wide range of perspectives, including what they liked and didn't like about the content presented in the wireframe, and their preferences and ideas for future iterations of the resource. Codesign Round 1 feedback was broad in nature to inform the development of a prototype to facilitate more specific feedback. All participants agreed with the six main topics of the website (i.e., information provision, risk assessment, signs and symptoms, self-management, healthcare team management and services), so these remained the main sections when converting the wireframe to Prototype v1.0. In addition, based on participant preferences, eight new separate self-management pages were added: goal setting, talking to healthcare professionals, physical activity, healthy eating, healthy weight, quitting smoking, alcohol consumption, and stress reduction. Participants' emphasis on information being presented as briefly and simply as possible was honoured in Prototype v1.0, with options for users to access more detailed information via links, if desired. Website user engagement was identified as important in Codesign Round 1, and Prototype v1.0 addressed this by including pictures, colour and activities. An example of pages of Prototype v1.0 are shown in Figure 12 [A-F].

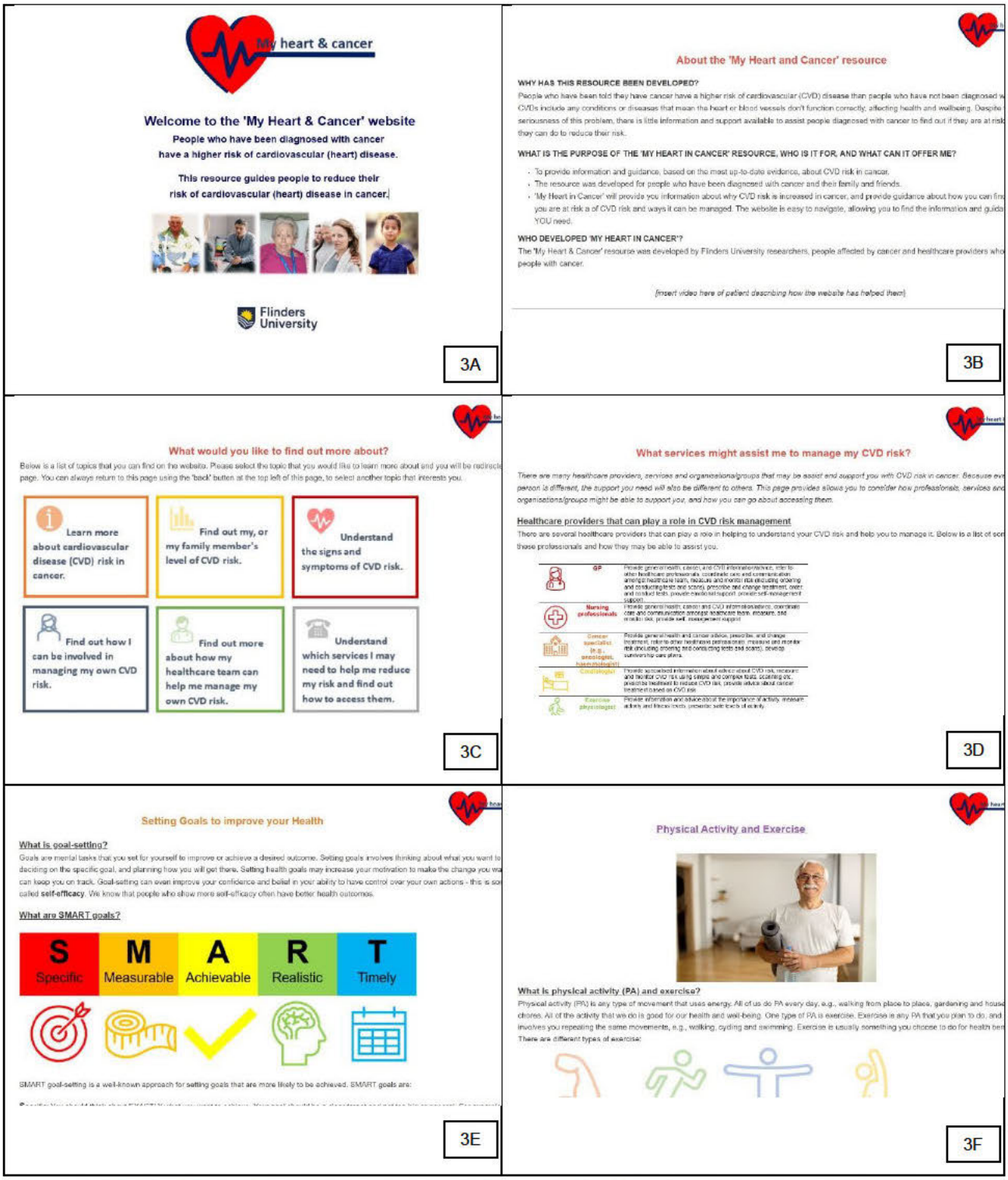


Figure 6 (A-F) - Example frames from prototype of “My Heart and Cancer” informed by Codesign Round 1, presented in Codesign Round 2

Codesign Round 2

Between April and May 2024 11 individuals (5 patient advocates and 6 healthcare providers) participated in Codesign Round 2. All 11 participants had already participated in Codesign Round 1. The five remaining Round 1 participants were unable to participate in Round 2 due to illness (n = 1) or unavailability (n = 5) Participant demographics are summarized in Table 8. One focus group of two patient advocates was conducted (face-to-face), with the remaining nine participants preferring individual interviews (6 face-to-face, 3 online). All participants only participated in one session. The focus group lasted 32 minutes, 51 seconds, and individual interviews lasted between 23 minutes, 27 seconds and 64 minutes and 35 seconds.

Qualitative descriptive data analysis led to identification of 51 codes, with participants' feedback and preferences categorized into five topics (Content, Design and Interactivity, Layout, Navigation, and CVD risk information and support is important for people with cancer) and 15 sub-topics. The topics, sub-topics and examples of quotes are reported in Table 9 and are narratively reported below.

6.6.1.1 Topic 1: Content

Participants provided feedback regarding the content of information included in the 'My Heart and Cancer' website. Most responses were positive, with participants describing specific components of the website as "*excellent"* (risk assessment page), *empowering* (self-management information), and "*handy" (*links to resources and services). However, participants also made suggestions to overcome what they perceived to be missing from the website, e.g., strengthening the message to engage in physical activity (not just exercise).

Some participants expressed that the level of detail throughout the website was "*comprehensive"* and "*understandable",* but others indicated that some sections required changes because they felt *overwhelmed*. For example, some participants were concerned that there was too much detail included in the 'CVD and cancer' information provision page, and one participant argued that the information about scans (to assess CVD risk) was "*too much".* To address concerns about excessive detail and complexity, participants suggested reducing complexity of language, using more pictures, 'hiding' some information in a link/pop-up box, and removing some information altogether (e.g., detailed information about scans).

6.6.1.2 Topic 2: Design and Interactivity

Participants liked the use of icons, pictures and videos throughout the website, describing pictures as *"cute"*, and videos (especially those including patients) as a "*really powerful"* way of engaging users. Two participants suggested more pictures and graphics should be included throughout. Activities were described as *"fantastic"* (activity to facilitate goal setting), and a "*good idea"* (list of risk factors that patients can select to assess overall risk), but there were also several suggestions

for how activities could be further improved. For example, one healthcare professional suggested adding information to ensure the goal setting activity emphasizes that users should choose goals based on the problems they perceive to be most important to them.

One participant commented the next iteration of the website should be "*fancier"* and another expressed there was a "*disconnect"* with the title using the term 'heart' because this term doesn't include stroke and blood vessel conditions.

6.6.1.3 Topic 3: Layout

The layout of the website pages was discussed, with some respondents emphasizing the importance of including the *most important* information at the top of each page. The inclusion of 'Takeaway points' at the top of pages was suggested to provide users with a summary of what they can expect to find on the page. Participants also suggested the layout could be improved by arranging text as dot points rather than in paragraphs, and by integrating pictures and videos throughout sections of text. Respondents also commented that the list links to resources and services needed to be better "*organised"* (e.g., under sub-headings or in 'boxes') and that activities should be situated at the top of each page.

6.6.1.4 Topic 4: Navigation

Preferences for navigation throughout the website were discussed. Suggestions included that there should be a 'Scroll down for more' button on each page so users know there is more content and that the contents of each page should be listed at the top with the capability to 'skip' down according to the user's interest. Links to external credible websites throughout the 'My Heart and Cancer' website were determined to be "*really important"* and "*handy"*.

6.6.1.5 Topic 5: CVD risk information and support is important for people with cancer

Participants discussed the importance of providing CVD risk information and support to people with cancer, perceiving many people may not "*fully understand"* they are at higher risk. For example, communicating CVD mortality risk was described as "*quite powerful"*, and guidance for those experiencing distress was described as "*really important"*. In addition, establishing and promoting the credibility of the website was identified as important as there can be a lot of *noise* on the Internet, and it can be confusing to know what is "*legitimate"* and "*reliable"*.

The findings of Codesign Round 2, informed the development of a Microsoft Word prototype of the content and format of the website, with comments describing requirements for navigation and website operations (such as activities etc.). A summary of the types of revisions made is shown in Figure 13. Examples of pages of the Word prototype are presented in Figure 14. The Word prototype was checked for content accuracy by a Medical Oncologist and a Cardiologist.

Table 9 - Codesign Round 2 topics, sub-topics and quotes

Topic	Sub-topics	Quotes
Content	There is information missing	[It is important to highlight to users that] *"it's normal to feel how you're feeling and it's not a mental health concern. It's situational normalcy. It's hard to write that because then you don't wanna minimise it. But very much, that's what I would say to families."*
	Too much detail	*"Yeah, I think I would probably hide a lot of the anatomy and physiology stuff maybe behind the link so that when people are looking at it that it's not, it's not quite as technical."*
	Good level of detail/understandable	*"It's really good. I think it's written in a way is understandable even for probably, you know, like that high school age child, which I think is good."*
	Typographical and grammatical errors	*"Sometimes you've got a healthcare as one word, and sometimes you've got it as two. And I think in this paragraph alone, you've said healthcare team 9 times."*
Design & Interactivity	Like pictures and videos	*"Yeah. I love this…I love the pictures."*
	Need more pictures and videos	[Patient videos on another website were a] *"really powerful message that you know, as a patient, I could really identify with. So, I think you know of a patient talking about this is really would really sort of appeal."*
	Like activities	*"You get an idea* [about your level of risk from the risk factors activity]. *Because I feel like you don't think about it unless someone asks you which I like. I like that idea."*
	Improve overall design	*"I think we can make it fancy."*
Layout	Change order of information/pages	*"So, do you even put alcohol earlier than the smoking* [on drop-down list of lifestyle behaviours for self-management]? *Because yeah, people drink alcohol and smoke these days, only like 13 percent or something smoke."*
	Needs dot points	*"But I do like dot points…the dot point is a really good way to make things less complex."*
	Insert pictures/videos to 'break up' text	*"Yeah, the ones* [sections] *with a lot of dense text, I think break it up a little bit with some graphics."*
	Need to add summary/takeaway points	"[Could include] *a condensed version of [the page] like when you look at your textbook, whenever you start a new chapter, yeah, there's always a little blurb. Yeah. And The thing is, sometimes I have read that blurb and I'm being like, yeah, there's nothing to do with what I wanna do."*
Navigation	-	*"Like you go to the page that you want to go to and there's like a little navigation thing at the top of that page saying like, click here…*[based on] *what do you want to know?"*
CVD risk information and support is important	Importance of website	*"I think maybe cancer survivors themselves don't fully understand* [about their CVD risk]*, they could easily think I'm I'm the same* [level of CVD risk] *as everyone else, but they do need to understand that it is higher without frightening them."*

for people with cancer	Credibility	*"It could be very difficult to work out what's actually legitimate and reliable and what's not, so that is really important* [to include the information that Flinders researchers developed the resource]*."*

Content	Design and Interactivity
• Small additions made to website content, e.g., highlight physical activity in addition to exercise, emphasise importance of prevention, clarify risk management before, during and after cancer treatment. • Content simplified and detail reduced throughout the website by removing sections, reducing language complexity, and replacing text with pictures for easier understanding.	• More pictures and videos were incorporated into the website wherever possible, and resolution of pictures was improved where needed. • An extra four videos were filmed, including one featuring a patient. • Activities: • Goal setting activity: added explicit step-by-step guidance of how to develop SMART goals based on individual priorities; • Questions for healthcare team activity: reduced the number of questions and allowed for order to be modifiable according to user's priorities; and • Risk factor assessment activity: calculates and reports total number of risk factors a user selects as affecting them. • Colour scheme, headings, logo and infographics were modified and made consistent throughout to improve overall design.
Layout	**Navigation**
• Reorganised order of information on pages according to priority/importance. • 'Takeaway points' added to the top of each page. • Text organized into dot points where appropriate. • Text, pictures and videos were better integrated. • Links to external resources, support and services presented in separate boxes for easier engagement.	• Floating 'scroll down for more' button added to each page. • Content of each page listed as introduction with user able to 'skip' to that topic according to their priority. • Drop-down boxes on toolbar allow navigation from any to another throughout website (in addition to separate navigation page).

Figure 7 - Types of revisions made to 'My Heart and Cancer' based on Round 2 Codesign

Learning about CVD and cancer

On this page you can learn: what is CVD and which types most commonly affect people who have been diagnosed with cancer; why it is important to understand CVD risk; and why people who have been diagnosed with cancer have a higher risk of cardiovascular disease (CVD). In addition, you can learn more about the heart and cardiovascular system.

TAKE-AWAY points

- ✓ People diagnosed with cancer are more likely to be at risk of CVD than those who have not been diagnosed with cancer.
- ✓ People with cancer may experience CVD risk because their cancer treatment can damage their heart and blood vessels. Also, cancer and CVD have many similar risk factors including increasing age, physical inactivity, poor diet, smoking etc. Finally, some cancers can cause changes in the body, such as inflammation, that negatively affect cardiovascular health.
- ✓ Understanding CVD risk is important because you and your healthcare team can reduce your risk and prevent/minimise negative outcomes.

What is CVD?

- Cardiovascular disease (CVD) is a term used to describe a range of conditions affecting your cardiovascular system, which includes the heart and the vessels that carry the blood around your body.
- There are certain CVD conditions that are more likely to occur in people who have been diagnosed with cancer.

Click the icons or titles in the image below for more information about each CVD.

Cardiomyopathy/ congestive heart failure (CHF) Cardiomyopathy: heart muscle damage, meaning blood not pumped well. May lead to CHF, where organs don't get enough Oxygen.	**Arrhythmia** Irregular heartbeat.	**Problems with the pericardium (outer membrane of the heart)** Including pericarditis: swelling; and fibrosis: thickening or scarring.
Coronary artery disease When the heart's blood vessels are damaged and/or blocked.	**Myocarditis** Swelling of the heart that can lead to other heart problems including affecting the heartbeat.	**Damage to heart valves** Narrowing, stiffening, or leaking of the heart valves.

Why is understanding your level of CVD risk important?

- It is important that you understand if you have CVD or are at risk because there are often things that you and your healthcare team can do to reduce your risk and improve your health.
- People with CVD can experience many serious negative effects, such as heart attack, stroke, kidney disease and symptoms including shortness of breath, tiredness, and mental health concerns.
- We now know that people who are long-term survivors of cancer are more likely to die of CVD than cancer.

Why do people diagnosed with cancer have a higher risk of CVD?

Cancer treatment

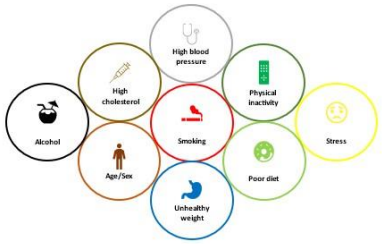
- Some cancer treatments, including chemotherapy and radiotherapy, can damage your heart. These may be referred to as cardiotoxic.
- It is not possible to list all the cardiotoxic cancer treatments because new treatments continue to emerge, as does understanding of cardiotoxicity of existing and new treatments. But, there is some more information here which may provide more information about the cardiotoxicity of certain treatments. You can also talk to your healthcare team.

Cancer can affect your heart directly

- Some cancers may increase CVD risk through changes in the body, such as inflammation.
- The way cancer directly affects the chance of CVD in the body is very complicated, but if you would like to read about this, this journal article discusses the topic.

Shared risk factors

- Cancer and CVD have many of the same risk factors, including physical inactivity, poor diet, overweight/obese, smoking, existing CVD, and excessive alcohol consumption.



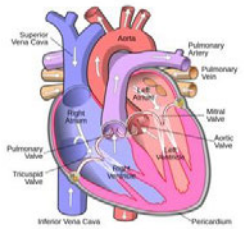
The heart

The heart is:

- the central part (organ) of the cardiovascular system.
- a large muscle that pumps blood around your body.
- is located between your lungs, behind your breastbone, slightly to the left.
- made up of four separate chambers, two at the top (also called atria) and two at the bottom (also called ventricles), and four valves.

Each section and valve of the heart has a separate role in making sure that blood moves where it needs to, for oxygen to be added at the lungs, to deliver oxygen and nutrients to the body, and to bring waste back from the rest of the body to be cleared. An electrical signal causes your heart to pump in stable rhythm so that the blood moves through the cardiovascular system as it is needed.

For an interactive 'tour' of the heart, please click here.



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The cardiovascular system

- The cardiovascular system is made up of the heart, blood, and circulatory system.
- As described above, the heart is a pump that pushes blood from the heart to the lungs and all parts of your body including the organs and the muscles.
- The blood must travel through the lungs to receive oxygen which is needed by all parts of the body.
- The blood also contains nutrients which are needed by all the cells of the body, and collects waste (especially carbon dioxide) and carries it back to the heart where it is directed to the lungs, liver and kidneys for removal from the body.
- The circulatory system is a complex system of blood vessels that carry the blood throughout the body. The vessels that take the blood from the heart to the rest of the body are called arteries, arterioles, and capillaries. The vessels that bring the blood from the rest of the body to the heart are called veins and venules.

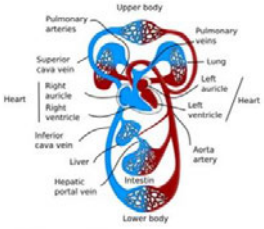

Figure 8 - Example of Microsoft Word prototype informed by Codesign Round 2

Website development

The ‘My Heart and Cancer’ website was developed and refined between May and August 2024. For the purposes of the iterative nature of the development and refinement of the website, and the need for testing before being appropriate for public use, the website is hosted on a private server. However, Figure 15 provides a summary description of each page of the website.

6.6.2 Stage 2: Usability testing and website finalisation

Five people affected by cancer participated in face-to-face, individual usability sessions. Sessions lasted between 21 minutes and 28 seconds and 67 minutes and 10 seconds.

As shown in Figure 16, through descriptive analysis of data, a total of 165 references were categorised into 46 codes, which were mapped to four of the topics identified in Codesign Round 2 (Content, Design and Interactivity, Layout and Navigation). Figure 16 provides an overview of topics and sub-topics with quantitative summary of codes, references and respondents.

6.6.2.1 Topic 1: Content

All participants provided feedback about the content of the website, with a total of 55 references related to this topic. As shown in Figure 16, these references were classified into four sub-topics: Content is appropriate; Language/wording is appropriate; Add/remove content (or detail); and Change wording for clarity/accessibility.

Seven favourable comments were made about three aspects of the website content, including encouraging communication with healthcare team, inclusion of tips on all behaviour-change pages, and links to relevant organizations and services. For example:

> *“…ah, this this is perfect. I love this. Just a whole list of community support groups.”*

In contrast, all five participants expressed preferences for changes to the content (including the level of detail provided) on a total of 12 occasions. Suggested included adding a link to the ‘Patient Charter of Rights’, adding information on vaping throughout ‘Quit smoking’ page, explaining that some CVD risk factors have a greater impact on overall risk than others, removing links to unhelpful resources on the ‘Services’ page, and emphasising that exercise is safe for most people.

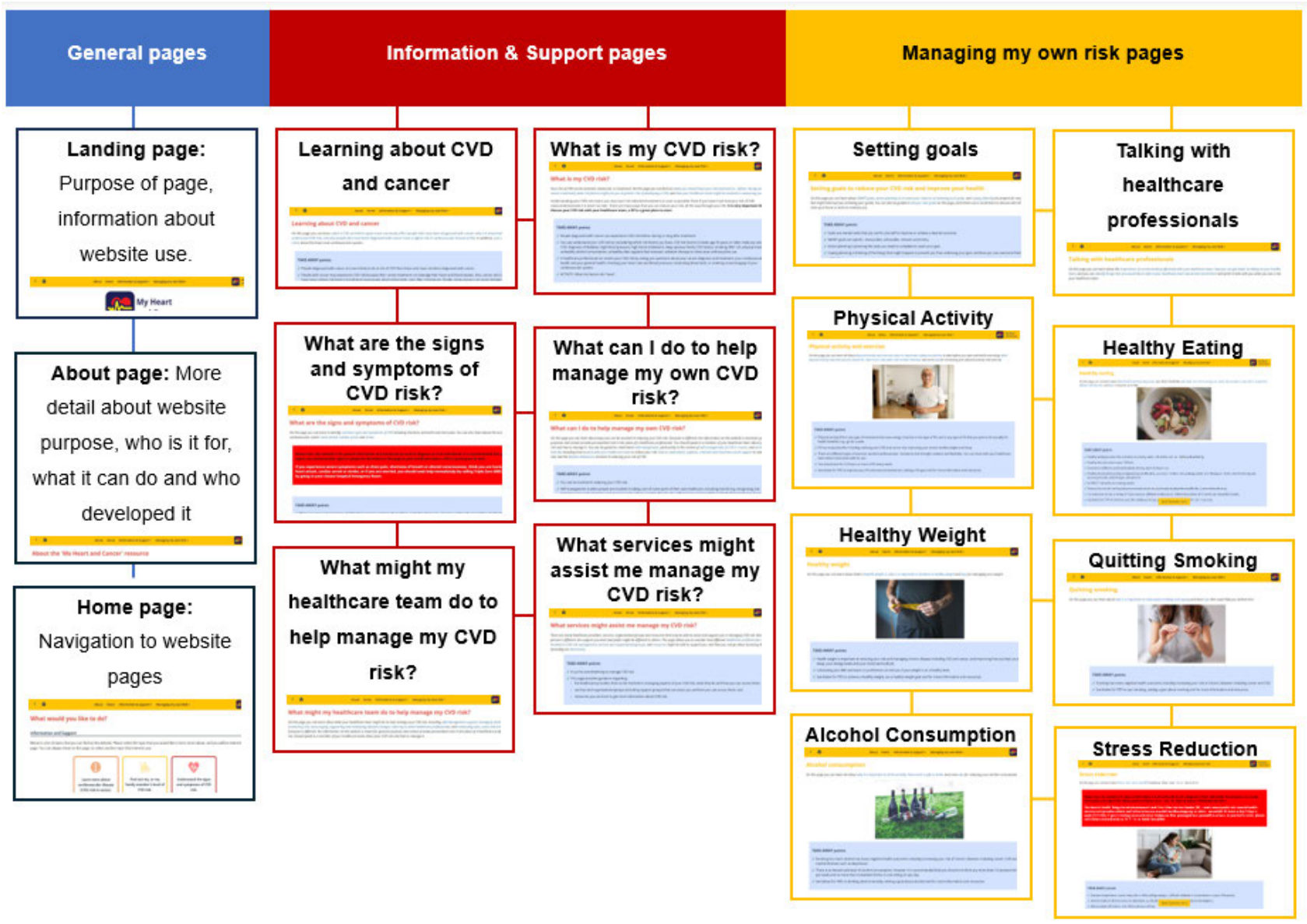

Figure 9 - Overview of website

> *"*[I think you should be] *a little bit more positive, as in most people will be safe to do some type of exercise, but see* [a] *healthcare professional"*

The language and level of detail presented throughout the website was commended by all participants a total of 27 times. Language and content were described as *straightforward, empowering* and *solution based*. About one section of the 'CVD risk and cancer' page, one participant stated:

> *"That's good. You know that that's pretty succinct and palatable"*

Another participant praised the directness of the website:

> *"I've got no issue with that* [saying you are more likely to die of CVD than cancer as a long-term survivor]*. I'm a person that's really upfront and I prefer the world to be upfront with me."*

However, another participant was not as complimentary about the website stating CVD mortality risk:

> *"I wouldn't…use the term die. Particularly if these people already have cancer? Yeah, I'd say something like to be impacted by."*

This was one of nine suggestions made by participants for how the website content could be improved. Other preferences included: reducing the detail and complexity of the goal-setting page, simplifying the concept of self-management, ensure dietary advice is not judgmental, inclusion of information in another language, and removing links requiring a high level of understanding of health and healthcare:

> *"I wish people would read healthcare, but they're not going to comprehend it. I'd get rid of it* [link to journal article]*."*

6.6.2.2 Topic 2: Design and Interactivity

All participants provided feedback about the design and interactivity of the website, with a total of 51 references related to this topic. As shown in Figure 16, these references were classified into two sub-topics: Engagement enhancers are favourable (design, activities, pictures, videos); and Improve engagement enhancers.

All participants made favourable comments (29 references) about the tools used to enhance the engagement of the website (i.e., design, activities, pictures and videos). Twelve of these comments (4 participants) referred to the design or style of the website, indicating appreciation of the *colours, fonts, presentation* and *consistency* of design throughout. For example:

"The setup's the same. Yeah, nice. So, it's consistent and easy to find things."

Two participants made some suggestions (5 references) for changes related to design, particularly related to ensuring text and background colours allowed for ease of reading. For example:

"Instead [of red boxes and red text] *have like the exclamation point in the exclamation sign in the triangle* [for important information]*, because I think most people will see that and go warning and then they'll go that's something* [important]*."*

Four participants (7 references) noted that they liked the activities included within the website, including the risk factor activity (users select which risk factors apply to them from a list), the talking to healthcare professionals activity/aid (users can type in questions about their health and care to aid communication with their healthcare team), and the goal-setting activity (users are guided through setting their own goals for health and care). Participants liked that they could print out the information they have added as part of engaging in the activities.

"OK, this [goal-setting activity] *is good… Ohh like it…So they can type things in here and then can they print it off or what?"*

There were also suggestions for how to improve the activities. Two participants discussed how the identification of risk factors in the risk factor activity could be used to further individualise the experience of users, where users who select a particular risk factor are automatically directed to advice/support for managing that risk factor, to setting a related goal via the goal setting activity, or adding a related question in the talking to healthcare professionals activity. One participant queried the purpose and appropriateness of the activity to calculate energy requirements:

"So, calculating your energy requirements. It's a hard one, isn't it? In terms of do we do you get them to calculate that? I'm just wondering what will they do with that? What do we want them to do with that information? So yeah, are we then expecting them to count their calories, for example?... So, if you're focusing more on healthy eating, should it be more…content is more around getting food groups and eating. Yeah, food groups and diet?"

Ten positive comments were made about the use of pictures and videos throughout the website including:

"[Including a video] *helps as well for people that aren't good at reading information, they take it better by seeing it."*

Minor changes were suggested to improve the use of pictures, with one participant encouraging some resizing of pictures:

> *"I'd make those images* [on physical activity page] *just a bit smaller. Yeah, honestly, they're just taking up space. Like they're not telling me anything, but it's nice to have some visual stimulus."*

Similarly, preferences for changes to the video were minor, including adding a 'cover' for each video with the title and a 'play' button, and discussion around the best location on the page for the videos (participants had conflicting preferences for placement at the top of page vs bottom):

> *"I probably have* [video] *at the bottom, to be honest. Just I think logically about other websites, a lot of the time the video is* [at] *the bottom because it's not an introduction."*

> *"I think definitely what you say in that video needs to go up front…I've already read through the chunk at the website. So, I think that needs to go up front."*

6.6.2.3 Topic 3: Layout

All participants provided feedback about the layout of the website, with a total of 20 references related to this topic. As shown in Figure 16, these references were classified into three sub-topics: Layout is favourable; Improve individual 'page' layout; and Layout improvements throughout website.

Three participants made a total of six favourable comments about the layout of the website. One participant indicated the *quite liked* the layout because it was *not overwhelming*. Five comments praised the inclusion of takeaway points at the top of pages to provide a summary of what can be found on the page. For example:

> *"I think the takeaway points* [are] *really good because people will go…ohh this interests me. I'll keep on reading."*

All participants contributed their preferences for how the layout of the website could be improved (14 references). These included discussions about the order in which information should be presented on the page, where participants had varying, often conflicting preferences. For example, for the CVD and cancer information provision page, one participant felt information about the heart and the cardiovascular system anatomy and function could be left out or hidden behind a button to be selected only if the user wanted to find out, whilst another wanted this information to be more prominent on the page.

> *"But I think yeah, just having that stand out a bit more, yeah, because again body of text, it's at the bottom, people go halfway and go, oh, cool…. And then they're gonna have* [to go] *back to the top."*

6.6.2.4 Topic 4: Navigation

All participants provided feedback about the navigation of the website, with a total of 39 references related to this topic. As shown in Figure 16, these references were classified into four sub-topics: Navigation within website is favourable; External website links are favourable; Improve navigation within website; and Improve links to external websites.

Participants indicated they liked navigation within the website (8 references), including that users can link to pages within the website from the specific navigation page or the dropdown lists in the toolbar, they can follow the links from one page to another (e.g., from 'Managing my own risk' to health behaviour change pages), and they select hyperlinks at the top of pages to take them straight to the information on the page relevant to their needs:

> *"So, they're* [sections in intro] *hyperlinked then. So, if I hit that…I'd just go straight down the page. Cool."*

Respondents also liked the links to other websites (8 references):

> *"I like that list* [of healthcare professionals and what they do for CVD risk]. *And yeah, the information…then about what they…*[do]. *And then you can link to find* [for example] *GP."*

Participant advice for improvements to navigation included making the title on each page consistent with the titles on dropdown and navigation lists; ensuring the names of the About page, Home page and Navigation page are more intuitive to users; and changing the structure of the introductory information (currently presented as a sentence presenting all sections of the page that are hyperlinked), to asking the user what they want to learn about with options as dot points:

> *"Somehow phrase it…I'm interested in how it works? Or…What do I really want to know? And then they can just link [to] it that way."*

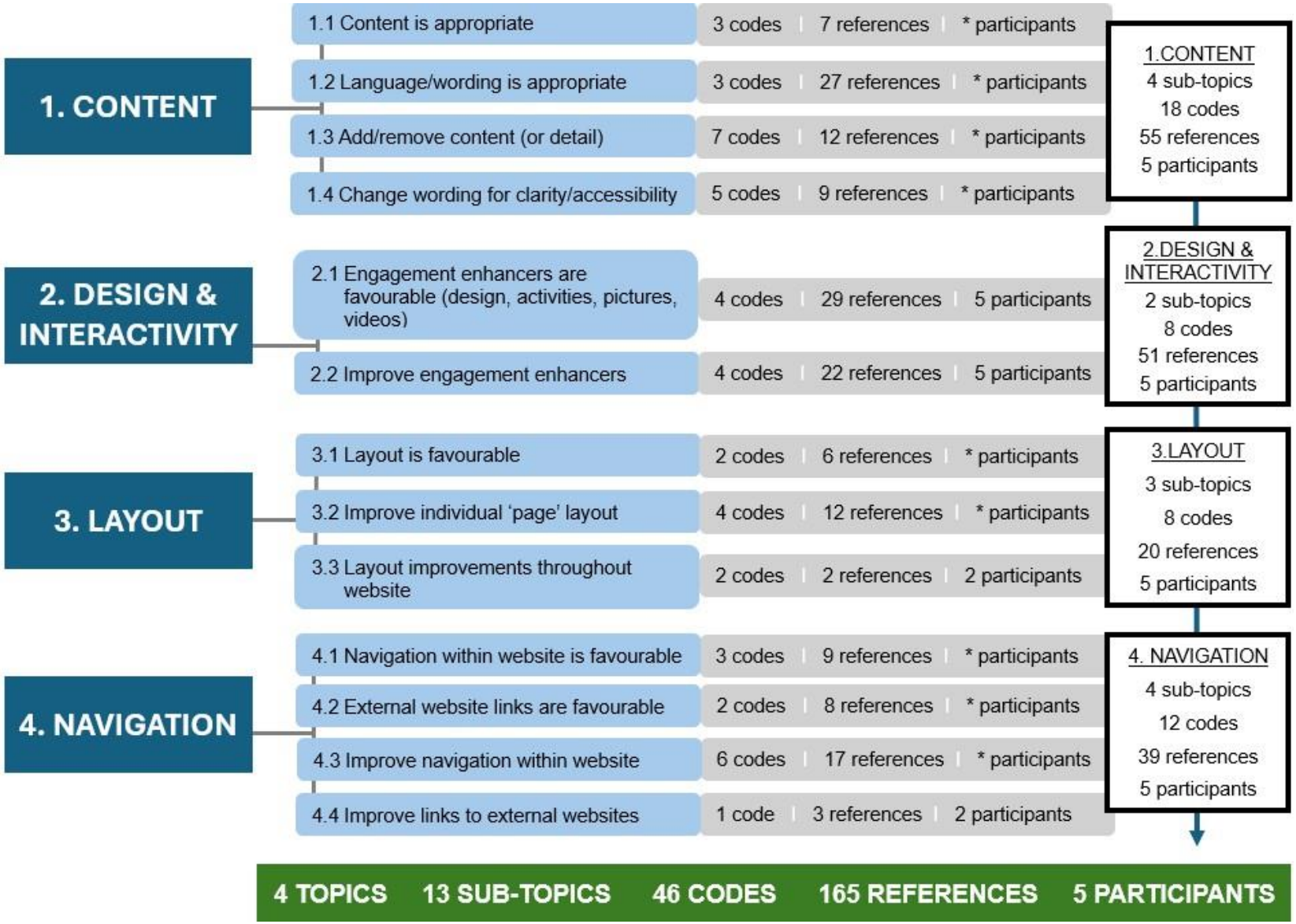

Figure 10 - Overview of topics, sub-topics, codes, references and respondents from usability testing

Based on participant feedback and discussion amongst the research team, 30 revisions were identified and applied to refine the website (shown in Figure 17). Five examples of pages in the final website are shown in Figures 18-22.

Content

1. *Add link to Australian Charter of Healthcare Rights (Australian Commission on Safety and Quality in Health Care) to 'Talking with healthcare professionals' page.*
2. *Add vaping to the title and throughout 'Quit smoking' page where relevant.*
3. *Add statement to all website 'pages' providing guidance regarding seeking help for distress.*
4. *Clarify that not all CVD risk factors have an equal impact on overall CVD risk.*
5. *Advise the 'My Heart and Cancer' is a credible website, and that users should beware the credibility of other sources.*
6. *Emphasise exercise is safe for most people.*
7. *Remove links to resources providing information regarding CVD risk in cancer that do not provide adequate guidance for users.*
8. *Use more empowering language around dietary and weight.*
9. *Reduce text around definition of self-management, focus on what CVD risk self-management looks like.*
10. *Reduce detail/complexity of goal-setting information.*
11. *Remove links to complex sources, i.e., academic paper about the understanding how cancer impacts the cardiovascular system, and Nutrient Reference Values.*

Design and Interactivity

12. *Add plain coloured cover to all videos with title, description of content and 'play' button.*
13. *Relocate all videos to the bottom of 'page', with link to the video at the top of page.*
14. *Resize pictures throughout website as needed for ease of reading.*
15. *Clarify the purpose of energy requirement calculation activity, i.e., to provide personal context to information/guidance about energy balance.*
16. *Fix print function where required.*
17. *Change colour-scheme (text and background) to ensure adequate contrast for ease of reading.*

Layout

18. *Ensure all links are blue text, underlined.*
19. *Separate information/guidance for users aiming to gain weight vs lose weight.*
20. *Hide 'The Heart' and 'The Cardiovascular system' information behind a 'tile' that can be clicked for users wanting more information.*
21. *Reduce text throughout (e.g., replace with diagrams/pictures) where possible.*

Navigation

22. *Change title of 'Home' page on toolbar to 'What would you like to do'.*
23. *Clarify instructions regarding navigating via 'What would you like to do' page, and dropdown options and ensure consistency between titles of pages, dropdown options and 'What would you like to do' page options.*
24. *Add floating 'back-to-top' button so users can navigate back to top of page, at all times.*
25. *Ensure consistency in how users navigate to external websites (EITHER via icon/picture or by blue, underlined text)*
26. *Change structure of introduction on each 'page' to facilitate users easily navigating to section of page they are interested in.*
27. *Fix 'broken' links throughout website and ensure external websites appear in new browser.*

Figure 11 - Revisions to 'My Heart and Cancer' informed by findings of Usability testing

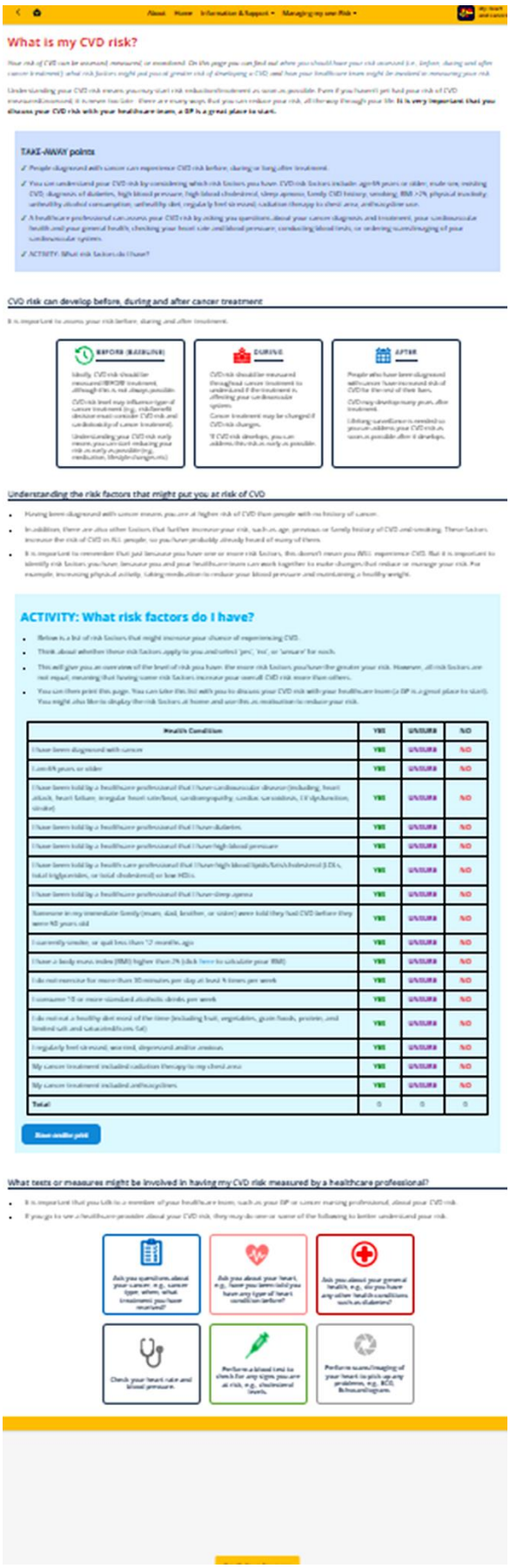

Figure 18 – Screenshot of example page of the final ‘My Heart and Cancer’ website (What is my CVD risk?)

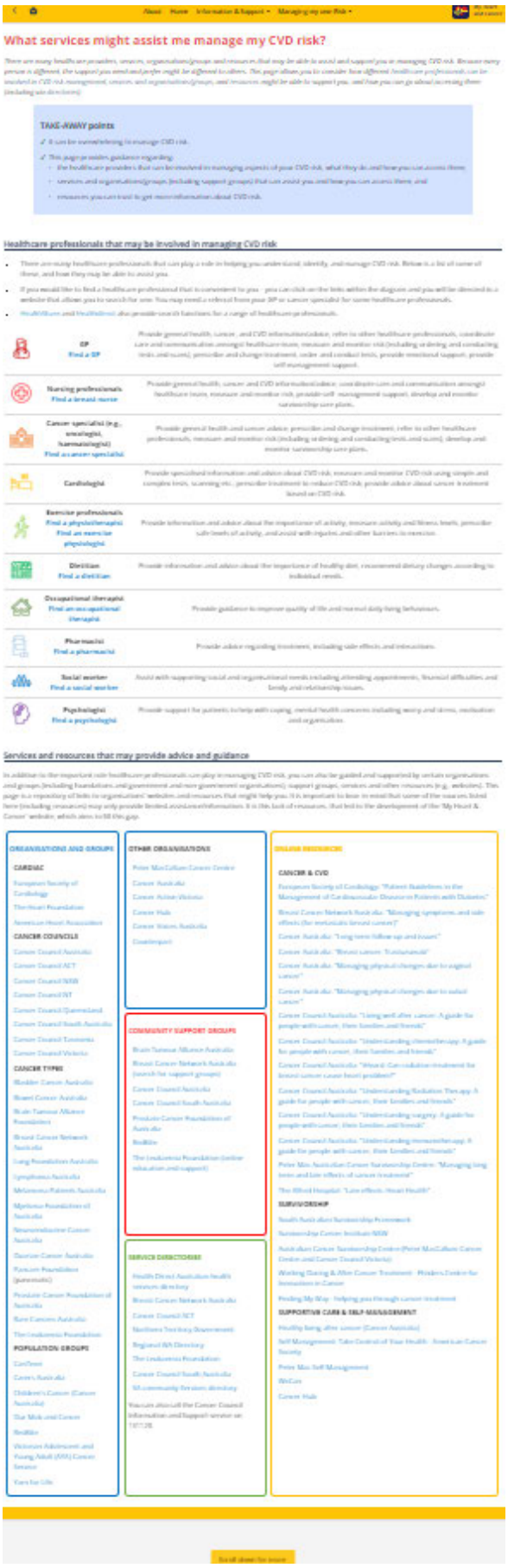

Figure 19 – Screenshot of example page of the final ‘My Heart and Cancer’ website (What services might assist manage my CVD risk?)

Figure 20 – Screenshot of example page of the final ‘My Heart and Cancer’ website (Talking with healthcare professionals)

Figure 21 – Screenshot of example page of the final ‘My Heart and Cancer’ website (Stress reduction)

Figure 22 – Screenshot of example page of the final ‘My Heart and Cancer’ website (Goal setting)

6.7 Discussion

'My Heart and Cancer' is the first patient-facing website developed to solely target CVD risk assessment and management in cancer. Key recommendations from participants throughout codesign and usability testing related to the amount, level of detail and presentation of information; the importance of using design and interactive activities to engage users; and the need for easy navigation throughout the website and to external credible information and support. Feedback was addressed iteratively until the website was finalised. We simplified, summarised and reduced text wherever possible but provided options (links) for users to access further information/detail if desired. We added pictures and videos and improved the website design and further strengthened activities and practical self-management tips to enhance ease-of-use and interactivity (improved instructions and functionality). To optimise navigation throughout 'My Heart and Cancer', consistency of design, presentation and language was ensured throughout the website. The website is informed by evidence and user preferences and facilitates an experience that can be tailored to individual needs. Hence, 'My Heart and Cancer' is a promising approach to addressing the problem of CVD care in cancer in the ever-increasing population of cancer survivors.

Participants were satisfied with the topics addressed in each section of the website (i.e., general information about cancer and CVD risk, CVD risk assessment, CVD signs and symptoms, self-management, healthcare team management and access to services and resources), with feedback focusing on preferences for amount, level of detail and presentation of information, rather than content. This aligns with the strength of evidence for best practice for the assessment and management of CVD in cancer, particularly the ESC Guidelines on Cardio-oncology (6). Participant satisfaction with the provision of general information about cancer and CVD risk also aligned with our research team's previous findings that many people affected by cancer were unaware, or only somewhat aware of the increased risk of CVD in cancer (239), and cancer care providers' assertions for the importance of education in approaches to improve CVD care (216). In addition, the current study elicited positive feedback regarding the focus of the website on self-management and patient empowerment and activation, which also aligns with previous research (reported in chapters 4 and 5) in which people affected by cancer expressed that being involved in their own care is empowering, and that healthcare professionals experienced many barriers to implementing adequate CVD care alone. Moreover, there is strong evidence that self-management is critical for effective cancer care (260, 261), and activated cancer patients are more satisfied with aspects of their care (e.g., feel their treatment aligns with their values) and better adhere to treatment and cope with treatment side effects (262).

Participants' preferences for aesthetic design features, pictures and text presented as bullet points and interspersed with videos and pictures aligns with previous research (263). This research elicited consistent positive responses for the inclusion of interactive, user-centred functions (e.g.,

activities in which the user sets goals, identifies their own CVD risk factors, and identifies questions for their healthcare team), which aligns with adult learning theory concepts including that learning is most effective when it is directed by the individual, focuses on goals, and builds knowledge (264). Furthermore, the website's capacity to provide an experience tailored to user needs and preferences is supported by previous research examining cancer survivors' perspectives that websites provide an opportunity for individualised support and information provision (261, 265).

The findings of the research reported in this chapter highlight the importance of conducting multiple rounds of codesign and usability testing. For example, some topics were raised multiple times in subsequent rounds, despite changes made in response to feedback. Effectively, this allowed the opportunity to 'check' if changes met the needs of users and further improve the website where needed. In addition, new topics arose across the study, perhaps because participants were unable to identify website issues/concerns until more obvious problems had been addressed.

6.7.1 Strengths and limitations

There were important limitations of this research, with most participants residing in South Australia (n = 10) and all residing in Australia. In addition, given the relatively small sample size, not all cancer types and healthcare professions involved in care provision were able to be represented. In addition, demographic data were not collected from participants. Lack of diversity of demographics and health characteristics potentially limits the transferability of findings and appropriateness of the website in other areas where resources, services, and patient needs and experiences differ. In contrast, the study strengths included the comprehensive methodological approach used to codesign and test usability of the 'My Heart and Cancer' website. In particular, the strong consumer engagement approach (i.e., collaborating with people affected by cancer and healthcare providers to develop and test the website) increases the likelihood that the 'My Heart and Cancer' website will provide effective people-centred care and satisfy user needs (266).

7 CHAPTER SEVEN: SUMMARY, DISCUSSION AND CONCLUSIONS

7.1 Chapter overview

In this chapter, the rationale for how the research program progressed is presented, particularly with regard to how findings of each informed the next. The findings of the research program are then discussed and contextualised within what is already known. Strengths and limitations of the overall research program are presented, and clinical and research implications are discussed. Recommendations for future research are also stated, and the thesis concludes with summarising and concluding remarks.

7.2 Novel contributions of the doctoral research

This research program has led to the development of a comprehensive website to provide information and support to improve self- management of CVD risk in people diagnosed with cancer. We are not aware of a similar resource available elsewhere. This novel approach has been codesigned, using a patient-based approach, by people diagnosed with cancer, cancer care providers and cardio-oncology researchers using a rigorous methodological approach with strong philosophical underpinnings. ‘My Heart and Cancer’ is designed to facilitate patient activation, self-management and lifestyle behaviour optimisation to empower people with cancer to make positive changes to their health leading to better health outcomes. In addition, this research contributes new knowledge regarding consumers’ needs and preferences regarding CVD care in cancer, which can inform improvements in care episodes between patients and their healthcare team. This research program also produced the first summary and synthesis of review-level evidence for the effectiveness of lifestyle interventions in older people with cancer. Finally, the comprehensive methodology used to guide the entire research program serves as an example of a novel approach that could be applied in the development of other interventions. Specifically, critical realism philosophy underpinned all stages of the research program, and the principles of the person-based approach to intervention development (PBAID) and reflexive thematic analysis were followed so as to authentically align with the researcher’s worldview.

The thesis itself provides a unique contribution to the literature in that it provides a detailed account of the comprehensive and rigorous research process, in which existing evidence was summarised and combined with new understandings from cancer care providers and people diagnosed with cancer to iteratively develop a new approach to address the gap of CVD care in cancer. Stakeholders’ feedback was the foundation of all decisions in the establishment of the ‘My Heart and Cancer’ website and the thesis described the exhaustive process through which researchers made decisions to address the needs, overcome the barriers and enact the preferences of stakeholders in the development process.

7.3 Discussion of findings

Study-specific findings have been discussed in chapters 4, 5, 6 and 7, however this section provides high-level discussion about some of the main 'takeaways' based on the integration of findings from the entire research program. Specifically, this section discusses perspectives of cancer care providers and people affected by cancer in the context of existing cardio-oncology literature, and the 'My Heart & Cancer' website – and how its components align with the findings of the literature review (chapter 3), preferences of cancer care providers and people diagnosed with cancer (chapters 4, 5 and 6).

7.3.1 Perspectives of cancer care providers and people affected by cancer regarding cardio-oncology

The key findings of this study were that cancer care providers a) were aware of the topic of CVD care in cancer and considered it an important issue, b) could identify barriers to effective CVD care in cancer including that they felt they could not deliver CVD care alone, and c) had diverse preferences for a future approach to improving CVD care including education and digital tools. The findings of this research program include important contributions to limited existing literature regarding the perspectives and experiences of cancer care providers and people affected by cancer about CVD risk in cancer. Despite the limited existing literature related to CVD risk in cancer, it is important to consider if the findings of the current research align with what is available, and why or why not. In addition, some of the perspectives reported in this research may not be specific to CVD risk and are issues relevant to cancer care more broadly, e.g., staff barriers including lack of time and training. Thus, it is relevant to consider if findings of the current research are similar/different to perspectives reported in research examining other aspects of cancer care, e.g., survivorship care. In this section, the findings of this research are considered in the context of relevant existing literature.

7.3.1.1 Awareness and importance of CVD care in cancer

In this research, all cancer care providers reported being aware of the issue of CVD risk in cancer and perceived it to be important, whereas many people diagnosed with cancer were unaware, or only somewhat aware they were at risk of CVD, but all indicated they thought it was an important issue. In contrast, existing literature regarding cancer care providers' awareness and perceptions of importance have reported mixed results, with qualitative and survey studies finding majority of oncology and cardiology experts were unaware of the incidence of cardiotoxicity (232) and were unconcerned about cardiotoxicity (233), but another survey study reporting over 70% of cardiologists (n=106) felt potential cardiac complications were an important consideration of anti-cancer treatment selection (221). Given the proliferation of evidence and development of the ESC guidelines, it would be expected that cancer care providers' awareness of CVD risk in cancer would be increasing, however it is likely that this varies according to health care service, interest in

cardio-oncology of study participants, and the professions included in each research study. There have been no previous studies to examine patient awareness and perceived importance of the issue of CVD in cancer. However, the findings of the current research, that patients felt the issue was important (despite most not being fully aware of CVD risk), are consistent with the well-established evidence for the importance of provision of health information to patients to improve perceived control, reduced anxiety and better clinical outcomes (244). Contextualising the findings of this study with the existing evidence suggests that despite evidence indicating that the issue of CVD risk in cancer and information provision is important to patients, and some evidence that cancer care providers are aware of risk, there may be limited transfer of information from providers to patients.

7.3.1.2 Barriers to CVD care

This research identified various barriers to the provision of, and engagement in, CVD care in cancer. Cancer care providers felt concerned about their (and their profession's) capabilities and capacity to deliver CVD care alone, reported a lack of time and a lack of training needed to provide effective CVD care; and perceived patient-level barriers may include socioeconomic disadvantage, lack of motivation and having a fatalistic outlook. Interestingly, a previous study involving cancer care providers also reported they perceived socioeconomic disadvantage and a fatalistic outlook as patient-level barrier to engaging in CVD care (232). However, majority of patients did not identify barriers to engaging in CVD care (which could be because many had not previously been aware of CVD risk so had not had an opportunity to consider potential barriers). The only barriers reported by patients were related to financial restrictions to engage in care and being preoccupied with cancer. Greater understanding of patients' perceived barriers to CVD care is needed, but requires engagement from participants with existing awareness of CVD risk; such research would shed light on whether there are barriers specific to CVD care (as compared to well-established barriers to cancer care more broadly, e.g., lack of social support, insurance/financial concerns, and inadequate communication with cancer care providers (267)). Lack of time, lack of training and conflicting role identity are commonly reported perceived barriers to implementing cancer care interventions (237, 268) and relate to under-resourced workforces, inadequate training, and poorly defined scopes of practice. Cancer care providers' perspectives regarding lack of time and training are unsurprising given the limited number of individuals and health services that have received certification from the International Cardio-Oncology Society (ICOS), which is the only recognised certification program globally (95). Lack of development and lack of implementation of specific cardio-oncology clinical pathways may impact providers' confidence in their own scope of practice and roles and responsibilities related to CVD care. Similarly, clinical care pathways are known to improve teamwork, which is directly relevant to the finding of the this research, that providers felt they couldn't deliver CVD care alone (269). In fact, a multidisciplinary approach was identified as an enabler to improved CVD care by both cancer care providers and people affected by cancer in

both the qualitative studies reported in chapters 4 and 5, and the codesign reported in chapter 6. People affected by cancer identified several health care professionals who they felt would be able to effectively provide CVD care. This is consistent with well-established evidence of the importance of multidisciplinary health care approaches to improve patient outcomes, workforce satisfaction, staff communication and decreased hospital length of stay (270). In this research participants identified the 'chasm' between cardiology and oncology professions where there are differing views about many aspects of care including cardiology referral and assessment. This is consistent with recent cardio-oncology expert panel recommendations developed to address gaps in evidence which includes statements highlighting the need for oncology and cardiology to collaborate and the importance of a multidisciplinary approach (271). It is noteworthy that even with the release of the comprehensive ESC cardio-oncology guidelines, cancer care providers still identify lack of training and being unsure of roles and responsibilities as concerns, and there remains a lack of clinical pathways which tend to be developed based on evidence-based guidelines. This suggests a lack of translation of the guidelines into practice, which could be due to limitations identified since the release of the guidelines, including that several recommendations were based on limited evidence (94), recommendations assume a level of resources not available in many services, and the role of nursing in CVD care is not well-defined (272).

7.3.1.3 Diverse preferences for potential solutions to the problem of CVD risk in cancer

Cancer care providers and people affected by cancer expressed diverse ideas, preferences and potential solutions to improve CVD in cancer throughout the research program (studies reported in chapters 4, 5 and 6). These included cardio-oncology clinics, clinical care pathways and education. In addition, preferences for specific components of an improved approach included a multidisciplinary approach, information provision to patients, support to empower patients to self-manage aspects of CVD risk and support for behaviour optimisation. Interestingly, there were several views and opinions expressed by participants throughout this research program that were in contrast with one another, including preferred amount of information provided and manner of information provision (e.g., website vs printed materials vs talking with member of health care team). Some people diagnosed with cancer argued the importance of leading or being involved in their own health care, whereas cancer care providers were more focused on which type of health care professional should deliver care. Diverse preferences (between health care providers and patients, as well as within these groups) for healthcare are commonly reported in the literature (273). Differences between patients may be due to individual characteristics, e.g., different previous experiences with health care where people are more likely to select an approach they have experienced positively (274). Existing literature has proposed that differences between patients and health care providers with regard to treatment can be influenced by health care providers' tendency to be more cautious than patients regarding potential risks, whilst patients were more likely to focus on potential health benefits (273). This could partially explain some of the

current findings, where cancer care providers expressed the importance of communicating risks (e.g., signs and symptoms of CVD and safety of lifestyle behaviour change) and people diagnosed with cancer were very positive about their capacity and willingness to make behaviour changes.

Although it is useful to understand why there may be diversity in preferences for a new approach to CVD care in cancer, the most important conclusion from synthesising this data is that a new approach must be individualizable and must be able to tailor to many differing needs and preferences. In addition, it is important to appreciate that no single approach will improve CVD risk in all people with cancer.

7.3.2 'My Heart and Cancer' – components of the website

This thesis reports the comprehensive approach, based on the Person-based Approach to Developing Interventions (PBAID) framework, that led to the development of the novel 'My Heart and Cancer' website. The aim of the website was to provide information and support to people diagnosed with cancer to self-manage aspects of their own CVD risk and their overall health. Through the iterative codesign process, various website components and concepts were selected to constitute the website, including but not limited to information provision, self-management, patient activation, and lifestyle optimisation support, and uses techniques to encourage user engagement and to provide an individualised experience tailored to the needs and preferences of the user.

7.3.2.1 Lack of awareness and perceived importance of CVD in cancer – information provision

Patients' lack of awareness and perceived importance of understanding the issue of CVD risk in cancer necessitated that information provision would be a strong focus of 'My Heart and Cancer'. Information provision is a key component of many interventions targeting disease management, given patients who have their information needs met report being more satisfaction, improved QoL and reduce anxiety and depression (275). The website was structured into six sections (information about CVD risk in cancer, CVD risk assessment, CVD signs and symptoms, self-managing aspects of CVD risk management, health care team's role in CVD risk management and access to resources and services) based on the ESC guidelines on cardio-oncology. These sections (and a 'rough' description of the content to be included) were presented to codesign participants in round 1 to prompt discussion. Throughout the iterative stages of codesign and usability testing, there were no suggestions to deviate from the six sections nor significant changes to the content. This is likely due to the fact that participants who were aware of CVD risk in cancer might be familiar with the well-established evidence and recommendations for what CVD care should look like in cancer (which the contents of the website were based on), and the people who were less aware might have been content to follow the suggestions of others with regard to this. In addition, the appropriateness of the content may reflect that the findings of the qualitative studies reported in

chapters 4 and 5 were accurately interpreted in terms of informing the first version of the website (wireframe).

7.3.2.2 Patient-facing website, self-management and patient activation

The choice of a patient-facing website as the type of intervention to address the problem of CVD risk in cancer was strongly informed by the qualitative findings (chapters 4 and 5) which identified the importance of patient activation and self-management. Patient activation refers to patients having the skills, confidence and knowledge to manage their health, and is linked to improve patient outcomes including reduced CVD risk factors (276). Self-management is "the individual's ability to manage the symptoms, treatment, physical and psychosocial consequences and lifestyle changes inherent in living with a chronic disease", and self-management support is provided by others to increase the ability of the individual to self-manage (101). In addition to informing the type of intervention, patient activation and self-management support were key concepts incorporated and applied to the content and layout of the website. This was achieved through the inclusion of a webpage dedicated to supporting users to self-manage CVD risk, that can be navigated to from the website toolbar. This page defines self-management, why it is important, and specific examples of how to self-manage aspects of CVD risk (e.g., lifestyle optimisation). Furthermore, self-management and patient activation are encouraged throughout other sections of the website, e.g., 'tips' sections on lifestyle optimisation pages, goal-setting advice, activities that users can interact with, and advice for how to engage with health care providers effectively. There is evidence that self-management interventions can lower symptom distress and improve self-efficacy in cancer (273), and knowledge and QoL in people with heart failure (277). However, self-management experts have argued that self-management support is not as advanced in cancer as it is for other chronic diseases and have identified six priority areas as part of a 'call to action' to improve self-management in cancer (102), of which four align with aspects/techniques of the 'My Heart and Cancer' website and its development. By providing information about self-management and using various techniques to educate users about how to self-manage, the website closely aligns with priority area one ("prepare patients and survivors for active involvement in care"). The patient engagement that occurred throughout website development provides an example of action 2 ("shift the care culture to support patients as partners in cocreating health and embed self-management support in everyday health-care provider practices and in care pathways"). Findings related to self-management from the qualitative and codesign studies in this research program advance self-management literature ("advance the evidence and stimulate research on self-management and self-management support in cancer populations"). Finally, the website has the potential to expand reach of self-management support ("expand reach and access to self-management support programs across care sectors and tailored to diversity of need and stimulation of research to advance knowledge"). The PhD candidate is unaware of any other self-management interventions to reduce the impact of CVD risk in cancer.

7.3.2.3 Lifestyle optimisation

All qualitative and codesign participants supported the importance of including information and support to optimise lifestyle behaviours, with an emphasis of quitting smoking, physical activity and healthy weight. This is consistent with the strong evidence base for the importance of health lifestyle in cancer, CVD and coexisting disease. In particular, the ESC guidelines for cardio-oncology include recommendations related to healthy lifestyle (6), and the ESC Guidelines for Patients has a strong focus on lifestyle behaviours, specifically physical activity, healthy diet, healthy weight, alcohol moderation and quitting smoking (278). Despite guidelines, there has been a lack of translation of evidence into interventions which target lifestyle behaviours in people with cancer to manage CVD risk (279). In addition, the findings of the review of systematic reviews of the effectiveness of lifestyle interventions in older people with cancer (reported in chapter 3) provide support that lifestyle optimisation also has benefits for older people (who represent a large proportion of the population with cancer) despite having biological and social differences to younger people with cancer. Therefore, optimising lifestyle behaviour was determined to be a necessary key component of the 'My Heart and Cancer' website. Users can navigate to separate 'pages' within the website that provide information and support (including tips, goal setting and links to other sources) for physical activity, diet, healthy weight, quitting smoking, alcohol moderation and stress reduction. Given there was a lack of behaviour-change interventions targeting cardio-oncology, the Health Belief Model (HBM) was used as a theoretical framework to guide the incorporation of information and support that aims to encourage users to change their lifestyle behaviours. The HBM focuses on how factors such as beliefs about what negative outcomes could occur with poor behaviour and what likely benefits may occur with behaviour change, contribute to whether a person will make changes (280). There are six constructs of HBM that can be applied in the context of behaviour change to manage CVD risk in people diagnosed with cancer: 1) perceived susceptibility to CVD risk; 2) perceived severity of CVD; 3) perceived benefit of making lifestyle changes and managing CVD risk; 4) perceived barriers to behaviour change; 5) self-efficacy to believe in the individual's ability to make changes; and 6) increasing cues to remind individuals to engage in behaviour change. The way in which the lifestyle behaviour change advice and support was incorporated into the 'My Heart and Cancer' website was achieved thoughtfully and intentionally using the HBM constructs as a guide. For example, the strong emphasis on information provision about CVD risk in cancer (including why CVD risk is higher in people who have been diagnosed with cancer compared to those who have not) encourages users to consider their susceptibility to CVD risk. Likewise, providing an overview of the more common CVDs associated with cancer means users become more aware of disease severity. The detailed section on goal setting includes a section about 'Coping Planning' which refers to identifying potential barriers to achieving goals (e.g., behaviour change) so that one can create a plan for how they can be overcome should they arise. The 'My Heart and Cancer' website presents healthy behaviours positively, so users appreciate the benefits of engaging in these behaviours. The

website aims to optimise self-efficacy in several ways, including via its focus on empowering people to self-manage aspects of their health and disease, and by including simple achievable tips related to behaviour change. Activities throughout the website have the function to print goals, questions for healthcare professionals and CVD risk profile, which can serve as cues for action.

7.3.2.4 Diversity of preferences – importance of individualisation of intervention

Given the diversity of preferences related to CVD risk reduction interventions in cancer, the 'My Heart and Cancer' website was created so that each user experience would be tailored to their individual needs and preferences. For example, people with cancer's perceptions varied with regard to the amount of information they wished to receive about CVD risk in cancer, therefore the website was developed in a way that individuals would first be presented with a brief summary of information about a topic but had the option to navigate to more detailed descriptions. Likewise, there are 14 separate webpages within the website, each addressing a different topic and users can navigate to any of them from every page meaning they do not need to 'wade through' information that they do not wish to engage in. Each page provides 'takeaways' at the top of the page with links to sections below so they can navigate directly to what they are interested in. The comprehensive approach to ensuring 'My Heart and Cancer' can tailor information provision and support according to the users' needs aligns with literature arguing for the importance of customisation of information provision in cancer (281).

7.3.3 'My Heart and Cancer' – design and development process

A major strength of the research program was the comprehensive approach to developing the website based on the feedback and preferences of stakeholders, specifically people affected by cancer and cancer care providers. This participatory approach involved several challenges to be reflected upon. It was critical to balance the feedback and preferences of stakeholders with evidence-based content that was accurate. This was addressed by responding respectfully to participants that changes to the content were not possible if it changed the meaning of the information in a way that would mislead users. At times there were conflicts between stakeholders' input, which required discussion amongst stakeholders in the first instance. Where disagreement remained, the researchers engaged in discussion and consulted relevant research literature or other similar resources to determine the best way forward. There was a need to balance broad applicability of the website with specificity of information and to provide adequate detail whilst maintaining accessibility and equity for generalisability, and this was mostly addressed through presenting information simply but with options to link to other more detailed resources. The development of the 'My Heart and Cancer' website also required regular communication between the PhD candidate and the website developer. The PhD candidate was required to develop adequate website development knowledge and skills in order to communicate effectively with the website developer and to understand what was possible in terms of translating stakeholder preferences into a website whilst maintaining accuracy and accessibility.

7.4 Strengths and limitations of the research program

There were various strengths and limitations of the research program. The majority of participants, particularly in studies 1 and 2, were either treated at or employed by the same clinical service in Southern Adelaide, South Australia. Given there are variations in many aspects of health services such as workforce training, resources and special interest of employees, there may also be differences in perceptions and experiences related to cardio-oncology. This limits the generalisability of findings and could potentially impact the appropriateness/relevance of the website to different populations. However, compared to studies 1 and 2, the codesign study (study 4) included a greater proportion of participants who received/provided care at services other than in Southern Adelaide. In addition, a key finding of all studies was that perspectives and experiences were diverse, and therefore a key focus in the development of the website was that it was capable of catering to a range of needs and preferences. Also, when considering the findings of the qualitative and codesign study in the context of existing (albeit limited) data, there was little evidence of substantial differences in perceptions across different populations. Another limitation of the research was that people who predominantly speak a language other than English were not sampled, and the samples did not show diversity in race/ethnicity or level of socioeconomic advantage which are known to influence the care experience. There was an attempt to recruit purposively with respect to achieving diversity in gender, cancer type (people diagnosed with cancer), and profession (cancer care providers). A study-specific limitation was the drop-out of participants between round 1 and round 2 of the codesign study. This was unfortunately due to people being unavailable in the time where the second round needed to be conducted in order to complete the research in a timely fashion (within the requirement of the candidature). Another study-specific and important limitation of the research was that there was limited/no review-level literature examining the effectiveness of diet, smoking and alcohol consumption in older people with cancer. Likewise, there has been a lack of research examining the mechanisms that may explain differences in potential differences in effectiveness according to age (e.g., impact of sarcopenia in physical activity effectiveness).

It is also important to consider potential limitations affecting technology-based interventions in healthcare. The use of any website requires a level of digital literacy, which cannot be assumed for all people, and some people who experience low levels of education, lower socioeconomic status and older people may be unable to access and effectively use computers and websites (282-285). In addition, some populations have no or unstable access to broadband internet services required for website use (283). These factors lead to inequity of access to technology-based interventions, often called digital exclusion (285).

An important strength of the overall research program was that the research program was strongly and consistently informed and guided by the PhD candidate’s understanding of their own

philosophical, ontological and epistemological worldviews. Identifying, and deeply understanding the researchers' own philosophy and values (i.e. critical realist view) facilitated the design of a research program that consistently and explicitly aligned philosophically, from epistemology, to ontology, methodology and methods (including data collection, data analysis, interpretation and dissemination of findings). Specifically, by identifying that critical realism recognises that truth is made up of objective reality and interpretation by humans, a mixed methods approach with quantitative and qualitative components was selected, with all qualitative research focusing on understanding, and developing an approach informed by, the perspectives of key stakeholders (i.e. people diagnosed with cancer, cancer care providers, and carers). In addition, the application of reflexive thematic analysis ensured that the researcher's own views and biases were not only reflected on but also appreciated as being critical to the construction of knowledge. A truly patient-centred approach to intervention development is difficult to achieve given that researchers' coordination of research can often lead to their voices being more influential. However, in this research program, the extensive work by the PhD candidate to understand and embrace their own philosophical viewpoint, led to all research tasks being conducted with a focus on ensuring that findings and decisions were truly patient-centred and informed equally by the views of key stakeholders and researchers. Multiple rounds of qualitative interactions with different stakeholders (i.e. studies 2, 3 and 4) is also a strength of the research program, as it allowed for the contribution of a large number of stakeholders (i.e., a total of 47 participants provided feedback leading to the website development), and created an iterative approach to approach development where ideas were integrated and then could be refined later.

7.5 Future research recommendations

It is anticipated that 'My Heart and Cancer' will undergo further efficacy testing. First, this could involve a pilot mixed-methods hybrid implementation-preliminary effectiveness study to assess the feasibility, acceptability and preliminary effectiveness of the website. The PhD candidate foresees that feasibility may be assessed as demand (i.e., uptake rate – proportion of people who the website address is provided to (by a health care provider) that visit the website and provide online consent to participate in the research); retention (i.e., proportion of consenting patients who show reasonable use/engagement in the website) and engagement (i.e., average number of minutes participants use the website for, how many and which pages within the website are visited, number of activities engaged in). The Theoretical Framework of Acceptability (TFA) online questionnaire could be used to assess the eight constructs of the TFA (affective attitude, burden, ethicality, perceived effectiveness, intervention coherence, self-efficacy, opportunity, costs and general acceptability). It is anticipated that preliminary effectiveness may involve assessment (via pre- and post-website use surveys or interviews) of outcomes including knowledge/awareness of CVD risk in cancer, self-management skills, self-efficacy, intended behaviour-change, and healthcare/resource utilisation.

If the findings of the pilot hybrid implementation-effectiveness study indicate that the 'My Heart and Cancer' website is adequately feasible, acceptable and effective (with regard to the preliminary measures assessed in the pilot study), a randomised controlled trial (RCT) could be conducted as a more rigorous assessment of the effectiveness of the 'My Heart and Cancer ' website in affecting outcomes including risk factors (e.g., smoking, physical activity, healthy weight, diet, blood pressure and blood lipids) as well as knowledge, self-efficacy and self-management.

It is anticipated that the 'My Heart and Cancer' website will also be evaluated for cost-effectiveness. This would involve comparing the costs and benefits of the website against 'usual care'. Direct economic costs could be estimated, as well as resources saved through avoiding CVD events, with decision-analytic modelling being a potential approach to achieve this (286).

In addition to further evaluations of the 'My Heart and cancer' website, the findings of the review of reviews reported in chapter 3, identified a lack of review-level evidence for the effectiveness of lifestyle behaviour optimisation interventions in older people with cancer (with the exception of physical activity). Furthermore, there is a need for better understanding about why there are differences in the effectiveness of interventions according to age. Identifying other demographic and health factors (including sex, socioeconomic factors and comorbidity) that influence effectiveness of lifestyle optimisation interventions is also important to inform new approaches that aim to improve patient outcomes, including CVD risk in cancer.

7.6 Practice implications

The thesis has important clinical implications by demonstrating gaps in care that need to be addressed and offers a potential clinical tool should the efficacy be confirmed. It is envisaged that the website could be launched and promoted to consumers (people diagnosed with cancer and cancer care providers), potentially via member organisations (e.g., Cancer Council, Cancer Voices, Clinical Oncology Society of Australia, Multinational Association of Supportive Care in Cancer, The Heart Foundation etc.) and professional bodies whose members include cancer care providers (e.g., Dietitians Association of Australia, Cancer Nurses Society of Australia, Royal Australian College of General Practitioners etc.). People with cancer could then be informed of the website through their member organisations or their health care team (or via an Internet search engine).

As reported in chapter 4, cancer care providers have identified that a lack of time, being unsure whose role it is to provide CVD care and being concerned that they cannot manage CVD care alone, are significant barriers to CVD care in cancer. It is anticipated that cancer care providers being able to provide patients with a link to information and support will reduce the impact of these barriers. General practitioners (GPs) are well-placed to play an important role in enabling and encouraging people with cancer to access and engage in the 'My Heart and Cancer' website. The provision of health information and coordination of care are often delivered by GPs to people with

cancer, and patients are often in regular contact with their GP (287, 288). If GPs are aware of the website, they will likely have the opportunity to introduce it to their patients, and the information and support provided by the website can assist GPs to provide the care needed by their patients. GPs will also have an important responsibility in responding to the needs that may be identified through patients' engagement with the website, e.g., patients may wish to discuss their level of risk with their GP after completing the risk identification activity in which they gain an improved understanding of the number of CVD risk factors that apply to them. In addition, many patient preferences reported in chapter 5 are met by receiving information and support via the 'My Heart and Cancer' website, given they are empowered to make their own choices regarding accessing information and support. In particular, patient activation, seeking information and knowledge, and being supported to self-manage and optimise lifestyle behaviours may lead to improved CVD care (including risk assessment and management) and reduced CVD risk, and are associated with many other positive outcomes including improved communication between patient and health care team, QoL and survival, and reduced anxiety and depression. Information and support provision through a website is also likely to be a cost-effective approach to CVD care both directly (through saving time and cost of health care provider educating the patient) and indirectly, where patients are encouraged to self-manage and optimise lifestyle behaviour to reduce risk which can be less expensive than health service interventions.

Increased understanding of the perspectives of people who have been diagnosed with cancer and health care professionals can also lead to improvements in clinical practice. Patients who feel their perspectives are understood and respected by their health care team are more likely to report being satisfied with their care and to have improved health outcomes, compared to those who feel they are misunderstood. Similarly, health care providers who report feeling as if their perspectives are recognised, report they have better work satisfaction and provide better quality care to their patients.

7.7 Conclusion

CVD risk is an important competing morbidity and mortality risk for people who have been diagnosed with cancer. However, despite the significance of the problem of CVD in cancer, many people with cancer do not receive adequate CVD care. This research program contributes new in-depth and rich data that improves understanding of people with cancer and cancer care providers' experiences and perspectives regarding CVD risk in cancer. This knowledge is critical to informing future research and the development of new interventions, but also can inform current clinical practice, e.g., encouraging cancer care providers to inform people affected by cancer of their increased CVD risk, and clarifying roles of cancer care providers with regard to their provision of CVD care within health care services. However, the high impact of this research program was the development of the first patient facing digital tool to support people affected by cancer to manage

CVD risk. Given the evidence of inadequate awareness, identification, and management of CVD care in cancer, the website developed through this research offers an accessible option to help address this gap, leading to improved outcomes for people with cancer.

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9 APPENDICES

Appendix 1: Knowles et al. 2022 (132), published paper: "Physical activity interventions in older people with cancer: A review of systematic reviews"

Appendix 2: Knowles et al., 2023 (216), published paper: "Reducing the impact of cardiovascular disease in older people with cancer: a qualitative study of healthcare providers"

Appendix 3: Topic Guide for Qualitative Study of Healthcare Providers and People Diagnosed with Cancer (reported in chapter 4, Appendix 2)

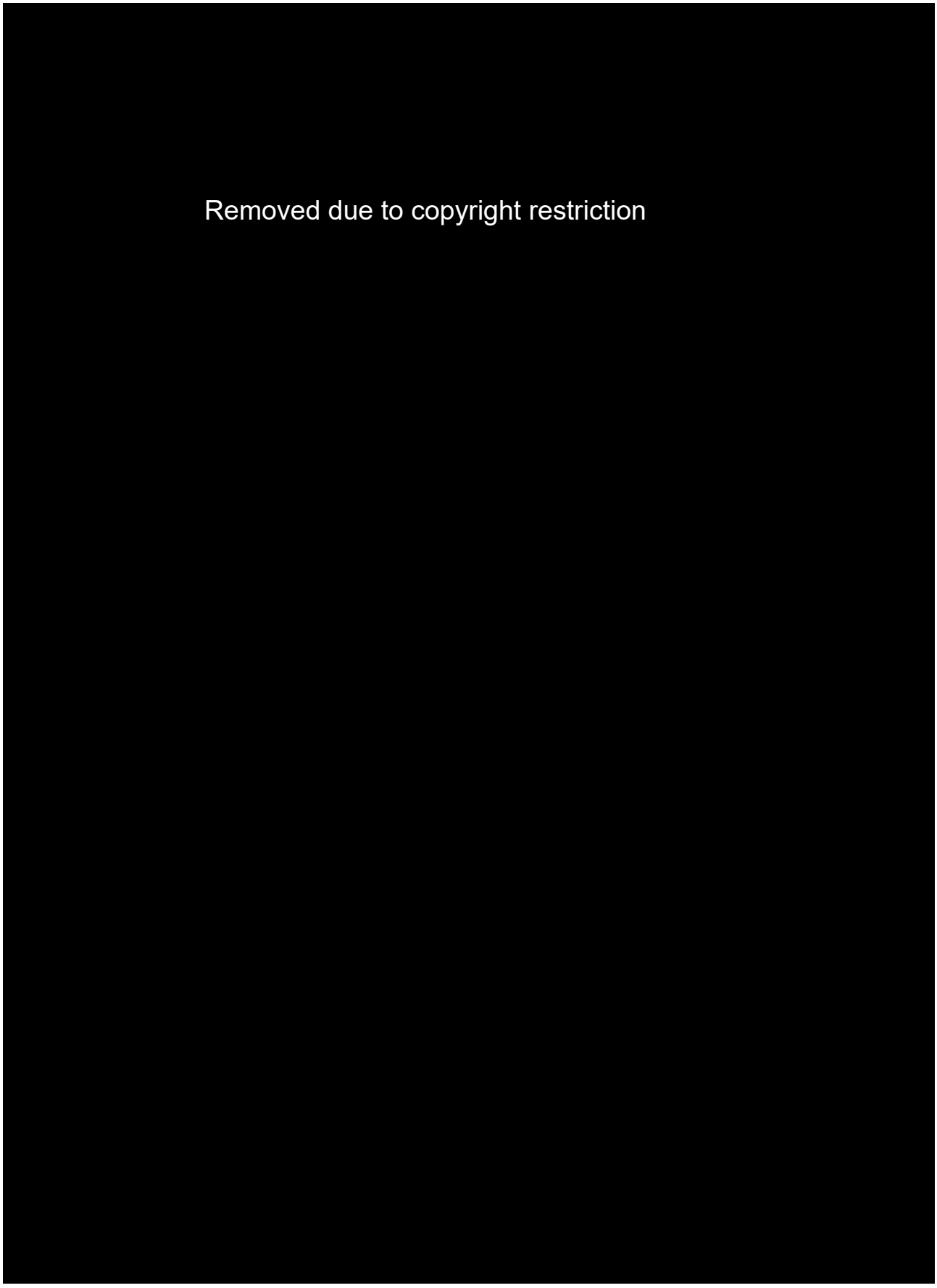
Appendix 4: Knowles et al., 2023 (239), published paper: "There could be something going wrong and I wouldn't even know": a qualitative study of perceptions of people with cancer about cardiovascular disease (CVD) risk and its management”

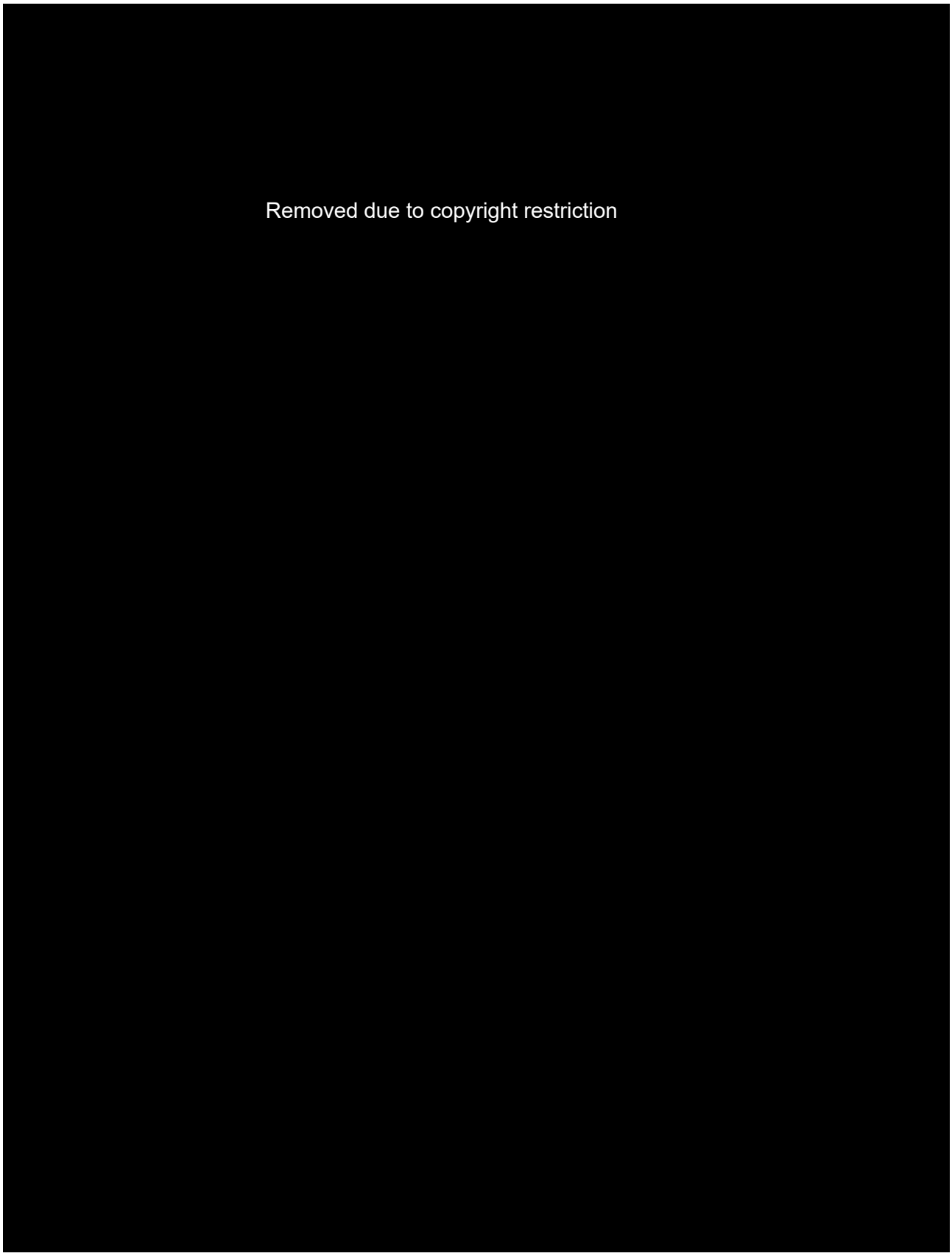
Appendix 5: Paper submitted to Journal of Cancer Survivorship, 2025: “My Heart and Cancer’: Codesign and usability testing of a cardiovascular disease risk management website for cancer survivors”

Appendix 6: Topic Guide for the co-design of a web-based resource to support self-management of CVD risk in people with cancer.

Appendix 7: Wireframe with Prompts for the co-design of a web-based resource to support self-management of CVD risk in people with cancer.

9.1 Appendix 1: Knowles et al. 2022 (132), published paper: “Physical activity interventions in older people with cancer: A review of systematic reviews”

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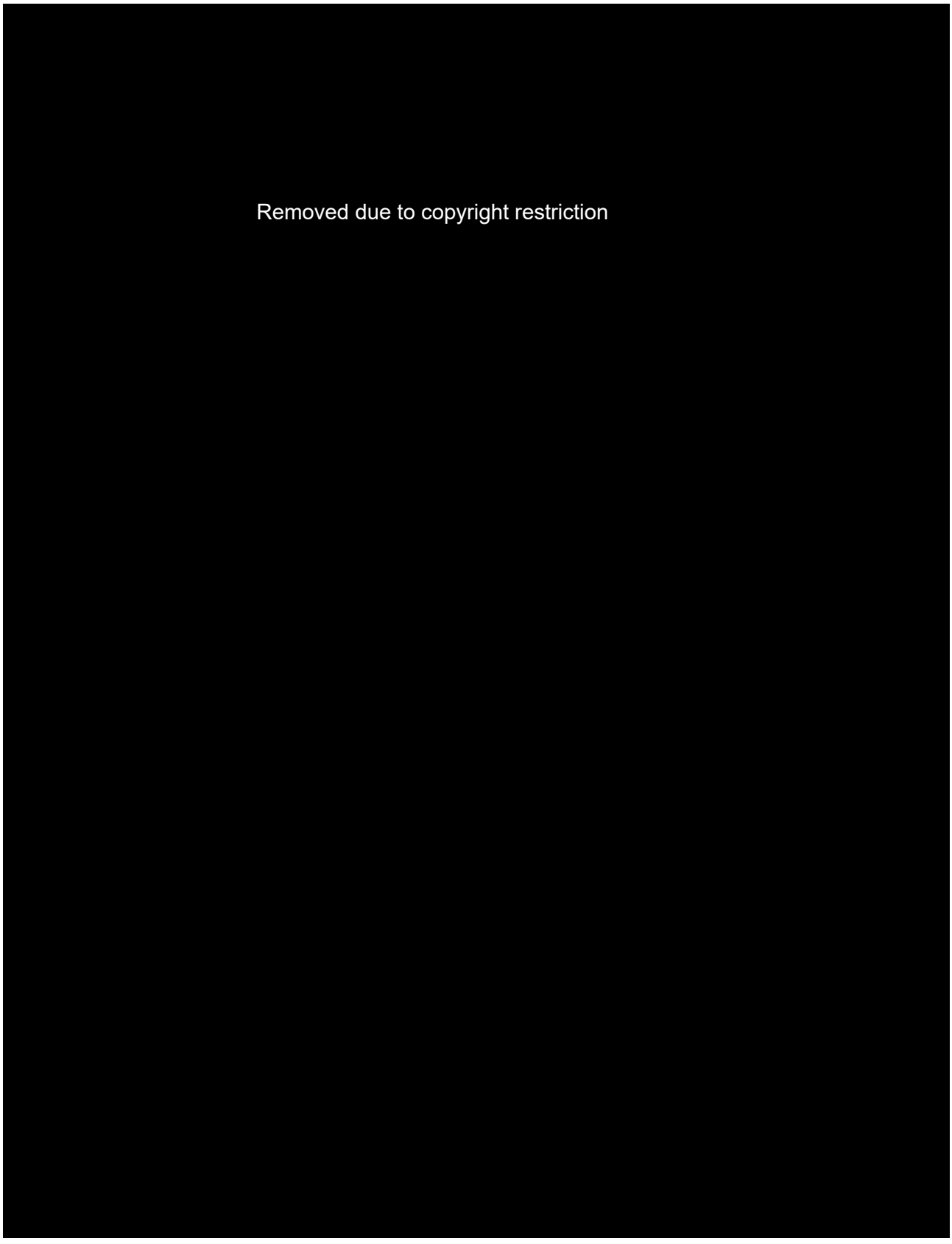
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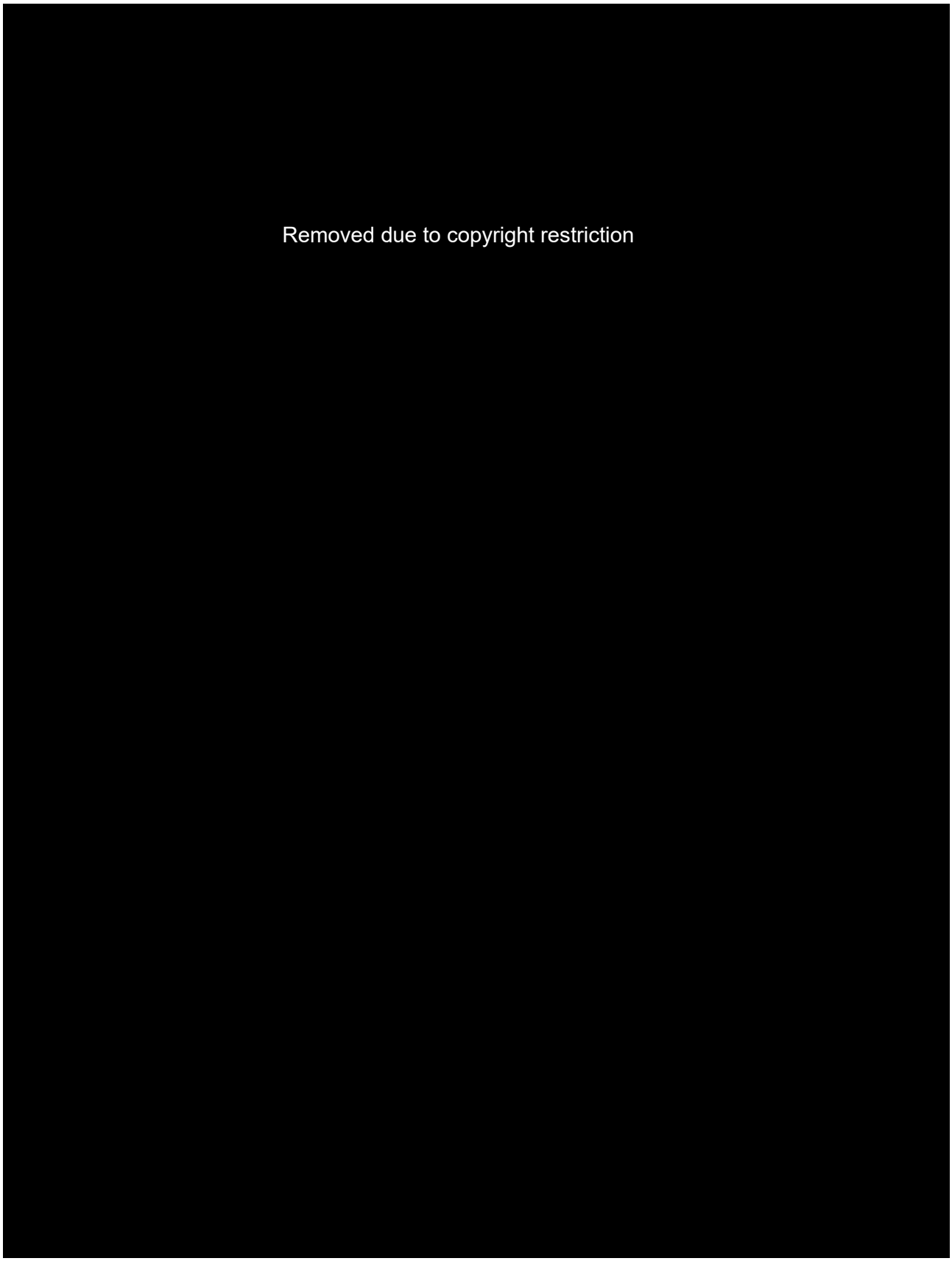
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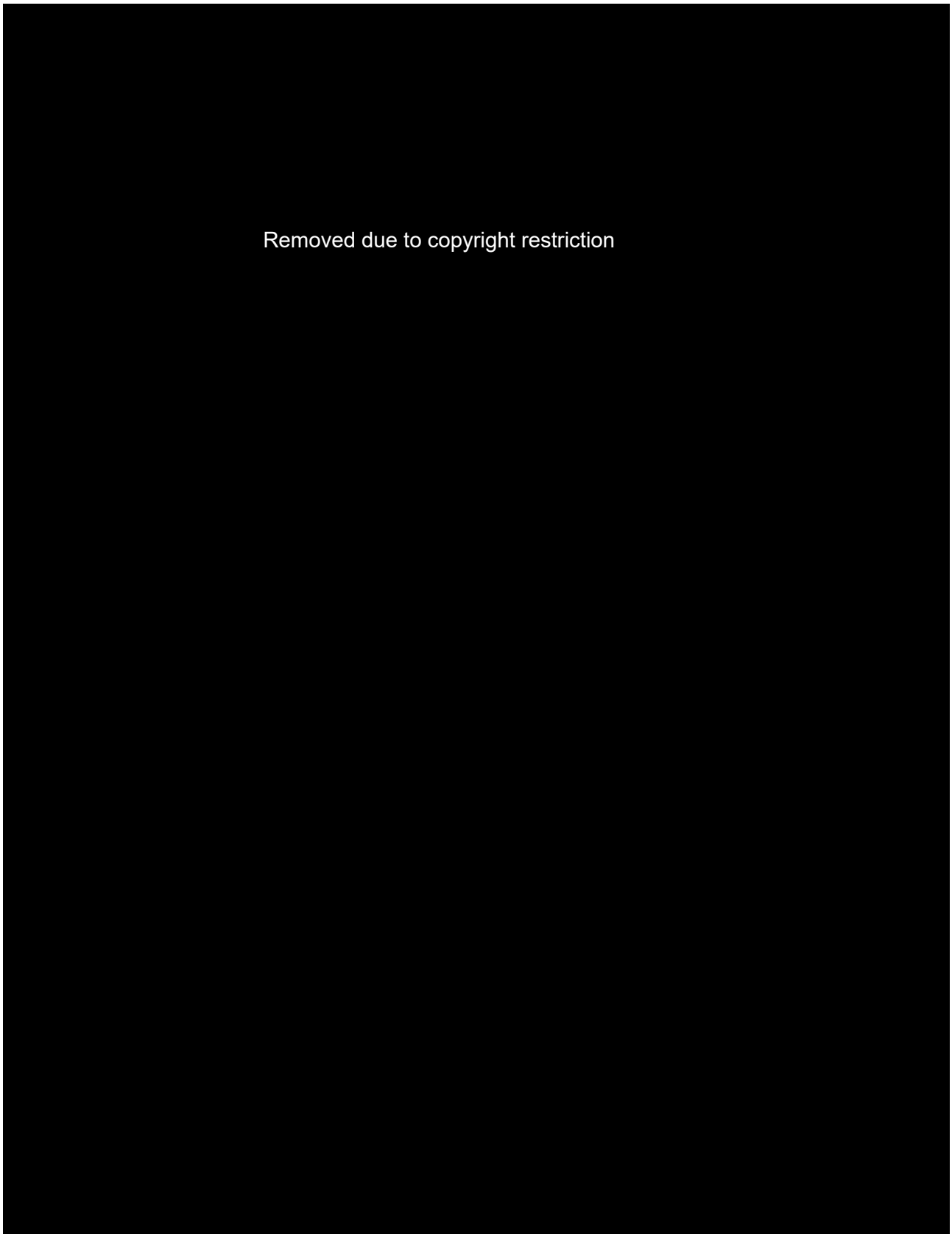
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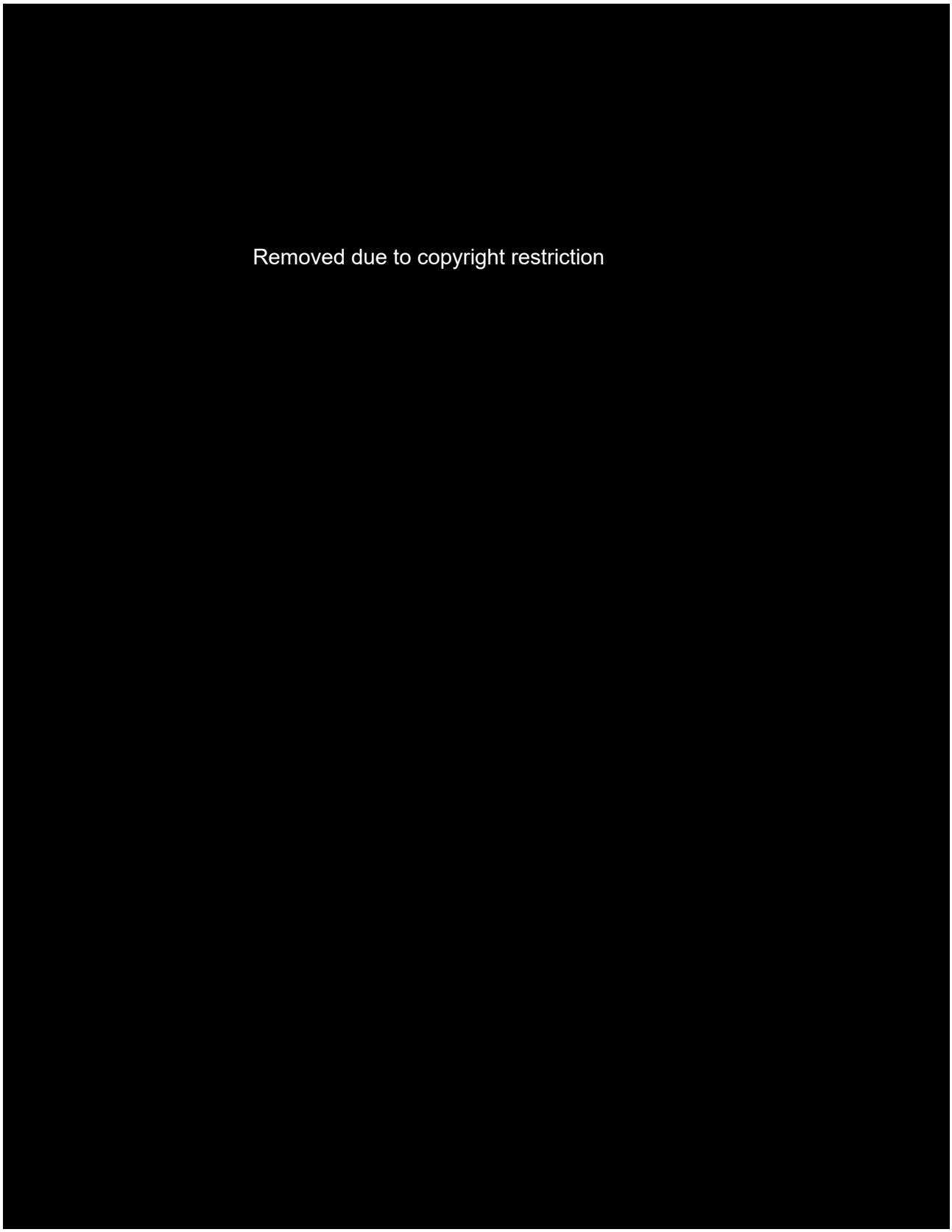
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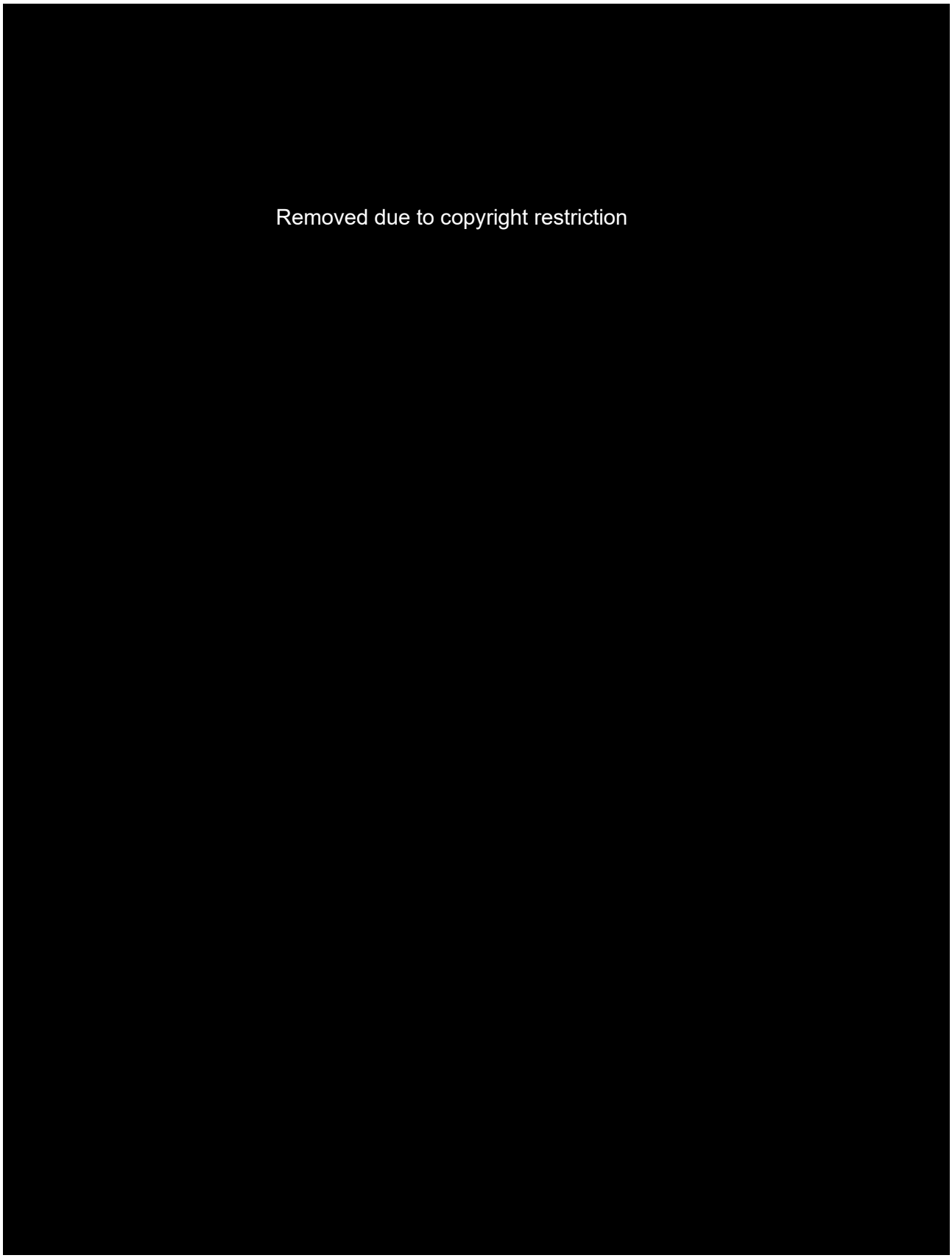
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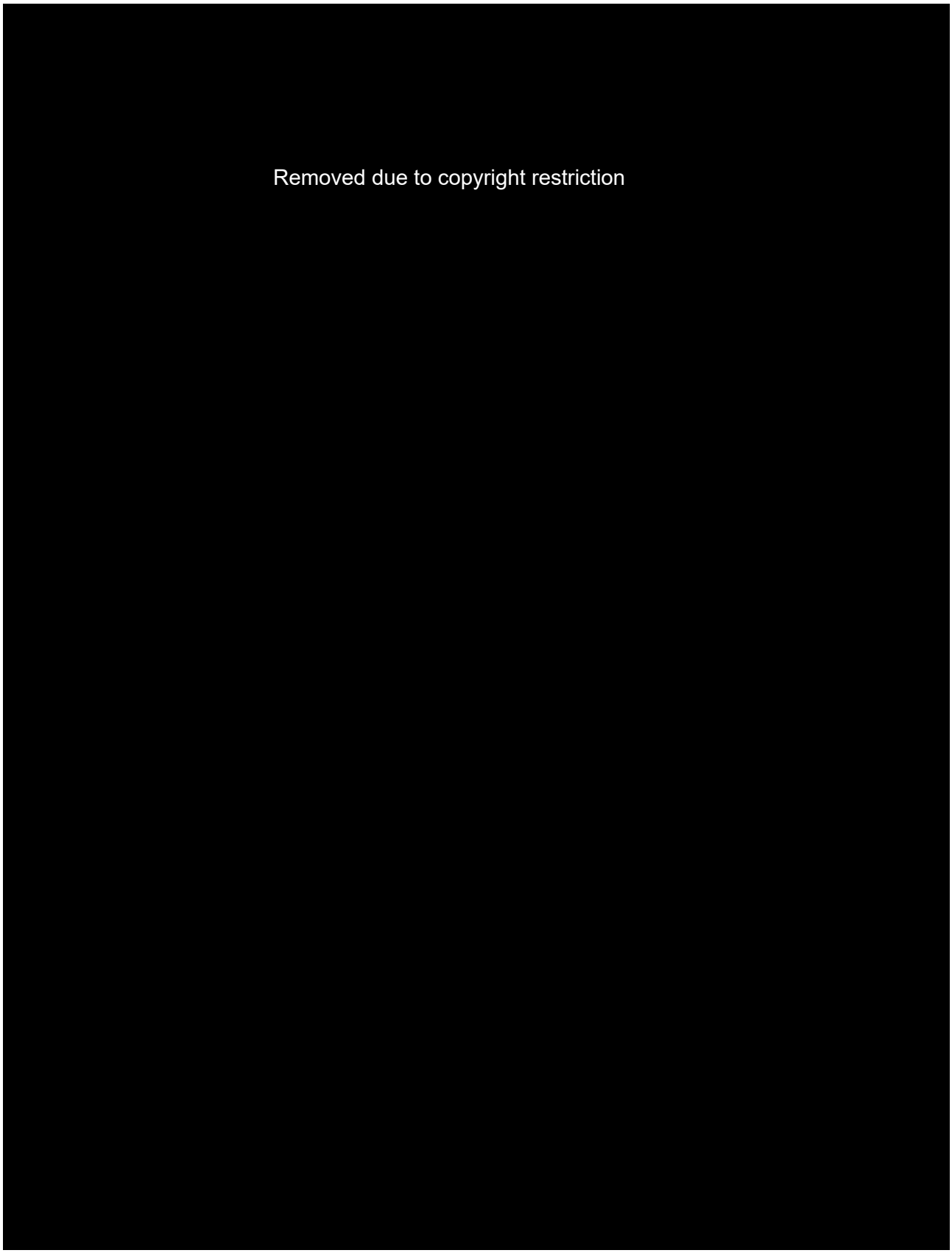
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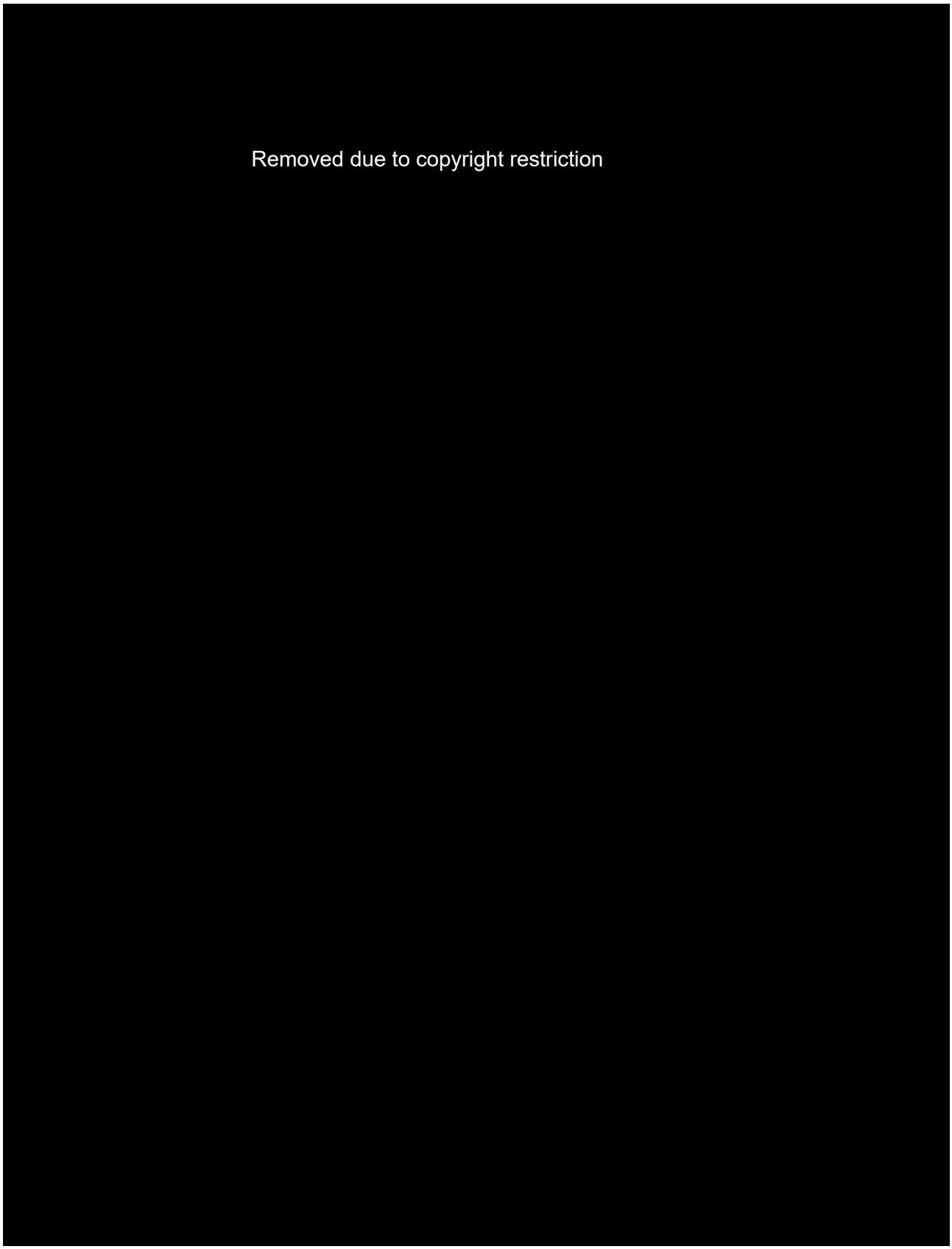
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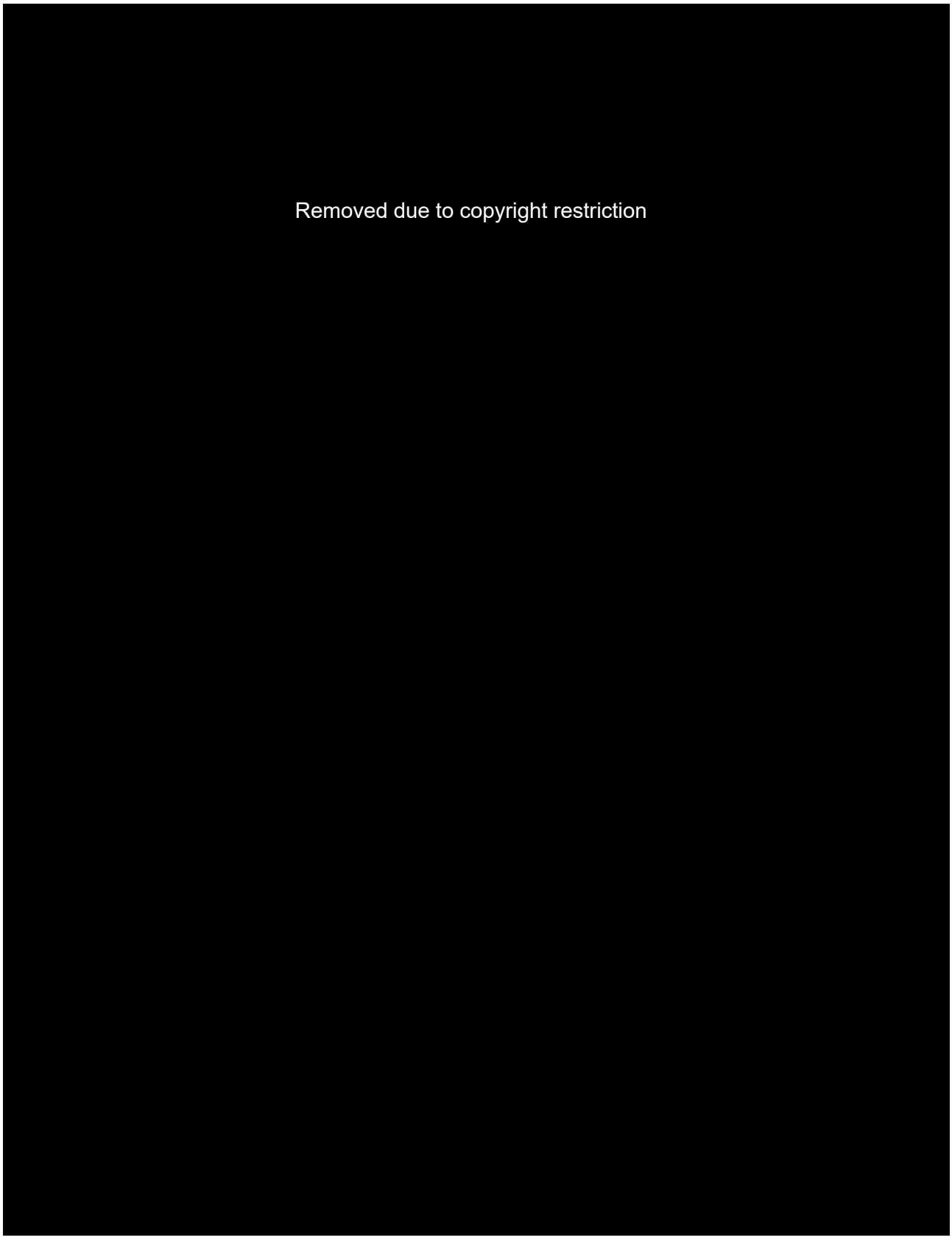
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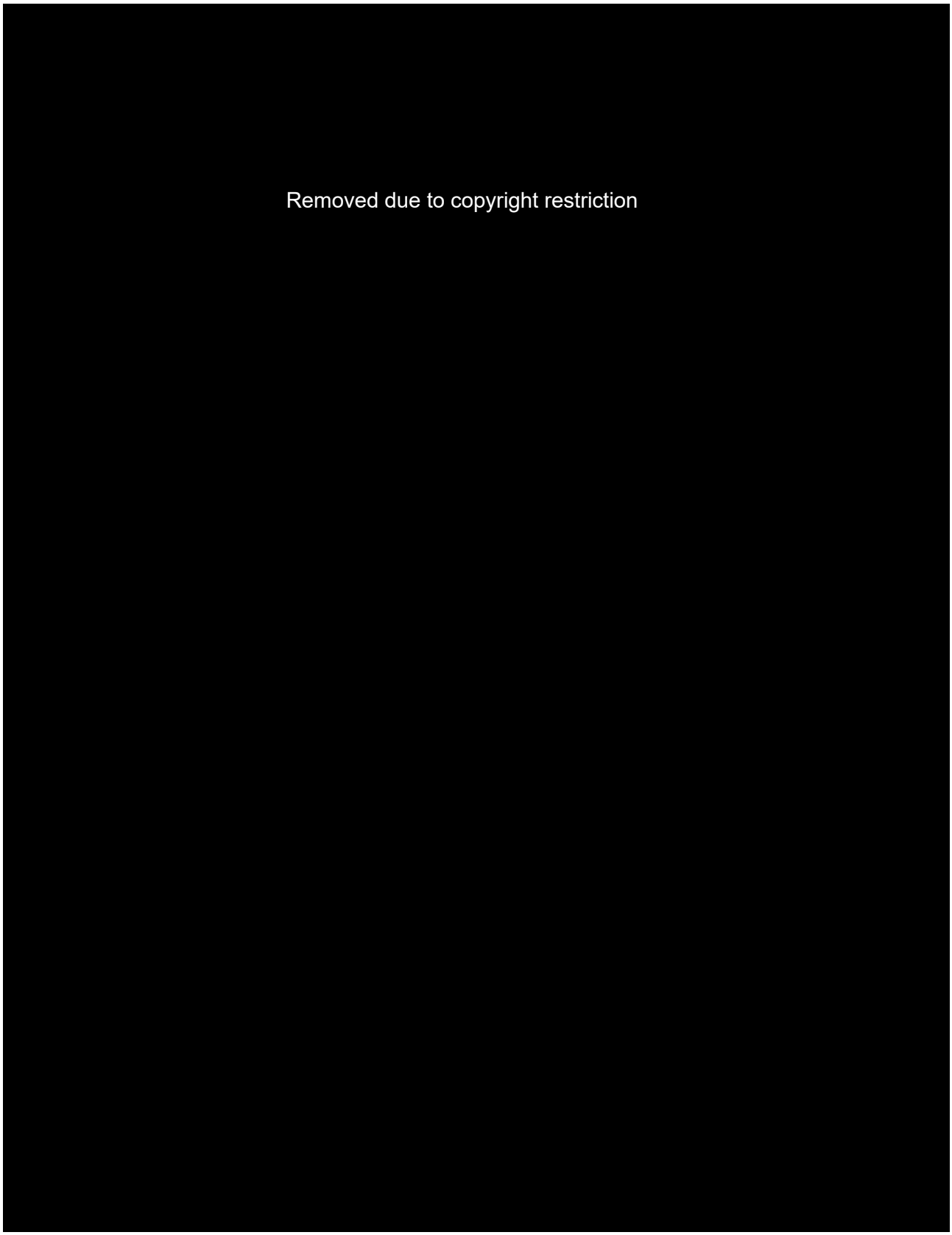
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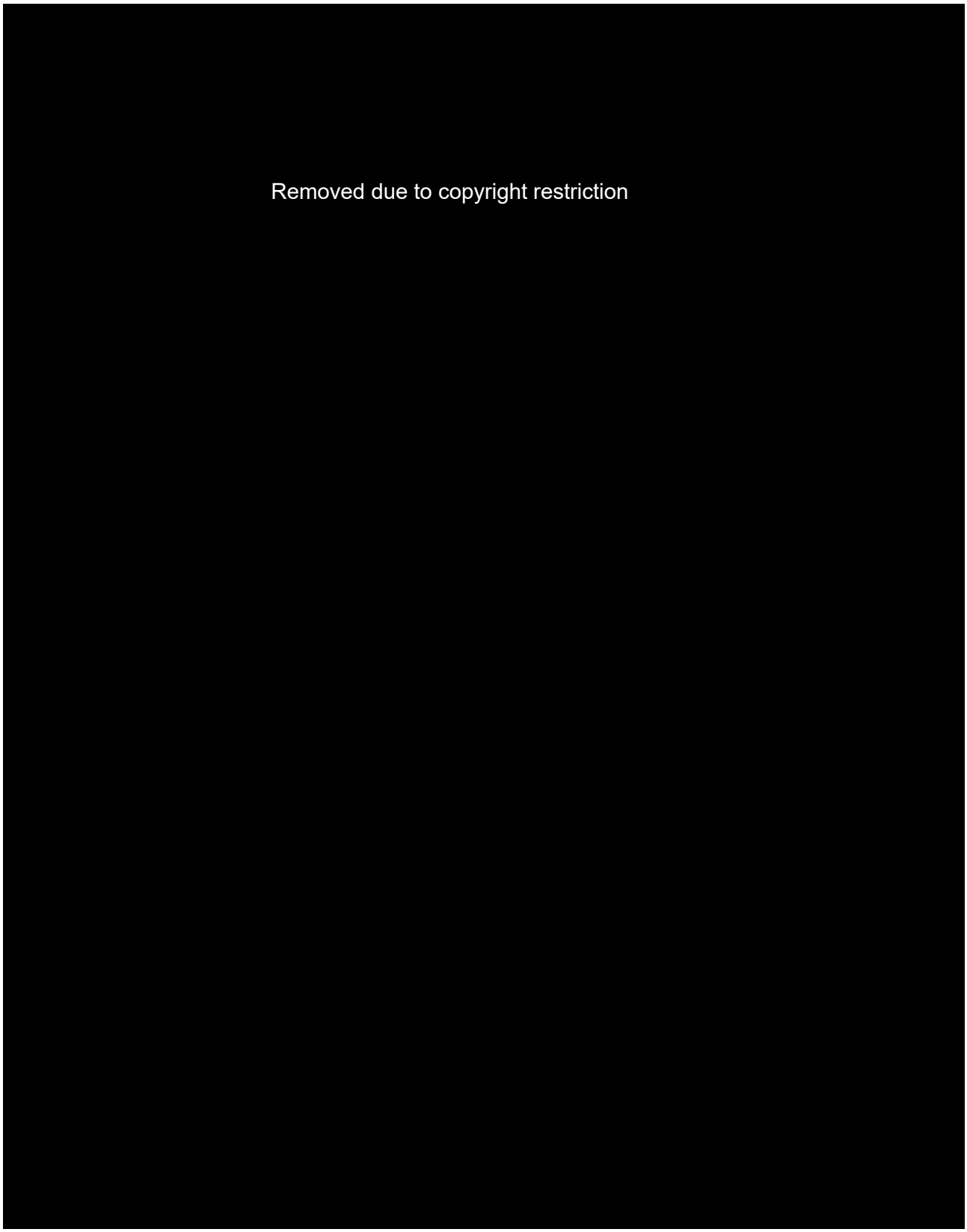
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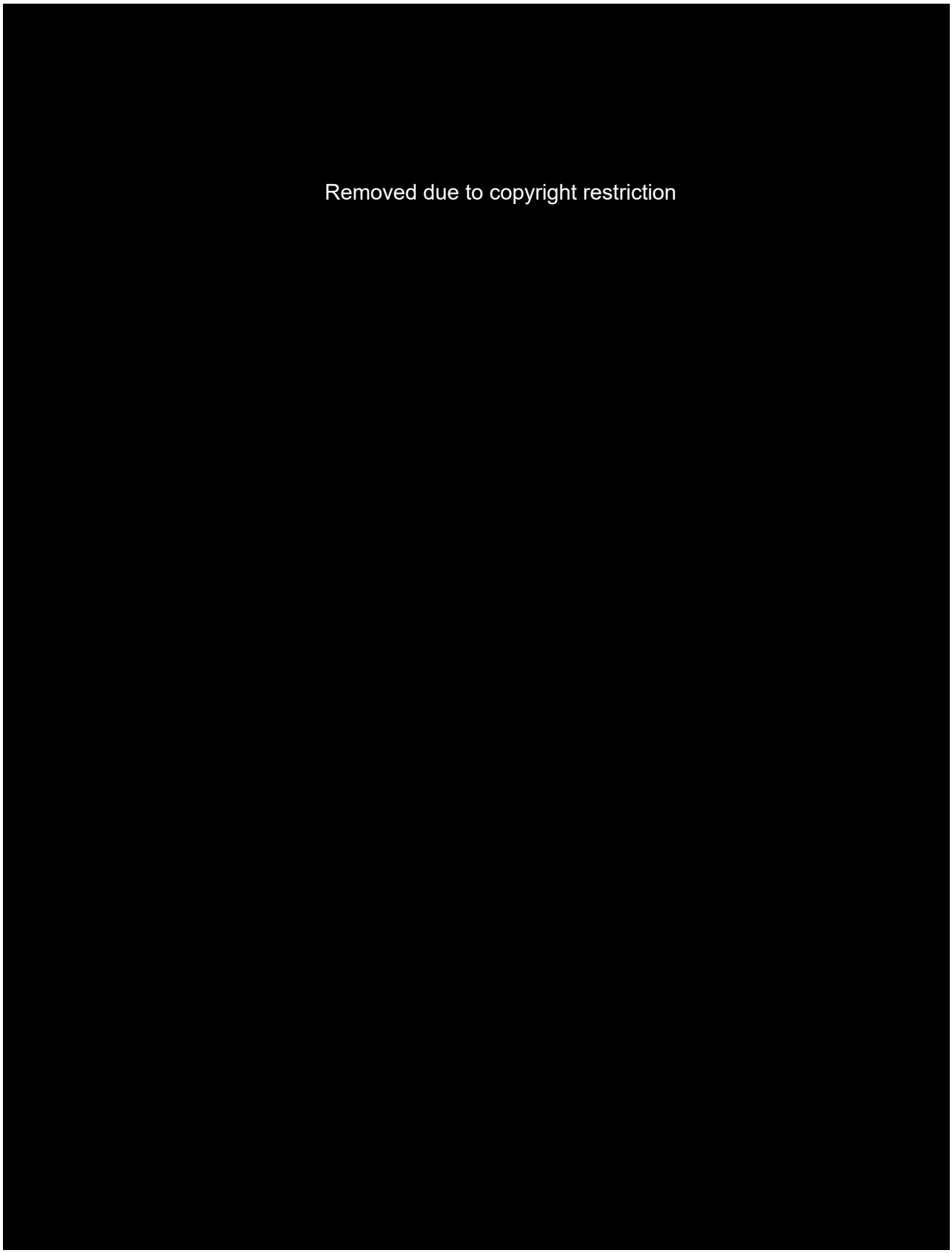
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9.2 Appendix 2: Knowles et al., 2023 (216), published paper: "Reducing the impact of cardiovascular disease in older people with cancer: a qualitative study of healthcare providers"

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Reducing the impact of cardiovascular disease in older people with cancer: a qualitative study of healthcare providers

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Abstract

Purpose Cancer survivors are at greater risk of cardiovascular disease (CVD) than cancer-free controls. Despite evidence-based guidelines recommending CVD risk factor assessment, surveillance and risk-reduction, many people with cancer do not receive adequate CVD care. To address potential barriers and enablers of care, we examined healthcare professionals' (HCPs) perceptions and experiences of CVD risk assessment and management in people with cancer.

Methods We conducted one focus group and 12 individual interviews to examine HCPs' perceptions and experiences of CVD care in care. We used reflexive thematic analysis to collect and analyse the qualitative data to construct and understand themes.

Results Twenty-one HCPs participated (8 oncologists, 5 nurses, 3 general practitioners, 2 dietitians, 1 cardiologist, 1 haematologist and 1 physiotherapist). Majority of HCPs were aware of CVD risk in cancer but were concerned they could not deliver CVD care alone due to system-level barriers including lack of time and training. HCPs also perceived patient-level barriers including socioeconomic disadvantage and fatalistic outlook. Despite barriers, HCPs suggested diverse solutions for improving CVD care in cancer including new models-of-care, clinical pathways, risk assessment/management tools and education.

Conclusions The diversity of perceived barriers and suggested solutions identified by HCPs suggests the need for a multilevel approach tailored to context. Future research involving people with cancer is needed to co-design acceptable interventions.

Implications for Cancer Survivors Improved understanding of HCP's perceptions can inform the development of new interventions to deliver CVD care to people with cancer to reduce morbidity and mortality.

Keywords Cardiovascular disease · Cancer · Healthcare providers · Perceived needs · Older people

Background

Cardiovascular disease (CVD) is a major cause of competing mortality and morbidity in people with cancer because of shared risk factors such as physical inactivity and smoking and the cardiotoxic effects of common anti-cancer treatments [1–4]. Older people with cancer, compared to their younger counterparts, are at greater risk of experiencing comorbidity [5–7] and have a higher all-cause and CVD mortality rate [8].

Evidence-based guidelines recommend CVD risk factor assessment, surveillance and risk-reduction as best practice supportive/survivorship care of people with cancer [9]. A wealth of evidence supports encouraging people with cancer to engage in healthy lifestyle behaviours, including physical activity [10–12], healthy diet [10], smoking cessation [13] and moderation of alcohol consumption [14]. However, many people with cancer do not receive appropriate assessment and monitoring/management of CVD and its risk factors [15], and older individuals with cancer are even less likely to be assessed for CVD risk than their younger counterparts, with preventive health services

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typically decreasing with age [16]. Understanding is limited as to why CVD risk identification and management is not routinely undertaken; however, data suggests a lack of guidance and resources to assist clinicians to identify risk [17] and lack of resources to manage this risk [18, 19]. Greater depth of understanding is needed about barriers, as well as preferences for CVD risk identification and management. Focused understanding of these issues particularly in older people with cancer is warranted given they are more likely to experience comorbid CVD, have higher all-cause mortality and may have different perceptions regarding barriers to and preferences for reducing the impact of CVD in cancer.

To address this gap, this study aimed to examine health care professional's (HCP) perceptions and experiences of the management of CVD and risk in older people with cancer.

Methods

Design

This qualitative study was undertaken as part of the broader program of research which aims to develop a new approach to CVD risk factor management in older people with cancer. The study involved focus groups and interviews conducted in person, via telephone and online.

Recruitment

HCPs were recruited through researchers' existing networks using a non-random, purposive sampling technique. Potential participants were informed of the project aims and study procedures (verbally and via the Participant Information and Consent Form [PICF]) before they indicated consent by signing the PICF. Participants could choose whether they participated via focus group or individual interview, and in-person, online or telephone.

Study procedures

Data was collected via focus group or individual interview. All interviews and focus groups were conducted by the same investigator (RK) with assistance from another (EK) for the focus group. The sessions were semi-structured using a topic guide (see Appendix 1) to collect the perceptions and experiences of HCPs around the central phenomenon of CVD in older people with cancer. Recruitment continued until the researchers perceived enough data to conduct rich and meaningful analysis and to develop a report that is interesting, informative and can inform future research and clinical practice. This approach aligns with the premise that "new" data can always be collected and ceasing data collection is a pragmatic decision based on the objectives of the research [20].

Data analysis

The focus group and interviews were audio-recorded and transcribed verbatim. We used the RTA approach to data analysis, underpinned by a critical realist paradigm to address our research objectives. RTA involves the development, analysis and interpretation of a range of qualitative data in which the researcher is involved in the construction of knowledge around a central phenomenon [21]. We used NVivo to assist with coding and theme development, and our analysis progressed through frequent discussions involving all researchers.

The analysis was conducted according to the six phases of the RTA framework [21] (i.e. data familiarisation, coding, initial theme development, review of themes, refinement, reporting). Semantic and inductive analysis predominated our approach to the generation of themes, in which the researchers identified themes explicitly communicated by the participants during focus groups and interviews. However, to increase the depth and richness of analysis, we also employed a latent approach to the analysis of some themes, in which we further discussed and analysed data to uncover the underlying meaning of participants' contributions. We practiced reflexivity throughout the analysis process to identify, understand and consider the impact of our own perspectives, perceptions and beliefs on the construction of knowledge in our research. The data analysis approach was iterative and recursive, as discussions and drafting of findings often led to new ideas and perspectives which required further discussion and analysis. An example of the flexible and iterative approach we used during both data collection and analysis was that although we aimed to encourage discussion about CVD and cancer with a specific focus on older people, we identified that many responses did not include differentiation between older and younger people. This was unpredicted but we determined that it occurred organically through the research process and chose to allow flexibility and authenticity in the application of the research methodology.

Ethics

Ethics approval was granted by the Southern Adelaide Local Health Network Ethics Committee on 22 January 2020 (HREC/19/SAC/309).

Results

A total of 21 HCPs participated in the research. Nine HCPs participated in one online focus group which lasted 59 min; and 12 HCPs participated in an individual interview

(face-to-face $n=9$; telephone $n=2$; online $n=1$), ranging from 12 to 53 min duration (median = 36 min).

The analysis identified four themes and 11 subthemes (Fig. 1).

Theme 1: Majority of HCPs are aware of CVD risk in cancer and consider it an important issue to address

Majority HCPs indicated that they were aware people with cancer had a higher CVD risk and summarised reasons for the co-existence of these diseases. For example:

> …toxicity of treatments we do for cancer, so for many of our chemotherapy or target treatments have a cardiovascular effect – that's one. Second is that some cancers have similar risk factors for development of the cancer as to cardiovascular disease, so its obesity, diet, smoking – Medical oncologist

But one HCP (GP) mentioned they were not aware of the impact of cancer diagnosis on CVD risk.

> I guess I'm not really well aware of that impact of increased risk [of CVD with history of cancer)…I don't think in my mind I factor in specifically as cancer survivors being at higher risk unless specifically their treatment has been flagged as being a potential risk factor. – GP

Sub-theme 1.1: HCPs consider CVD risk important

HCPs from a range of disciplines highlighted perceived importance of CVD risk in cancer. There was a strong focus on the perceived importance of weighing up the (cardiotoxic) risk and (anti-cancer) benefit of anti-cancer treatment.

> And if a patient has, for example, say, 20%, 30% risk of death just because of their cardiovascular risk it doesn't make sense to give them toxic treatments for 1% or 2% improvement. – Medical oncologist

Intervention to reduce CVD risk was identified as potentially improving patients' quality of life.

> …they've [typical lung cancer patient getting high dose radiotherapy] got a 20% chance of having a CV event in 2 years. Yet those patients are often not referred because you got people saying they've got such a poor prognosis there's no point. But if you could potentially prevent a cardiovascular event from

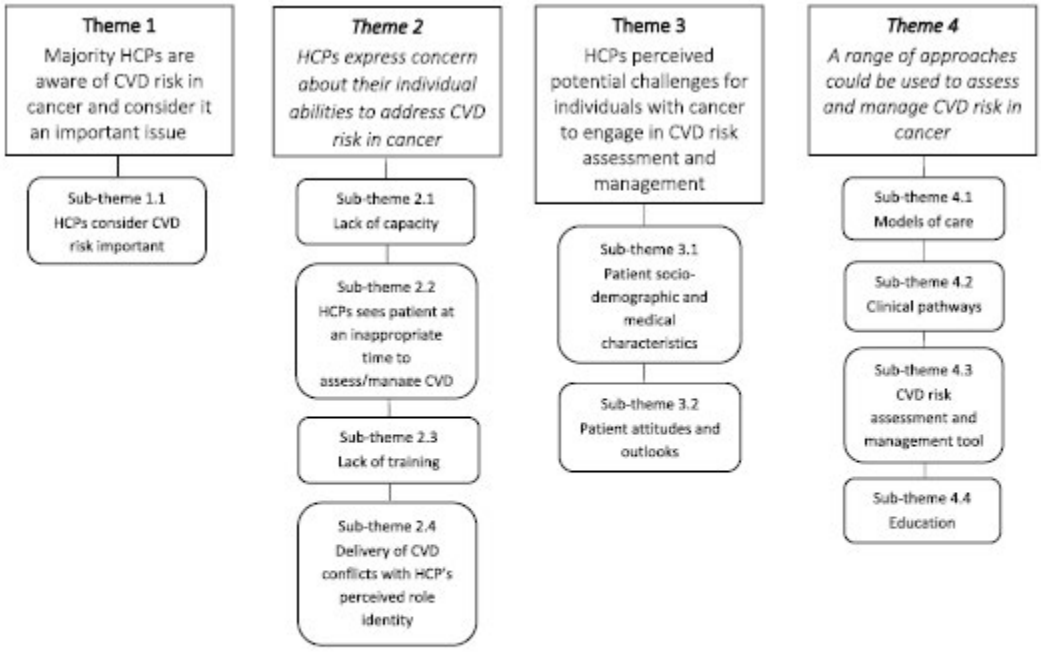

Fig. 1 Themes and sub-themes summarising HCP's perceptions of CVD risk identification and management in older people with cancer

a QOL perspective in the few years they've got remaining, why wouldn't you…? – Cardiologist

Theme 2: HCPs expressed concern about their individual abilities to address CVD risk in cancer

Majority of participants expressed concerns about their ability to deliver CVD care to people with cancer because of lack of capacity, training, inappropriate timing or perception of CVD care as outside of their role identity.

Sub-theme 2.1: Lack of capacity

Lack of time was the most common barrier to delivery of CVD care. For example, dietitians discussed how time limitations precipitated the need for prioritisation of cancer-related needs over CVD, and the need for referral of patients with CVD-related issues to community dietetics services.

I think it's all about priorities and so because everyone has limited time everyone aims at looking at the cancer. – Dietitian

A lack of adequate resources and services and inadequate cohesion/coordination of tasks by different professions involved in cancer care were identified as potential barriers to the provision of CVD care in cancer. A cardiologist commented that there was an inadequate number of cardiologists appropriately trained for providing cardio-oncology care and linked this to the absence of training programs.

there's probably only about 30 cardiologists in the country that have got an interest, there's 2 that are certified with the ICS which is sort of the de facto forming international group interested, and there's about 2 or maybe 3 who have done international overseas fellowships. There's no training programs in Australia, no requirement for training, so we couldn't deal with all the work anyway. – Cardiologist

A dietitian mentioned that hospital-based dietitians did not have the capacity to address CVD care in people with cancer, as their focus is on dealing with acute problems directly related to cancer.

we're just trying to make sure that we meet nutritional requirements, there's a lot of issues with inability to eat so it's not often around food groups or what you focus on when you think about cardiovascular health, because we're just trying to help keep them alive really and then the patients we keep long-term it's often around trying to improve quality of life. So, our work is very acute. – Dietitian

Participants communicated their perception that many patients did not receive survivorship care/post-treatment care, with one participant suggesting that this would be where CVD risk management would best fit.

…if the person comes out of the hospital with a clear survivorship plan, then there's a fair chance that it will be followed, but most people don't come out with a survivorship plan. – GP

A cardiologist identified that oncology and cardiology professions did not work together cohesively or communicate effectively, and this lack of connection between disciplines was perceived as a barrier to CVD care delivery.

…there is a disconnect between oncology and cardiology because there are different journals,… different language,…different side effects, reporting algorithms, different conferences and we sit on two sides of a chasm. It's only in the more recent past that there's been more movement towards bringing those two sides together – Cardiologist

Sub-theme 2.2: The time HCPs consult with patients is not the right time to raise CVD risk

Some participants expressed concern about *timing*; i.e. some felt the time at which they see their patient was not appropriate to introduce more information about another potential health problem. For example,

…when you see somebody for the first time you have to talk to them for nearly an hour about what their disease means and the side effects of the treatment and all of that and that's without at all talking about vascular risk status and so, I guess, partly that's an issue for my time because it already runs over but it's also an issue for them because they're often frightened and overwhelmed and it's not really the time to be trying to pile on more information. – Haematologist

…people have to be ready to take information on board, I don't think during the peak time of treatment would be so cool [to provide CVD risk assessment/education] –Dietitian

Sub-theme 2.3: Lack of training

HCPs (including a GP, oncologist and cardiologist) perceived inadequate training/education to be a barrier to the delivery of CVD care in cancer.

I don't feel like I have any guide, we know for example managing high BP, if you're a diabetic, your targets are much lower. If you've got a preexisting cancer, so am I aiming for a better target? What are the more important things to manage in terms of decreasing their CV risk? I don't think it's beyond our scope, I just feel like we

don't have the tools and the guidelines to direct those interventions precisely. – GP

Sub-theme 2.4: Delivery of CVD conflicts with HCP's perceived role identity

Many HCPs communicated their perception that delivering CVD care did not align with how they saw their professional role. Some HCPs explicitly described that they (or their discipline) were not appropriate to deliver CVD care. For example:

I'm not up to date on the optimum level to diabetes or blood pressure and I'm not interested in acquiring that knowledge. – Haematologist
I don't see my role managing patients' cardiovascular health. I think what I can do is assess how much I'm going to cause damage and whether or not that treatment is worth doing. But whether or not they need their hypertension to be controlled better, the most I can do is write a letter to the GP. – Medical oncologist

HCPs communicated that they perceived other professions as more appropriate for providing CVD assessment and management. For example,

whether the head clinician likes it or not, they're still the gatekeeper for a lot of referrals [as part of CVD care] – Dietitian
[patients could receive CVD care] if you had a nurse practitioner leading that program and the other nurse practitioners knew that… – Dietitian

Nurses identified GPs as being the most suitable for addressing CVD risk in patients because.

It's part of coordination and care and that's the GP, not like a snapshot of a nurse or a dietitian who has like one episode. – Nurse

A GP suggested that patients could play a role in the CVD care process through consultation with their healthcare team.

Some of them [patients] I think are so motivated and very invested in their health… GP

A haematologist stated that any of multiple professions could achieve this role.

I wouldn't say that there's one person to initiate that conversation, I can see lots of people being good people to initiate that conversation and that ranges from the GP, the medical oncologist, the surgeon, of the surgeons referring for radiation therapy, you know, the rad oncs, other people that are involved, breast care nurses, you know the McGrath foundation nurses, anybody that is involved in the care is in a good position to highlight the thought in the patient that they should think about it. – Haematologist.

Theme 3: HCPs perceived potential challenges for individuals with cancer to engage in CVD risk assessment and management

HCPs identified individual characteristics of patients with cancer that they perceived as barriers to engaging in CVD care. Some of these were demographic or medical factors, including level of disadvantage and prognosis. Other characteristics were related to patient attitudes and outlooks, such as low motivation and a fatalistic outlook.

Sub-theme 3.1: Sociodemographic and medical characteristics

One participant indicated that a patient's engagement in CVD assessment and management would be impacted by aspects associated with a patient's socioeconomic situation, e.g. financial barriers, health literacy and access to healthcare.

it's so difficult to predict who's going to react [to CVD assessment/management] because it's just all about the person and their socio-economic situation… – GP

Being isolated was also identified as reducing the likelihood that some patients would engage in CVD assessment/management.

Always having to reach the people [to provide them with CVD care] that have actually distanced themselves through it all [cancer treatment], they're the harder – the unreachables, so that's always the challenge. – GP

Sub-theme 3.2: Patient attitudes and outlooks

One nurse and one GP discussed their perceptions that aspects of a patient's outlook or mindset would reduce their engagement in CVD care, including: being in denial about their disease, having an "alternative" approach to healthcare, being unwilling/reluctant to make changes, being less demanding/entitled and having a fatalistic outlook.

But it's also denial. All these people with their inbuilt defence mechanisms, so that's [introducing CVD care] really, really difficult. – GP
I've had one or two [patients] who are very alternative so I guess the prospect of … starting any other medication is … revolting [to the patient]. – Nurse.
one or two [patients] are like "I'm not quitting smoking, it's my only joy in life if I die of it then I'm ok." – Nurse.

Being less demanding and having a fatalistic outlook were both specifically raised in the context of older people with cancer:

> …they [the older person with cancer] almost have a sense of being a bit fatalistic, like I'm getting older so why would I bother? – GP
> …they [the older person with cancer] come into the doctor and they don't want to waste your time [asking questions about CVD risk], they're a bit more old school, they're not as entitled or as demanding… – GP

Other participants noted that they perceived patients may interpret the offer of CVD care as overservicing or exploitation:

> …some of the things they [the patient] are worried about is that this is just a money-making thing for the business and that's why you're referring, that goes down very poorly. – Cardiologist

Theme 4: A range of approaches could be used to assess and manage CVD risk in cancer

HCPs discussed a diverse range of solutions and approaches which could improve delivery of CVD care in cancer, including new models of care, clinical pathways, tools and education. In addition, participants discussed the specific components they perceived as important in approaches to CVD care in cancer, including automaticity, communication, and a patient-centred approach.

Sub-theme 4.1: Models of care

HCPs discussed a range of models of care for the identification and management of CVD in individuals with cancer. These included cardio-oncology clinics; care models led/coordinated by selected professions (i.e. GPs and nurses); and multi-disciplinary/teams-based models.

A range of HCPs from nursing, haematology and allied health discussed the potential for a cardio-oncology clinic. For example:

> I would prefer it if there were a kind of cardio-oncology clinic that could see people, even if it's once, and make an assessment and give them a package of advice. – Haematologist

HCPs (including a nurse) suggested a nurse-led model of care, such as that used in other areas of care, could also deliver CVD care:

> I think that if you look at it in cardiology, cardiac rehab has these nurse-led multi-d team…, there's heart failure, there's hypertension and there's AF [atrial fibrillation], this is just an extension of those models of care, in reality we're not reinventing the wheel, we're just stealing basically. – Nurse

Nurses highlighted the role of the GP in coordination of care, implying that this role makes GPs most appropriate for coordinating a cardio-oncology model of care.

> GPs coordinate care. A lot of our referrals more than often are from GPs…that's where we get medical histories from…the GP is getting the letters from us, from oncology, …. the physio, …. lymphedema assessment from the radiotherapist… So, they're the linchpin. – Nurse

Multi-disciplinary or teams-based approaches to care were discussed by a range of HCPs. Several asserted the success of multi-disciplinary teams in other areas of care, and highlighted that by involving a range of professions in the model of care less responsibility is felt by individuals.

> Well, I guess, I think the ideal arrangement [is] … a multidisciplinary team with cardiologists and specialists and so on together with the dietician and educator what have you. – Haematologist
> …you kind of build up a bit of a team and sort of a collaboration so people don't feel like they're always bothering the same person… – Physiotherapist

Sub-theme 4.2: Clinical pathways

HCPs discussed the potential for a clinical pathway to ensure coordinated CVD care in cancer.

> "Well, ideally there would be a referral pathway." – Dietitian

> "Yeah. I think it should be referral and integration so that the messages are transferred over to GP practice as well so when they move to specialty care that you have a clinical pathway where you've got integrative care." – Nurse

> "I think there needs to be a systematisation of the workflows, and that has to be balanced up against the workforce capacity to deliver the care." – Cardiologist

HCPs asserted the importance of protocols in providing care.

> "that's how these things will work best, you have a protocol, a system that just gets followed based on the best available evidence." – Cardiologist

However, there was also discussion about how protocols are specific to the health service and are unlikely to be transferrable to other services.

> the trouble [with developing a CVD risk reduction approach/intervention] is that every location, geo-

graphically, will have a slightly different solution in terms of the process because of the way pre-existing processes are there. – Cardiologist

Sub-theme 4.3: CVD risk assessment and management tool

Several participants voiced their support for the development and integration of CVD risk assessment and management tools to improve CVD care in cancer, including treatment decision-aides, risk stratification and education tools.

Participants varied in their opinions regarding what would be the most useful purpose of a tool in the area of cardio-oncology, with some asserting the need for the tool to aid in treatment decisions whilst others indicated they would prefer the tool to stratify patients according to level of risk so that care provision can be triaged accordingly.

a tool… that could provide me with some evidence in terms of that person's cardiovascular risk and particularly if it told me that they had a high risk of dying because of their heart problems, then that might actually influence the decision for the [anti-cancer] treatments that might be recommended for that patient – Nurse practitioner

Most HCPs preferred a digital tool, but some mentioned barriers to this indicating that some clinicians may be more likely to use a pen and paper version. Ipads, websites, and smartphones were identified as potential delivery modes for a digital tool.

[the tool has to be in the form of] either a phone app or it has to be online – Nurse

I think probably online portal, like I could just have it as a bookmark and then when I was seeing patients just kind of flick to that. – Physiotherapist

HCPs from a range of professions asserted the importance of specific aspects/components of a tool to deliver CVD care. Participants identified automaticity and embedding the tool into a current system (e.g. limited need for HCP to be involved in data collection/analysis) as being crucial.

…I think if you could use something … that's running in the back of EMR [electronic medical records] and pulls all the information and spits you out a risk, I think that would be helpful because then you know who to target. – Dietitian

I don't [want to] have to somehow input it [data about CVD assessment and management] back into the notes – GP

A lot of these kinds of tools, they should be automated into our work – Medical oncologist

Participants indicated that a tool should also facilitate communication, particularly between HCPs involved in the patient's care.

I just think there needs to be some sort of feedback to them [other HCPs], if you're doing some sort of screening that this has happened. - Medical oncologist

Participants identified that not all patients would be appropriate for the administration of a tool, and tools should be flexible so they can be tailored to the individual needs of different patients.

What I'm trying to actually say is that these tools are helpful, but we cannot actually use that on every patient, it just needs to be identify the situation where we can actually use it or individualise it for patients. – Medical oncologist

Sub-theme 4.4: Education

Participants also identified education and awareness in both HCPs and patients as important in delivering CVD care to people with cancer. A GP communicated that they would feel more capable of delivering CVD care if they were educated appropriately.

It's some guidelines or education [of GPs] that's kinda missing. – GP

Education of patients was identified by several participants as having a positive impact of integrating CVD care into cancer. This could, for example, lead to patients initiating conversations with HCPs about their CVD risk profile, and being more involved in the management of their own risk.

I think it's education of providers, I think its education of patients, particularly where we're looking at patient-centric care, patients being more involved in their health care making decisions, I think patients need to be made more aware. – Cardiologist

Discussion

The present study presents a comprehensive qualitative analysis of the perceptions of HCPs regarding the identification and management of CVD in older people with cancer. We found HCPs were aware of CVD risk in cancer and perceived it to be important but had concerns about their own ability to deliver CVD care. We also found a lack of consensus of HCPs' perceptions regarding the best way to reduce the impact of CVD in cancer.

Previous research specifically examining HCPs' perceptions regarding cardiotoxicity of anti-cancer treatment

reported some HCPs were not aware of the increased risk and associated poor outcomes of CVD in cancer patients and those that were aware did not perceive the relationship between CVD and cancer to be an important issue. For example, Koop and colleagues [22] reported that majority participants (Dutch oncologists, $n = 12$) were unaware of the incidence of cardiotoxicity and perceived cardiac surveillance as burdensome, and a recent survey ($n = 190$ Dutch cancer and cardiac specialists) found only 33.2% were concerned about the cardiotoxic effects of anti-cancer treatment [23]. However, in line with our research, a survey of 106 cardiology specialists in the US found that > 70% perceived potential CVD complications as an important consideration of anti-cancer treatment [24]. Many factors may influence awareness and perceived of CVD risk in cancer. For example, training and education in CVD risk in cancer vary across institutions [24]; and individual HCPs may have different preferences/interest in cardio-oncology [25]. It is possible that our findings reflect a growing awareness of the field of cardio-oncology through recent publications of recommendations and guidelines in this area [26].

A novel finding of our research was that HCPs were concerned about their (and their profession's) abilities to deliver CVD care in cancer alone. This finding has important implications for the development of future approaches to improve CVD care in cancer, where CVD care, like the rest of cancer care, is likely to require a teams-based approach. In addition, we are not aware of other research highlighting a perceived conflict between delivering CVD care and role identity in HCPs involved in cancer care. Although conflicting role identity was identified as a barrier in a systematic review of 43 papers examining staff-reported barriers to the implementation of hospital-based interventions such as the administration of screening tools and behaviour-change interventions, this did not include any research involving CVD care after cancer [27]. Our finding can inform future approaches that aim to improve CVD care in cancer, e.g. suggests the importance of clarifying HCP's expectations around their role and responsibilities, and providing them with the training they need to conduct expected tasks effectively.

Our research also identified HCPs' perceptions regarding patient-level barriers reducing engagement in CVD care, including socioeconomic disadvantage, lack of motivation, having a fatalistic outlook and adversity to more intervention. We could only locate one previous study that reported HCPs' perceptions regarding potential patient-level barriers [22], and this study also identified patient socio-economic disadvantage and having a fatalistic outlook as potential barriers to CVD care engagement [22]. In addition, we found that responses did not differentiate between older and younger people with cancer, which may suggest that there are no differences in perception of barriers (and preferences) related to age. Although our findings go some way to bridging the gap in evidence in this area, the critical next step of our broader research program is to examine patient-level barriers from research involving patients themselves and this will be the next step for our group. We are unaware of any previous research which has reported cancer patients' perspectives regarding barriers to engagement in CVD care.

We identified that there is a lack of consensus for a single approach to reduce the impact of CVD in cancer, with multiple suggestions including a new model of care, a clinical pathway, education and a tool to detect and manage CVD risk. Based on the findings of this research, we propose that effectively reducing the impact of CVD in cancer requires the development and implementation of a suite of intervention types. The diversity of solutions which have emerged in our research supports a complex multi-component intervention may be needed to reduce the impact of CVD in cancer. We also propose the diversity of barriers identified in our research supports the need for a multi-pronged approach, and that any intervention should be tailored to the context in which it will be delivered and input from people with cancer.

Strengths and limitations

The major strength of this research is the comprehensive, reflexive and flexible approach employing the RTA methodology to increase understanding of HCPs' perceptions regarding CVD in cancer. There are also notable limitations of our research. Majority of participants were employees of one hospital and although several professions participated in our research, there were small numbers from some disciplines (e.g. one cardiologist).

Conclusion

This qualitative study involving a range of HCPs suggests that while majority are aware of and appreciate the importance of CVD risk in cancer, they experience barriers to delivering care and suggest a diverse range of strategies for improving CVD risk identification and management. Future research involving cancer survivors is needed to co-design acceptable interventions to improve CVD identification and management in cancer.

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Author contribution All authors contributed to the study conception and design. Material preparation was performed by Reegan Knowles and data collection and analysis were performed by Reegan Knowles,

Emma Kemp and Bogda Koczwara. The first draft of the manuscript was written by Reegan Knowles and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Declarations

Ethics approval This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Southern Adelaide Local Health Network Ethics Committee (22/01/2020; HREC/19/SAC/309).

Consent to participate Informed consent was obtained from all individual participants included in the study.

Conflict of interest The authors declare no competing interests.

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9.3 Appendix 3: Topic Guide for Qualitative Study of Healthcare Providers and People Diagnosed with Cancer (reported in chapter 4, Appendix 2)

Co-design of a risk stratification tool to identify cancer survivors at risk of cardiovascular disease

Focus group and interview topic guide

Please note this topic guide will be developed iteratively depending on successive feedback from clinicians and cancer survivors; i.e. responses to these questions in earlier focus groups and interviews may inform the direction of later focus groups and interviews. Depending on the type of stakeholder participating in focus groups/interviews (e.g. consumers, cardiologists, oncologists), some topics in this guide may be emphasised or explored more or less than other topics, and different forms of the same question may be used in order to communicate relevant meanings.

Begin by introducing broad concepts relevant to the project, where appropriate (depending on participant type:

- What we mean by heart disease/cardiovascular disease
- What we mean by people with a history of cancer – e.g. people currently undergoing treatment for, or otherwise living with cancer (i.e. even if having 'treatment break' in treatment for metastatic cancer), and also people who are 'survivors', i.e. previous history of cancer that was successfully treated.
- Explore/clarify the concept of cardiotoxicity of cancer treatment and cardiovascular disease that may or may not relate to cancer treatment and emphasise that the discussion will relate to both.
- What we mean by cardiovascular disease risk, identification/stratification of risk, triage and management.

Introduce the concept of the Risk Stratification Tool:

- What we hope it can be used for
- What has been developed so far – i.e. the algorithm and what it is able to estimate
- Why we think it is important, and how we think it can lead to positive change in practice which can ultimately improve health outcomes for the cancer population
- Introduce that we want their feedback regarding preferences for the administration and format of the tool.

Move on to discussion topics:

1. What was/is your understanding of the risk of heart/cardiovascular disease in people with cancer or cancer survivors?

2. How important do you think it is for the risk of heart/cardiovascular disease to be identified in cancer patients and survivors?

3. In your experience how well is the risk of heart/cardiovascular disease for people with a history of cancer addressed? How do you think risk of heart/cardiovascular disease in people with a history of cancer is currently addressed? How effective do you think this is?

4. How easy or difficult do you think it is to identify the risk of heart/cardiovascular disease in people with cancer/cancer survivors? Why?

5. What needs do you think there are in addressing the risk of heart/cardiovascular disease in people with a history of cancer?

6. Are there barriers to effectively identifying the risk of heart/cardiovascular disease in people with a history of cancer? If so, what do you think these barriers are? How important/significant are these barriers? Consider barriers that relate to patients, providers, health system, society (ie media)

7. Are there facilitators/enablers/factors which can or do help in identifying the risk of heart/cardiovascular disease in people with a history of cancer? If so, what do you think these enablers are? How important/significant are these enablers? Consider barriers that relate to patients, providers, health system, society (ie media)

8. Do you think that the proposed cardiovascular disease risk stratification tool concept could assist in identify those at risk?

9. Please discuss your preferences for a proposed tool with regard to the following:

- Timing – when should the tool be administered to the patient/survivor? Ie start of treatment, end of treatment, at diagnosis etc.
- Who should administer the tool – e.g. cancer nurse, oncologist, cardiologist, other? Should the patient self-administer the tool after being directed to it by a care provider?
- What format should the tool be in, i.e. pencil and paper, tablet/smartphone app, website?
- How long should the administration of the tool take (i.e. ideally it should take no longer than ?)
- Should patients/survivors be re-screened? How often? At specific milestones in the cancer journey (i.e. beginning/end of treatment etc.) or annually/biannually?
- What training do you think will be required for the staff involved in the administration of the tool (i.e. what mode?)
- Stratification of risk: Stratification of risk refers to how patients are grouped according to the results they show after completing the tool (ie how much risk of CVD do they have), how do you think patients should be grouped? Cut-offs? Low, moderate and high risk groups etc?
- How do you think information about the level of risk should be disseminated, and to whom? E.g. alerts to care providers via the app/email? Information in electronic medical records? Oncologist, nurse, GP, patient, family, cardiologist?
- Management of risk: what should be in place for the referral/management pathway after risk is identified? Different pathways depending on risk? E.g. provide written information about reducing risk through behaviour change; refer to existing community programs for behaviour change, e.g. quitline etc; refer to cardiologist?

10. Do you have any specific concerns about the use of a tool to identify cancer patients and survivors at risk of CVD? What do you think could be barriers to the implementation of the tool?

11. Can you identify any positive outcomes you think could be associated with the administration of the tool, what are some enablers and facilitators for the use of the tool?

12. Do you think the development, evaluation and implementation of this risk stratification tool is worthwhile? Do you think there will be good uptake of tool by administrators and

patients/survivors? Would you be happy to use the tool? Do you think it has the potential to reduce the impact of CVD in cancer patients/survivors?

Any other comments?

9.4 Appendix 4: Knowles et al., 2023 (239), published paper: "There could be something going wrong and I wouldn't even know": a qualitative study of perceptions of people with cancer about cardiovascular disease (CVD) risk and its management"

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"There could be something going wrong and I wouldn't even know": a qualitative study of perceptions of people with cancer about cardiovascular disease (CVD) risk and its management

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Abstract

Purpose Despite being at higher risk, many people with cancer do not receive adequate cardiovascular disease (CVD) risk assessment or management. The purpose of this research was to examine people with cancer's perceptions, experiences and needs regarding CVD risk factor awareness, assessment and management.

Methods We conducted 15 individual interviews to examine people with cancer's perspectives regarding CVD care in cancer. Reflexive thematic analysis was utilised to collect and organise data into themes and to synthesise findings.

Results Fifteen people (6 males) diagnosed with diverse cancer types participated. Majority participants were not or only somewhat aware of CVD risk in cancer, but all expressed it was an important issue. A diverse range of priorities and needs for CVD care was discussed, including some participants' prioritisation of dealing with cancer and preferred amount, type and manner of information provision and support. Websites and brochures were identified as potential solutions for optimising CVD care.

Conclusions Codesign methodology should be used to engage patients in the development of flexible, tailored resources to increase awareness of CVD risk and strategies for its management.

Implications for Cancer Survivors Perceptions of people with cancer regarding CVD care can inform new interventions that reduce the impact of CVD in cancer.

Keywords Cardiovascular disease · Cancer · People with cancer · Perceived needs

Background

Cancer is associated with increased risk of cardiovascular disease (CVD) and resulting morbidity and mortality because of shared risk factors (e.g. smoking and age) and cardiotoxic anticancer treatments including radiotherapy and chemotherapy [1–4]. Older people are particularly vulnerable, given they have higher rates of both cancer and CVD compared to their younger counterparts [5–7]. Guidelines recommend people with cancer receive CVD risk factor assessment, surveillance and be assisted to reduce their risk [8, 9] including support to engage in healthy lifestyle behaviours, such as physical activity [10, 11] and smoking cessation [12].

Despite evidence and guidelines, many people with cancer do not receive adequate CVD risk assessment and management because of multiple reasons including clinician lack of time, resources or belief that this is not their role to do so [11, 13–15]. Older people may be even less likely to receive adequate CVD care, given there is evidence that preventive health services are delivered less frequently as age increases [15].

In previous research conducted by the authors, health care providers (HCPs) reported patient-level factors that they perceived may impact patients' engagement in CVD care

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(including socioeconomic disadvantage, a fatalistic outlook and aversion to further medical intervention) [16], but to the authors' knowledge, no research has examined perceptions of people who have been diagnosed with cancer regarding their awareness of CVD risk in cancer, barriers and enablers to engaging in CVD risk assessment and management, or preferences for improved approaches to CVD care in cancer. Therefore, the aim of this research was to examine people with cancer's perceptions and experiences of CVD risk factor awareness, assessment and management in cancer.

Methods

Design

This was a qualitative study involving individual interviews with people with cancer.

Eligibility and recruitment

People aged 18 years or older, diagnosed with any type of cancer regardless of stage or prognosis, and at any stage on the cancer continuum (e.g. during treatment, survivorship) were eligible to participate. People with cancer were recruited using a non-random, purposive sampling technique. Clinicians working at Flinders Medical Centre, a large metropolitan, tertiary referral centre in Southern Australia (oncologists and oncology nurses) and known through researchers' existing networks, agreed to introduce the research to potential participants. A recruitment flyer and Participant Information and Consent Form were provided to potential participants by their clinician, and the contact details of patients willing to be contacted were provided to researchers. A researcher (RK) then contacted all potential participants by telephone and arranged informed consent and interviews for participants (either in person or via telephone).

Study procedures

The same researcher (RK) conducted all semi-structured individual interviews. Participants were prompted to discuss their experiences and perceptions around CVD risk in cancer. We continued to recruit participants until we perceived adequate "information power" [17], that is, sufficient data to address the aims of the research, to provide a meaningful contribution to the research literature and to inform future research and practice, particularly in the development of a new approach to CVD risk identification and management in people with cancer. Ceasing recruitment based on reaching adequate information power aligns with the principle that original data may continue to emerge with subsequent interviews, and the decision to cease recruitment is therefore pragmatic [17].

Data analysis

Interviews were audio-recorded and transcribed verbatim. We used NVivo (Version 1.3) [18] to assist in coding and theme development, and the construction and interpretation of findings occurred through a series of discussions between all researchers.

Reflexive thematic analysis (RTA), underpinned by a critical realism, was used to analyse data. Our analysis, as per the RTA framework [19], involved data familiarisation, coding, initial theme development, review of themes, refinement and reporting. The majority analysis was semantic and inductive, meaning the construction of knowledge was based on the data explicitly communicated by participants in their interviews. However, we also used latent analysis to identify more complex meanings which underlie participants' responses. RTA is an approach that acknowledges the role of the researcher in the construction of knowledge derived from data collection, analysis and interpretation(19). The researchers practise reflexivity through all stages of analysis to analyse how our own perceptions and experiences influence the construction of knowledge derived from the analysis. The process of the construction of knowledge was iterative, recursive and flexible, where new data and ideas arose in subsequent interviews, through researcher discussions and drafting of results.

Ethics

Ethics approval was granted by the Southern Adelaide Local Health Network Ethics Committee on 22 January, 2020 (HREC/19/SAC/309).

Results

A total of 15 people ($n=6$ male) participated in the research. Thirteen interviews were conducted via telephone, and two were conducted in-person. Six participants had been diagnosed with breast cancer, one with oesophageal cancer, one cervical cancer and one rectal cancer. Six participants did not report the type of cancer they had been diagnosed with. The interviews lasted between 10 min, 33 s and 46 min, 21 s (median = 23 min, 1 s).

The analysis identified two themes, one of which had four subthemes (Fig. 1).

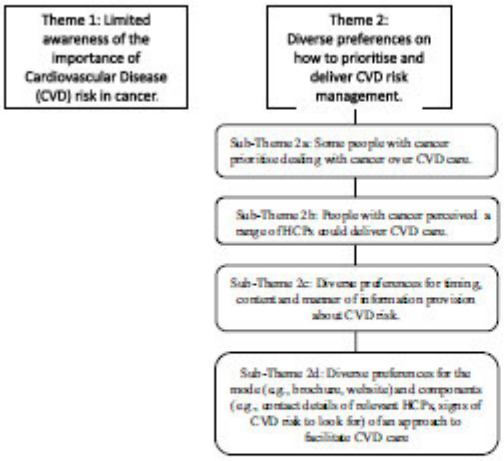

Fig. 1 Overview of themes and sub-themes summarising people with cancer's perceptions of CVD risk identification and management in people with cancer

Theme 1: Limited awareness of the importance of CVD risk in cancer.

The majority of respondents indicated that they did not know CVD risk was increased in cancer and had not been told about this by anyone in their cancer care team. For example, "I don't think I knew that it [cancer] really affected the heart."

Others indicated that they deduced there was a risk, without having been explicitly informed by anyone in their cancer care team.

> *"He [my oncologist] mentioned the word toxic chemotherapy… I knew exactly what he meant… [the oncologist told me it was] just toxic. Yeah, nothing [specific] to do with the heart. I know, it's my understanding that that that kind of chemotherapy actually destroys the heart muscles, reduces the ejection fraction."*

Some were unsure as to whether they had been informed of increased CVD risk, querying their own capacity to absorb information at the time it was provided.

> *"At the beginning I wasn't really aware of it [CVD risk] at all. It [CVD risk] may have been mentioned to me perhaps in passing earlier on, but because you're taking on board so many other things and you're so concentrated on what's happening to you with your cancer, I don't really remember even considering it or thinking that it could be a concern back then".*

> *…"I know it's silly, but they could have mentioned it [CVD risk], but the thing is I reckon for the first three months I didn't hear a word that they said."*

A minority of respondents were aware of increased CVD risk, most of whom had been informed of this by their oncologist.

> *"Yeah, especially after radiation that it [CVD risk] could definitely affect me."*

All respondents agreed increased CVD risk is an important issue and that it is important to be aware of it.

> *"Oh, look, I just like to know, that's all. There's no reason, I just want to know what's happening, you know? I don't want to be – I want the doctor to tell me the truth about stuff like that."*

Some participants acknowledged that informing patients about increased CVD risk could elicit negative emotions, but all but one reported they wanted to be fully informed despite this. For example, one participant said:

> *"I want them to tell me [about CVD risk…irrespective of how devastating it would be…"*

Only one participant suggested they did not want to be told about CVD risk:

> *"And I just don't know that it's fruitful to be told of all the things that might go wrong because then you almost manifest that to happen."*

Theme 2: Diverse preferences on how to prioritise and deliver CVD risk management. *management*

Diverse preferences for when, how and who should be involved in CVD care were discussed.

Sub-theme 2a: Some people with cancer prioritise dealing with cancer over CVD care.

A small number of respondents discussed they prioritised dealing with cancer over CVD care.

> *"I suppose the big picture's trying to sort the other – the cancer out".*

Sub-theme 2b: People with cancer perceived a range of HCPs could deliver CVD care.

Participants identified HCPs they perceived to be appropriate to assist them to self-manage their needs and provide CVD assessment and management, including nurses, oncologists

and GPs. They provided reasons for why they had determined these HCPs suitable for this role. For example,

> *"Because you can get in to see the GP usually a lot easier than you can the oncologist and if the GP's doing ECGs and he's checking your blood pressure and all the other general medication and issues, I think the GPs do one that actually know about it and do something about it for you."*
> *"…he's [the GP] supposed to be the guy that takes care of me and the oncologist is the guy who looks after the cancer itself. So, this heart disease, it's not part of the oncology treatment, it's a separate issue. So, therefore, your GP should be the guy that's says, alright, cancer – we can start expecting heart disease as well."*
> *"these guys [nurses] see everyone every day constantly and they don't back down, they come up again and try and help support you."*

One participant communicated that a range of HCPs could effectively guide them to manage aspects of their CVD care:

> *"Everyone seems to be fairly knowledgeable [about everything health-related]… so I really wouldn't mind who [guided me]."*

Sub-theme 2c: Diverse preferences for timing, amount and manner of information provision about CVD risk

Some respondents felt the timing of CVD risk assessment and management was important and could impact their engagement with CVD care. Respondents had specific ideas about *when* would be appropriate, and this varied from participant to participant. For example, some participants would prefer to engage in CVD risk management after treatment:

> *"[At the end of treatment] I would have a capacity to think okay, now I'm getting back into the swing of life… I think I would have the mental capacity to process the information…"*

In contrast, another participant expressed a preference for information to be provided earlier in the cancer continuum:

> *"I'd rather know all of it [cancer and associated risks including CVD risk] in one go, or like spaced out so I kind of absorb it and then I know the next bit and the next bit, but I want it all relatively soon."*

There were also diverse preferences for *how much* information should be provided, suggesting that flexible and tailored information provision approaches are needed. For example,

> *"I'm the sort of person that needs to know basically what's going on, I don't need to get into the really nitty gritty, but I like to know and then I try and process it and then I try and get on with it…"*
> *"Sometimes you can get bombarded with stuff you don't need to know."*

Other participants reported a preference for being provided with a comprehensive amount of information about CVD risk. For example,

> *"I'd rather have all the information and then I can read back through it if I need to, if I feel like I need to…"*
> *"I want to know all the information. Yeah. Yeah, definitely. I think that you can't advocate for your health for yourself if you're not informed."*

Although respondents reported they want to be informed of CVD risk in cancer, many communicated that the *way in which information is provided* should be carefully considered. For example:

> *"Definitely [CVD risk information should be] presented in a way that doesn't scare you more because you're already so scared."*

To illustrate the importance of the manner of CVD care, one participant gave an example of a negative experience of how they received care previously when they were admitted into hospital (after being diagnosed with COVID-19):

> *"One or two doctors need to get some bedside manner… but I probably would have if they had taken it differently – and it might sound a bit precious, but I do think if you can just do it a different way, just you're not as severe, do you want to be resuscitated or what?"*

Sub-theme 2d: Diverse preferences for the mode (e.g. brochure, website) and components (e.g. contact details of relevant HCPs, signs of CVD risk to look for) of an approach to facilitate CVD care.

A range of suggestions was provided by respondents regarding how CVD risk information could be provided and how people with cancer can be supported to undergo CVD risk assessment and management. A brochure and website for providing CVD risk information and guidance were suggested.

> *"Website is pretty good too. You can go on that website and go and read what to expect."*

Another respondent discussed their preference for support groups in which participants discuss and assist each other to navigate aspects of cancer (including CVD risk).

"So, I'd like to be able to have a resource or the opportunity to regularly check in with others going through similar treatments and processes and I suppose there's a warmth attached to that, talking to people that are going through similar experiences, but there's also a real knowledge base asking really targeted individual questions in the hope that, yeah, okay, someone else has had that same experience and this is what was advised to me, so it can either then build your confidence that everything's probably okay."

Other respondents indicated they would prefer they were informed about CVD risk and supported to manage their risk through direct interactions with HCPs. For example,

"Speaking to somebody [about CVD risk] really, but also reading, definitely where you can ask questions."

Respondents also discussed specific components of an optimal approach to reduce the impact of CVD in cancer including:

(a) Provision of information about CVD risk in cancer:

"I want to know all the information. Yeah. Yeah, definitely. I think that you can't advocate for your health for yourself if you're not informed".

(b) List of CVD risk-related symptoms/signs the person with cancer should be aware of:

"I mean, there could be something going wrong and I wouldn't even know. Sometimes I'm hopping around and think oh, okay, fine, you know? So, you just don't know what level of damage has happened or is happening and so, I don't know, if there is some sort of a measure…"

(c) List of HCPs/services that could be contacted to assist with CVD issues:

"I think it's…where to go to get advice if you feel you need to..."

(d) Self-management support:

"In the end, my health is my responsibility. I'm the one that needs to study up on these things and to understand how my body's going to respond to the cancer and I'm the one who needs to [deal with it]."

(e) Guidance/support for CVD risk reduction (including behaviour change):

i"If [I was advised that] a specific type of training will reduce your risk of heart damage…, I'd try and put them into my training…"

Discussion

This study of perceptions of people diagnosed with cancer regarding the CVD risk assessment and management shows that majority of respondents were not fully aware of CVD risk in cancer but once aware, they perceived it to be an important issue and had diverse preferences on how to prioritise and deliver CVD risk management.

The majority of participants in our study were relatively unaware of increased CVD risk in cancer, is concerning given guidelines which highlight the importance of CVD risk identification, monitoring and management in cancer [8, 9]. We also found that majority of people with cancer want to know about CVD risk, which aligns with evidence that providing patients with health care information can improve a patient's feelings of control, decrease anxiety and even improve clinical outcomes [20]. In contrast, some respondents expressed they may have been told about CVD risk but had not "absorbed" the information due to "information overload" and/or prioritisation of coping with their cancer diagnosis and treatment. This aligns with concerns of cancer care providers that people with cancer may be burdened by receiving information about CVD risk whilst dealing with cancer [16]. Our findings provide an example of the concept termed by Jensen et al. "cancer information overload" (CIO), where up to three quarters of people with cancer have reported being overwhelmed by information [21]. Given CIO can induce fatalistic thinking and reduced engagement in positive health behaviour [21], it is important to consider how to meet the expressed needs of patients to be health-informed, whilst also reducing the risk of CIO. Thoughtful consideration of how, how much and when information provision occurs may be able to achieve the balance between these opposing concepts.

We identified diverse priorities and preferences for CVD risk identification and management in cancer. This is unsurprising given the lack of awareness of CVD risk of majority participants, which implies limited (previous) consideration of the possibility and practicality of potential solutions. It is also important to acknowledge that diversity of health care preferences likely reflects differences in people (e.g. demographics, attitude/outlook and personalities) and their disease (e.g. cancer type and stage in continuum). Hence, our research highlights the need for a new approach to CVD risk identification and management that is holistic, multi-pronged, flexible and tailored to individual needs and preferences. The importance of consumer engagement in health research and services is well-established [22], including recognition that the preferences and ideas of consumers (in this case people affected by

cancer and cancer care providers) should inform new care approaches [22] through codesign methodology. The diversity of preferences identified in our research necessitates a comprehensive codesign approach (e.g. multiple rounds of discussion) to facilitate the development of ideas and preferences leading to approach design.

Examining perceptions of people affected by cancer regarding CVD risk in cancer facilitates comparison with the authors' previous research involving cancer care providers [16]. An important difference between the perceptions of people with cancer and those who provide cancer care was perceived barriers to CVD. Cancer care providers identified multiple barriers including perceived conflicts with role identity and lack of time and training, whilst people with cancer did not identify barriers (16). This may reflect patients' lack of awareness of CVD risk in cancer, meaning they likely have not considered potential barriers, and may perhaps also reflect health care consumers' trust in the Australian health care system. Meanwhile, HCPs are aware of CVD risk and that care is not always adequate, so they are more likely to have considered potential reasons for this. In contrast, an important similarity between people affected by cancer and HCPs' perceptions about CVD in cancer emerged, in that both had diverse ideas for solutions to optimise CVD care. This agreement reiterates the importance of future approaches to CVD care in cancer being flexible and individualised and emphasises the need for authentic and meaningful contribution of a broad range of stakeholders in the conceptualisation, design and implementation of CVD interventions for this population.

Strengths and limitations

This is the first study to examine people with cancer's perceptions and experiences of CVD in cancer. There were important limitations of our research. All participants were recruited from one health care setting and were of the same ethnicity, limiting extrapolation of findings to other contexts. We did not collect data from participants regarding cancer stage or phase on the cancer continuum (e.g. during active treatment, survivorship), nor the presence of existing CVD or CVD risk factors, meaning comparisons of perspectives according to demographics was not possible.

Conclusion

People with cancer tend to have limited awareness of CVD risk and have diverse preferences regarding how to prioritise and manage it. Future research should employ codesign methodology to engage patients in the development of flexible, tailored resources to increase awareness of CVD risk and strategies for management.

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Author contribution All authors contributed to the study conception and design. Material preparation was performed by Reegan Knowles and data collection and analysis were performed by Reegan Knowles, Emma Kemp and Bogda Koczwara. The first draft of the manuscript was written by Reegan Knowles and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Data Availability The data collected for this research is not available given the risk that the data may lead to the identification of participants.

Declarations

Ethics approval This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Southern Adelaide Local Health Network Ethics Committee (22/01/2020; HREC/19/SAC/309).

Consent to participate Informed consent was obtained from all individual participants included in the study.

Competing interests The authors have no relevant financial or non-financial interests to disclose.

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9.5 Appendix 5: Paper submitted to Journal of Cancer Survivorship, 2025: "My Heart and Cancer': Codesign and usability testing of a cardiovascular disease risk management website for cancer survivors"

TITLE PAGE

Title

'My Heart and Cancer': Codesign and usability testing of a cardiovascular disease risk management website for cancer survivors

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Abstract

Purpose

There is a lack of quality resources and support to address cardiovascular disease (CVD) risk in cancer, so we aimed to codesign a website for people affected by cancer, to self-manage CVD risk in cancer.

Methods

We conducted two rounds of codesign (via focus groups and interviews) with people affected by cancer and cancer care providers to iteratively develop a website to support people affected by cancer to self-manage CVD risk. Usability testing using the 'Think Aloud' approach facilitated further feedback about the website from people affected by cancer. We audio-recorded, transcribed and descriptively analysed round 2 codesign and usability sessions to inform website revisions and report findings.

Results

Codesign round 1 involved 16 individuals (7 people affected by cancer, 9 cancer care providers), with 9 participating in round 2. A further five people affected by cancer participated in usability sessions. Feedback was categorised into 5 topics: content, design and interactivity, navigation, layout and need for website. The website was developed iteratively, including 27 changes elicited from usability testing, until the final 'My Heart and Cancer' was developed.

Conclusions

'My Heart and Cancer' is the first website developed to support self-management of CVD risk factors in people diagnosed with cancer and may help to reduce the impact of CVD risk in cancer, which is associated with significant morbidity and mortality in this population.

approach to improving health outcomes for people affected by cancer (22, 23), including improving self-efficacy(24). The development of a website to provide information and support for CVD risk in people affected by cancer also aligns with needs and potential solutions and goes some way to addressing barriers to CVD care, identified by healthcare professionals and people affected by cancer in our previous qualitative research, including raising awareness and facilitating self-management. In addition, given preferences for information and support needs are diverse in these studies, a website can cater to individual preferences by allowing users to navigate to areas of interest and to access more detailed information if wanted.

In this study, we aimed to codesign and test the usability of a website for people affected by cancer, to support self-management of CVD risk in cancer.

METHODS

Study Design

Our study design was guided by the principles of the person-based approach to intervention development, in which the website was developed based on the perspectives of those who will use it (25). To develop the website, we utilized a qualitative two-round co-design methodology involving focus groups and individual interviews, supported by an external website developer (Stage 1). Qualitative methodology using the 'Think Aloud' approach (26) was then employed to examine the usability of the codesigned website (Stage 2).

Participants

Stage 1: Codesign

Participant group 1: people affected by cancer (n=8)

People aged 18 years or older diagnosed with any type of cancer, at any stage on the cancer continuum (e.g., during treatment or afterwards), and well enough to take part in an individual interview or focus group were eligible to participate. In addition, friends, family and informal carers of people diagnosed with cancer were eligible.

Participant group 2: Healthcare professional providing cancer to people affected by cancer (n=8)

Health care professionals who spend at least 10% of their work time providing care to people affected by cancer were eligible to participate.

Stage 2: Usability testing (n=5)

Participant Group 3: People aged 18 years or older, diagnosed with any type of cancer, at any stage of the cancer continuum, and who were available and able to attend an in-person usability session were eligible to participate in Stage 3.

Potential participants for Stages 1 and 2 were identified through the existing networks of researchers, using non-random purposive sampling in an attempt to achieve diversity in cancer types and sex of people affected by cancer (Stages 1 and 3), and healthcare professions (Stage 1 only). An introductory email was sent to eligible participants to provide a brief description of the study and a link to an online participant information and consent form. Those who provided informed consent were contacted to schedule an individual interview or focus group (Stage 1), or usability session (Stage 2).

Study procedures

Stage 1: Codesign

This stage involved two rounds of codesign sessions as either focus groups or individual interviews, conducted online or in-person by the same researcher (RK). For focus groups, people affected by cancer participated in separate groups to healthcare professionals.

Materials: Developing a wireframe for Codesign Round 1

Researchers developed a basic wireframe using Microsoft PowerPoint (27) to facilitate participant discussion regarding preferences for the structure, format and content of the website. Figure 1(A-J) shows the pages of the wireframe. The structure of the website was informed by existing literature (13, 14). We used this literature as a basis for six suggested sections: provision of information about CVD and cancer, assessment of CVD risk, signs and symptoms of CVD, self-management of CVD risk, healthcare professionals' role in CVD risk management, and accessing services and resources for CVD risk information and support. All other aspects, format and specific content of the website were not pre-determined, and the wireframe was developed to prompt codesign participants to contribute their ideas and preferences.

Procedure: Codesign Round 1

All Codesign Round 1 sessions were facilitated by the same researcher (RK). Sessions were focus groups of 3 or 4 participants, or individual interviews, conducted in-person or online according to participants' preferences. Only

participants of the same type (i.e., persons affected by cancer OR healthcare professionals) participated in the same session. A topic guide (see Supplementary 1) was used, along with the wireframe and prompts.

Each session began with the facilitator describing the purpose of the website. Participants were encouraged to speak at any time throughout the sessions, about specific aspects of the wireframe as well as to contribute general comments, ideas and preferences about the website more broadly. Participants were encouraged to discuss/indicate their preferences for:

- Website structure (i.e., whether the main sections of the website meet the needs of intended users);
- Website navigation (i.e., how users should be able to navigate from page to page within the website);
- Content (i.e., what information should be included on the website); and
- How to increase user engagement and interaction with the website (e.g., videos, pictures and activities).

Each slide of the wireframe represented one 'page' of the website. To facilitate discussion, multiple questions were incorporated to appear one-by-one on each page. The facilitator displayed each section of the wireframe (i.e., slide) sequentially, on a large monitor for in-person sessions or on the screen for online sessions. All participants had the opportunity to provide feedback about any part of the wireframe. Figure 2 illustrates an example of the questions presented for the landing page of the website. All sessions were audio-recorded, and the facilitator took written notes throughout. The perspectives of the participants in Round 1 were discussed by researchers in a series of in-person and email exchanges to identify how preferences for website structure, navigation, content and user engagement enhancement would be represented in a website prototype (version 1) for Codesign Round 2. This was an iterative process in which the researcher who conducted the co-design sessions developed aspects of the website prototype (version 1) based on Round 1 data and research literature, which were circulated to the wider research team for feedback. Revisions were made based on this feedback. Where there were differences in opinions between researchers, consensus was reached through discussion. This process continued until the prototype (version 1) was finalised for Codesign Round 2. At this point the name 'My Heart & Cancer' was suggested for the website. The website prototype (version 1) was developed using Qualtrics (28) a software program used to develop surveys and websites, to ensure that in the Codesign Round 2 participants were exposed to a website format and could provide informed feedback about content, navigation and formatting.

Procedure: Codesign Round 2

All Codesign Round 2 sessions were conducted as individual interviews (in-person or online), by the same researcher (RK). In these sessions, participants were exposed to all sections of the 'My Heart & Cancer' website prototype (version 1) using a laptop with Qualtrics software. Participants were encouraged and prompted to provide feedback about each of the sections of the website prototype (version 1) with regard to website structure, navigation, content, and user engagement and interaction. The researcher prompted participants to express their views about what they liked/disliked about website, and how it may be able to be improved.

All sessions were audio-recorded, and the facilitator took written notes throughout. Audio-recordings were transcribed verbatim, and data was analysed using qualitative descriptive analysis. Descriptive analysis effectively summarises data (29) and is an appropriate approach to understand relevant stakeholders' experiences about healthcare interventions (30). Using NVivo software (31), similar sentences and concepts were grouped into 'codes' which were labelled to describe the data contained (e.g., content is written at an understandable level, more pictures needed on website, use bullet points to reduce text, etc.). Next, codes were grouped into broader 'topics' and 'sub-topics' addressing similar aspects/components of the website.

A second version of the website prototype (version 2) was developed and transferred into a Microsoft Word (32) document. Preferences for the navigational/operational functions were annotated throughout this prototype (e.g., how user activities should work, how users can use 'buttons' to access more information). Multiple rounds of feedback from the research team were provided on subsequent iterations of the website prototype until all researchers were satisfied with the final website prototype (version 2).

The researchers engaged the services of an external website developer who used the Microsoft Word prototype (version 2) to create the 'My Heart and Cancer' website ready for usability testing. The researchers and website developer participated in a series of discussions via telephone/email to develop the final version ready for usability testing.

Stage 2: Usability testing and website finalisation

All individual usability sessions were conducted in-person by the same researcher (RK), using the 'Think Aloud' approach. In 'Think Aloud' procedures, participants are prompted to verbalise their thoughts and attitudes about all aspects of the intervention while they engage in the intervention being tested. The specific 'Think Aloud' procedure

we implemented was based on Beatty and colleagues (33) usability testing of a web-based self-guided psychosocial program for women with metastatic breast cancer, and Wu and colleagues' (34) testing of a smartphone application targeting smoking cessation in pregnant women. First, the researcher provided a brief overview of how and why the 'My Heart and Cancer" website was developed and explained the 'Think Aloud' procedure with an example of how the participant might verbalise their perspectives, whether these be positive or negative comments. Throughout usability sessions, the researcher occasionally provided explanations or descriptions if clarification was needed. If required, the researcher prompted the participant to continue to voice their perspectives, e.g., 'What do you think about this section?".

All sessions were audio-recorded, and the researcher conducting the usability sessions took field notes throughout. Audio-recordings were transcribed verbatim. Data were analysed by one researcher (RK) using qualitative descriptive analysis; however, in contrast to the Round 2 Codesign data analysis approach, after descriptive analysis we conducted an additional quantitative analysis to calculate the frequency of references within each topic (as per Beatty and colleagues (33)), including the number of participants that provided feedback relevant to each topic, and number of references per topic. These quantitative findings provided additional insight into the frequency of the issues raised, aiding decisions about whether/how they should inform changes to the website.

Qualitative and quantitative data emerging from the usability sessions informed the refinement of the 'My Heart and Cancer' website. Where decisions for website changes based on findings were simple and clearcut (e.g., fixing typos, specific changes where multiple participants expressed the same preference for change) RK made changes directly. For complex findings (e.g., participants' perspectives were varied or contradictory), RK made recommendations for how findings should inform website revision, and the research team engaged in email and in-person discussions until consensus was reached. All website changes were facilitated by RK with the assistance of the website developer where required.

RESULTS

Stage 1: Codesign

Codesign Round 1

From November to December 2023, 16 individuals (7 patient advocates and 9 healthcare providers) participated in Codesign Round 1. Participant demographics for Codesign Rounds 1 and 2, and usability testing are summarised in Table 1. Of 12 sessions conducted, two were focus groups (four and two patient advocates, respectively) and 10

were individual interviews. All participants only participated in one session. One focus group was conducted online and the other was in-person. Seven individual interviews were conducted online (1 patient advocate, 6 healthcare providers) and three were in-person. Focus groups lasted approximately 54 and 70 minutes; interviews lasted 26 minutes and 76 minutes.

Participants provided feedback throughout Codesign Round 1 sessions in response to question prompts presented with each of the 12 'pages' of the wireframe (see Figure 2a for example of wireframe page). The wireframe provided a framework for the topics of information that might be covered throughout the website and how they would be organized. Codesign Round 1 feedback informed the development of the first website prototype (Prototype v1.0) in which detailed information was added to broad topics presented in the wireframe; and using Qualtrics software aspects of design, layout and navigation were added to achieve website functionality/presentation. Participants' ideas led to naming the website 'My Heart and Cancer'. All participants agreed with the six main topics of the website (i.e., information provision, risk assessment, signs and symptoms, self-management, healthcare team management and services), so these remained the main sections of Prototype v1.0. In addition, based on participant preferences, eight new separate self-management pages were added: goal setting, talking to healthcare professionals, physical activity, healthy eating, healthy weight, quitting smoking, alcohol consumption and stress reduction. Participants' emphasis on information being presented as briefly and simply as possible was honoured in Prototype v1.0, with options for users to access more detailed information via links, if desired. Website user engagement was identified as important in Codesign Round 1, and Prototype v1.0 addressed this by including pictures, colour and activities. An example of a page of Prototype v1.0 is shown in Figure 2b.

Codesign Round 2

Between April and May 2024 11 individuals (5 patient advocates and 6 healthcare providers) participated in Codesign Round 2. All had already participated in Codesign Round 1. The five remaining Round 1 participants were unable to participate in Round 2 due to illness (n = 1) or unavailability (n = 4). Participant demographics are summarized in Table 1. One focus group of two patient advocates was conducted (in-person), with the remaining nine participants preferring individual interviews (6 in-person, 3 online). The focus group lasted approximately 33 minutes, and individual interviews lasted 23 - 65 minutes.

Qualitative descriptive data analysis of participants' feedback on Prototype v1.0 led to development of 51 codes, categorized into five topics (Content, Design and Interactivity, Layout, Navigation and CVD risk information and

support is important for people with cancer) and 15 sub-topics. Feedback led to multiple changes to the website. Topics, sub-topics, example quotes and changes are reported in Table 2. In addition, we provide a brief narrative summary of how participants' feedback informed the revision of the prototype to create Prototype v2.0.

Topic 1: Content

Most responses related to content were positive, with participants describing specific components of the website as "*excellent*" (risk assessment page), "*empowering*" (self-management information), and "*handy*" (links to resources and services). However, participants also identified some specific information that was missing, or the message was presented in a way that lacked emphasis of importance. As a result, we highlighted the importance of certain information, including the role of physical activity (not just exercise) in CVD risk reduction, and prevention of CVD risk (in addition to management of established risk).

Some participants expressed that the level of detail throughout the website was "*comprehensive*" and "*understandable*", but others felt that some sections contained "*too much*" information and felt "*overwhelmed*". To address differing preferences for amount and complexity of content, and thus provide an experience catered to the needs and preferences of the individual user, we further simplified and reduced the amount of written content wherever possible and replaced text with pictures and videos and provided options to access more detail via links if desired.

Topic 2: Design and Interactivity

Participants liked the use of icons, pictures and videos throughout the website, describing pictures as "*cute*" and a "*really powerful*" way of engaging users. Two participants argued for the addition of even more pictures which was implemented in the next iteration (Prototype v2.0). An interactive goal-setting activity was described as "*fantastic*", but there were also suggestions for how to improve activities, e.g., emphasise that users should set goals based on problems they perceived most important to them. Although there were positive comments about the design of the website, one participant commented the next iteration of the website could be "*fancier*", and we made improvements to the colour scheme and design to add sophistication.

Topic 3: Layout

Prototype v2.0 included various changes made to website layout based on participant's feedback. We re-ordered information on each page based on what was "*most important*", included 'takeaway points' to summarise page

Content

All participants provided feedback about the website content, (total 55 references), leading to 11 changes. As shown in Table 2, references were classified into four sub-topics: Content is appropriate; Language/wording is appropriate; Add/remove content (or detail); and Change wording for clarity/accessibility.

Seven favourable comments were made about the website content, including that it encourages users to communicate with their healthcare team, and the inclusion of a "*perfect*" list of community support groups that may provide further support and guidance. However, on 12 occasions participants advocated for content changes including adding clarification, detail or emphasis to sections, e.g., we added a link to the 'Patient Charter of Rights', added vaping throughout the 'Quit smoking' page, and used communication about the safety of engaging in physical activity that was "*a little bit more positive*". Language/wording were described as "*straightforward*", "*succinct*", "*palatable*" "*empowering*" and "*solution-based*", but participants also made suggestions for how communication of information could be further simplified/improved. For example, we removed reference to death when providing information about CVD risk outcomes, replacing with more likely to "*be impacted by*" CVD. Reducing detail, and removing some information altogether were also suggested, so we removed a link to an academic journal article, based on participants' feedback that many would be unlikely to "*comprehend it*".

Design and Interactivity

As shown in Table 2, participants provided feedback (51 references) about the design and interactivity of the website with two sub-topics: Engagement enhancers are favourable (design, activities, pictures, videos); and Improve engagement enhancers. Feedback led to six changes. Twelve favourable comments were made about the website design/style, ten about the use of pictures and videos throughout the website, and seven about the activities. For example, the website design/style was "*consistent*" meaning it was "*easy to find things*". There were also suggestions (n = 5) for further improvement, e.g., we added a 'warning' symbol (triangle with exclamation point) to signpost important information. Participants had diverse views on positioning of videos, with one suggesting it was "*logical*" to have them at the bottom of the page, and another arguing it "*definitely…needs to go up front*". Therefore, we decided on the placement of each individual video (i.e., top, middle or bottom of page) to best complement the text to achieve optimal flow of information. We improved activities based on participant feedback, e.g., we added a function to the risk factor assessment activity, where users who select a particular risk factor are

automatically directed to advice/support for managing that risk factor, setting a related goal via the goal setting activity, or adding a related question in the talking to healthcare professional activity.

Layout

All participants provided feedback about the layout of the website, with a total of 20 references related to this topic leading to four changes. As shown in Table 2, these references were classified into three sub-topics: Layout is favourable; Improve individual 'page' layout; and Layout improvements throughout website. Three participants made a total of six favourable comments about the layout of the website. One participant indicated the "*quite liked*" the layout because it was "*not overwhelming*". Five comments praised the inclusion of takeaway points at the top of pages to provide a summary of what can be found on the page. Several suggestions (14 references) were made for how layout could be improved, some of which were conflicting. For example, one participant felt general information about the heart and cardiovascular system should be more prominent whilst another felt it was too complicated. To address this, we made the titles for heart and cardiovascular system very prominent, but 'hid' the information behind a link so only people who were interested in this information would access it.

Navigation

All participants provided feedback about the navigation of the website (total 39 references), leading to six changes. References were classified into four sub-topics: Navigation within website is favourable; External website links are favourable; Improve navigation within website; and Improve links to external websites. Participants indicated they liked navigation within the website (eight references), but also made suggestions for improvement (17 references). Website changes were made based on feedback, e.g., altering the introduction for each website page. We replaced the general sentence outlining content, to frame as a question asking users for their learning preferences. Hyperlinked bullet points can facilitate direct navigation to desired information. Respondents also liked the links to other websites (eight references), particularly being able to access to external websites with search functions for healthcare professionals. We but made small changes related to linking to external websites based on one participant's feedback. We ensured all external websites opened in a new browser to allow easy return to 'My Heart and Cancer'.

DISCUSSION

We codesigned and established the usability of the first patient-facing website to target CVD risk assessment and management in cancer, 'My Heart and Cancer'. Key recommendations from participants throughout codesign and

usability testing related to the amount, level of detail and presentation of information; the importance of using design and interactive activities to engage users; and the need for easy navigation throughout the website and to external credible information and support. Feedback was addressed iteratively until the website was finalised. We simplified, summarised and reduced text wherever possible but provided options (links) for users to access further information/detail if desired. We added pictures and videos and improved the website design, and further strengthened activities and practical self-management tips to enhance ease-of-use and interactivity (improved instructions and functionality). To optimise navigation throughout 'My Heart and Cancer' we ensured consistency of design, presentation and language throughout the website. The website is informed by evidence and user preferences and facilitates an experience that can be tailored to individual needs. Hence, 'My Heart and Cancer' is a promising approach to addressing the wicked problem of CVD care in cancer in the ever-increasing population of cancer survivors.

Participants were satisfied with the topics addressed in each section of the website (i.e., general information about cancer and CVD risk, CVD risk assessment, CVD signs and symptoms, self-management, healthcare team management and access to services and resources), with feedback focusing on preferences for amount, level of detail and presentation of information, rather than content. This aligns with the strength of evidence for best practice for the assessment and management of CVD in cancer, particularly the European Society of Cardiology Guidelines on Cardio-oncology(8). Participant satisfaction with the provision of general information about cancer and CVD risk also aligned with our research team's previous findings that many people affected by cancer were unaware, or only somewhat aware of the increased risk of CVD in cancer(13), and cancer care providers' assertions for the importance of education in approaches to improve CVD care(14). In addition, the current study elicited positive feedback regarding the focus of the website on self-management and patient empowerment and activation, which also aligns with our previous research in which people affected by cancer expressed that being involved in their own care is empowering, and that healthcare professionals experienced many barriers to implementing adequate CVD care alone. Moreover, there is strong evidence that self-management is critical for effective cancer care (35, 36), and activated cancer patients are more satisfied with aspects of their care (e.g., feel their treatment aligns with their values) and better adhere to treatment and cope with treatment side effects (37).

Participants' preferences for aesthetic design features, pictures and text presented as bullet points and interspersed with videos and pictures aligns with previous research (38). Our research elicited consistent positive responses for

the inclusion of interactive, user-centred functions (e.g., activities in which the user sets goals, identifies their own CVD risk factors, and identifies questions for their healthcare team), aligns with adult learning theory concepts including that learning is most effective when it is directed by the individual, focuses on goals and builds knowledge (39). Furthermore, our website's capacity to provide an experience tailored to user needs and preferences is supported by previous research examining cancer survivors' perspectives that websites provide an opportunity for individualised support and information provision (36, 40).

Our findings highlight the importance of conducting multiple rounds of codesign and usability testing. For example, some topics were raised multiple times in subsequent rounds, despite changes made in response to feedback. Effectively, this allowed the opportunity to 'check' if changes met the needs of users and further improve the website where needed. In addition, new topics arose across the study, perhaps because participants were unable to identify website issues/concerns until more obvious problems had been addressed.

Strengths and limitations

There were important limitations of this research, with most participants residing in South Australia (n = 10) and all residing in Australia. In addition, given the relatively small sample size, not all cancer types and healthcare professions involved in care provision were able to be represented. Reduced diversity of demographics and health characteristics potentially limits the transferability of findings and appropriateness of the website in other areas where resources, services, and patient needs and experiences differ. In contrast, the study strengths included the comprehensive methodological approach used to codesign and test usability of the 'My Heart and Cancer' website. In particular, the strong consumer engagement approach (i.e., collaborating with people affected by cancer and healthcare providers to develop and test the website) increases the likelihood that the 'My Heart and Cancer' website will provide effective people-centred care and satisfy user needs (41).

Future research should examine efficacy and implementation of the website, ideally using a hybrid study design.

CONCLUSIONS

We employed a comprehensive and iterative approach to codesign and test the usability of 'My Heart and Cancer', the first website providing CVD risk information and self-management support to people affected by cancer. In response to participant feedback, we presented content simply with options to access more information/detail if desired; and we incorporated aesthetic and consistent design features, including pictures, videos and activities for

improved navigation and user-interaction. Our website has the potential to reduce the impact of CVD risk in people affected by cancer by improving awareness, understanding, and risk-reduction.

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STATEMENTS AND DECLARATIONS

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Competing Interests
The authors have no relevant financial or non-financial interests to disclose.

Author Contributions
All authors contributed to the study conception and design. Material preparation was performed by Reegan Knowles and data collection and analysis were performed by Reegan Knowles, Emma Kemp and Bogda Koczwara. The first draft of the manuscript was written by Reegan Knowles and Emma Kemp and Bogda Koczwara provided feedback on previous versions of the manuscript. All authors read and approved the final manuscript.

Ethics approval
This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Southern Adelaide Local Health Network Ethics Committee (06/07/2023 for Codesign – Project ID 6075; & on 28/06/2024 for Usability Testing - Project ID 4640).

Consent to participate
Informed consent was obtained from all individual participants included in the study.

9.6 Appendix 6: Topic Guide for the co-design of a web-based resource to support self-management of CVD risk in people with cancer.

Co-design of a web-based resource to support self-management of CVD risk in people with cancer

Topic Guide

Please note the discussion in these sessions will evolve iteratively throughout the session based on successive feedback and discussion from participants, and from findings of earlier sessions. Depending on the knowledge and experience of stakeholders in each session (e.g., patient advocates, health care professionals), some topics in this guide may be emphasized or explored more/less than other topics, and different forms of the same question may be used in order to communicate relevant meanings. Some sections will not be relevant to all stakeholders.

Introduction

- Begin sessions by introducing broad concepts relevant to the project where relevant – e.g., cardiovasulcar disease (CVD) risk in cancer, identification, assessment, management, codesign, web-based resource.
- Provide information about the broader research program – i.e., what we found in previous research regarding awareness, importance, barriers and preferences for solutions and how this informs the current research (i.e., the development of the list of potential components/format of the approach that they will be prompted to discuss).
- Describe rationale/purpose for developing the web-based resource.
- Describe rationale/purpose for using codesign and how we will utilize this approach (i.e., series of 2-3 codesign sessions, separate for HCPs and patient advocates)
- Remind participants participation is voluntary and they can withdraw at any time without consequence. Researchers will deidentify data in reporting of results where possible.

Presentation and discussion of potential components of the web-based resource

The session facilitator will present the potential components of the web-based resource to the participants. Each of the components will be discussed in turn and participants will be encouraged to provide feedback regarding whether they agree the component should/should not be included in the web-based resource, and/or what modifications should be considered.

The potential key components/formatting/approaches to be discussed will be:

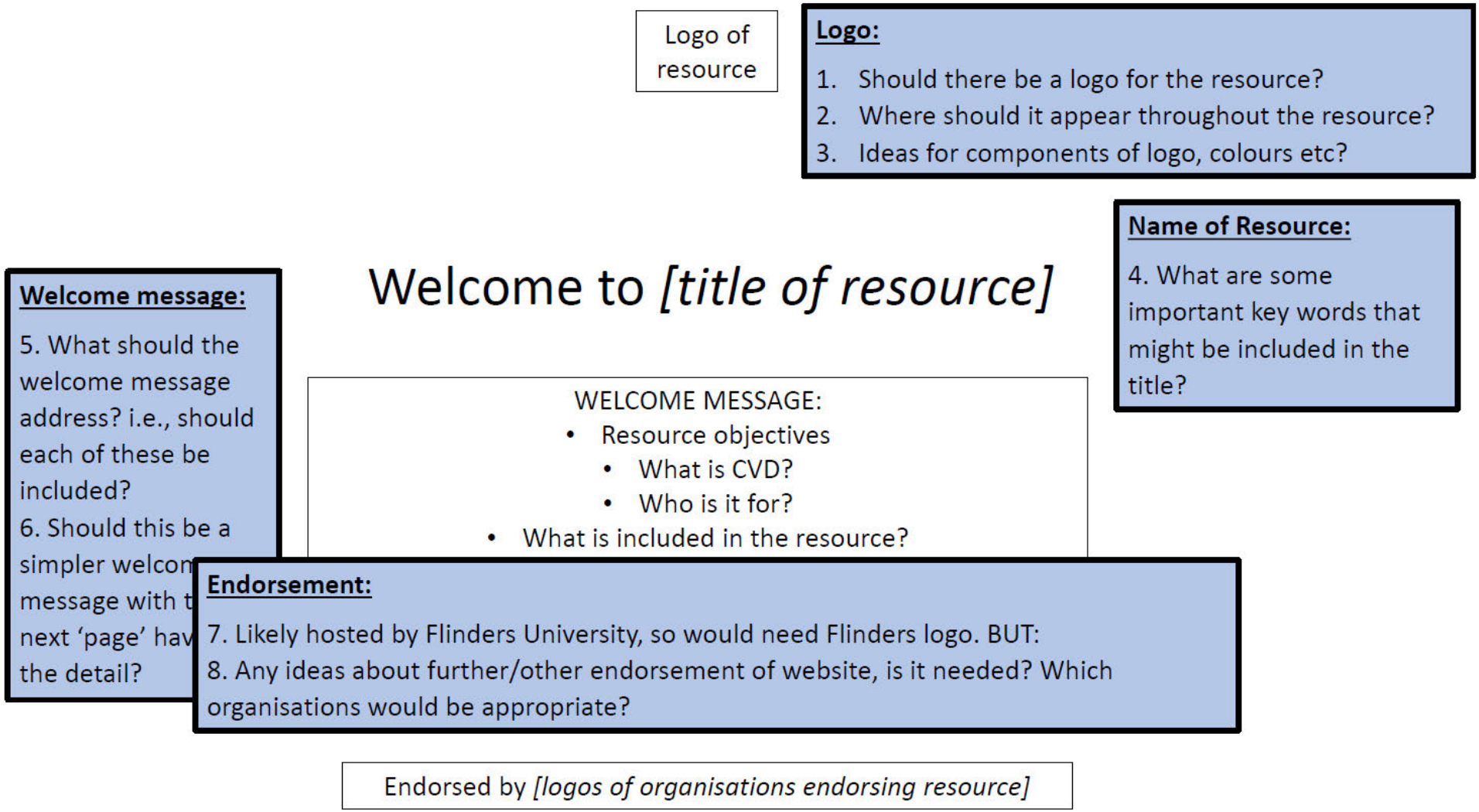
- **People can navigate to separate sections of the website according to if they are a person diagnosed with cancer, a carer/family/friend of someone with cancer, or a HCP.**
- **CVD risk information provision**, i.e., how will information be presented (e.g., video, text, audio etc.), how much information should be provided, options to navigate to more information?

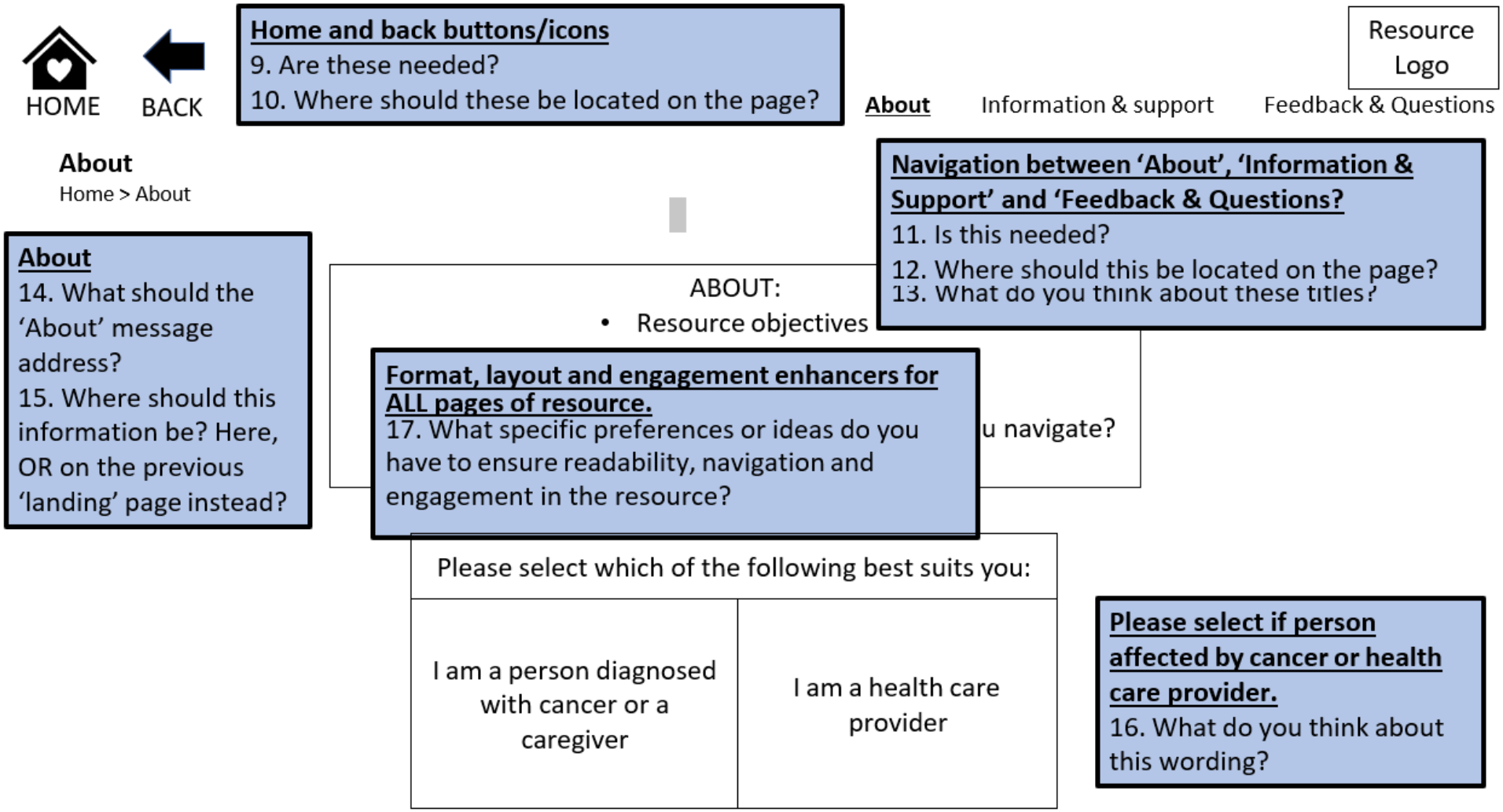
- **Focus on supporting self-management of aspects of CVD care,** i.e., education to people affected by cancer about how they can self-manage.
- **Questions prompts for navigation throughout website,** e.g., what do you want to do? Options might include learn about CVD risk, find a HCP/service, reduce my risk.
- **Links to other evidence-based resources** (e.g., guidelines).
- **Links to resources/services** (e.g., support groups, directory of relevant healthcare professionals).
- **Printable pages.** There was a diversity in preferences for how information is best received by PWC and HCPs, some indicated a preference for printed materials.

General feedback

Participants will be asked to suggest any additional components/formatting preferences they would like to be included in the web-based resource that had not already been discussed. They will be asked to provide any further comments about the web-based resource.

Appendix 7: Wireframe with Prompts for the co-design of a web-based resource to support self-management of CVD risk in people with cancer.




HOME
BACK
Home and back buttons/icons
9. Are these needed?
10. Where should these be located on the page?
Resource Logo
About
Information & support
Feedback & Questions
About
Home > About
Navigation between 'About', 'Information & Support' and 'Feedback & Questions?
11. Is this needed?
12. Where should this be located on the page?
13. What do you think about these titles?
About
14. What should the 'About' message address?
15. Where should this information be? Here, OR on the previous 'landing' page instead?
ABOUT:
• Resource objectives
u navigate?
Format, layout and engagement enhancers for ALL pages of resource.
17. What specific preferences or ideas do you have to ensure readability, navigation and engagement in the resource?
Please select which of the following best suits you:
I am a person diagnosed with cancer or a caregiver
I am a health care provider
Please select if person affected by cancer or health care provider.
16. What do you think about this wording?

Information & Support

Home > Information & Support > What guidance do you need?

TITLE of PAGE:

INTRODUCTION/WELCOME TO PAGE	**Title**	website, but you can choose from
the options below depending on wh	18. Ideas? Key words?	page to access another topic.

Options for topic
• Information p
• CVD risk asse
• Navigation to
• Signs and sym
• CVD risk mana

Introduction/welcome to page

19. What should be communicated here?
20. What do you think about the sentence: 'there is a lot of information and guidance, but you can choose what you want to see'?
21. What do you think about including instructions about coming back to this page to navigate to other topics?

Options for topics/guidance

22. What do you think about this title?
23. Does this need instructions that user can select what they would like more information about?
24. These are the topics/guidance we suggest including. What do you think about each? Any missing?

Information & Support

Home > Information & Support > Information provision: CVD risk in cancer

TITLE of PAGE:

INTRODUCTION/WELCOME TO PAGE

have not had cancer.

xperience CVD risk than people that

Why are people d

- Cancer and C
  existing CVD,
- Some cancer

e, smoking,

Title

25. Ideas? Key words?

Introduction/welcome to page

26. What do you think about the introduction/welcome?
27. Should anything else be included?
28. Should we add a summary/purpose of page/what will be included on the page?

Why are people diagnosed with cancer at greater risk of CVD?

29. What do you think about this section – content and wording?
30. What else be included?

Knowing about CVD risk is important

34. What do you think about including that CVD can be prevented and managed if we know about it?
35. What do you think about including that people who manage their risk have better outcomes? What examples could

How to get more information

37. What do you think about including this option to seek more information?
38. Ideas for specific links, services, providers to be included?

Information & Support

Home > Information & Support > CVD risk assessment

TITLE of PAGE:

CVD risk assessment is important before, during and after treatment

43. What do you think about this section – content? Wording?
44. Should anything else be included?

Introduction/welcome to page

40. What do you think about the introduction/welcome?

What are CVD risk factors?

45. Any factors missing?
46. How much information should be included here?
47. All information appears on page, or click link for more information if you want it?
48. Should a list of anti-cancer therapies that are most likely to cause CVD risk be included?

What might CVD risk assessment involve:

49. Anything missing?
50. How much/what information about each assessment type should be included here?
51. All information appears on page, or click link for more information if you want it?

What might CVD risk assessment involve: Imaging/scans, blood tests, questions about lifestyle, etc.

Information & Support

Home > Information & Support > Navigation to support/services

TITLE of PAGE:

INTRODUCTION/WELCOME TO PAGE

time they need it, and can lead to be

ive the support they need at the

n ptoms.

Services and Sup

List of services ar

s, local hospit ls

– others?

Title

52. Ideas? Key words?

Introduction/welcome to page

53. What do you think about the introduction/welcome?

54. What do you think about including the definition of navigation? Does this make sense?

Services and Support

57. Should this include a list of services and support?

58. How might these be grouped? Support groups, health care professionals, general, non-government organisations etc. OR grouped according to what people's needs are (overlap?)

59. Should there be a list of actual people that could be contacted for support in different areas?

60. Should there be an explanation of what these support/services can do to help?

Information & Support

Home > Information & Support > Signs and symptoms of CVD risk

TITLE of PAGE:

INTRODUCTION/WELCOME TO PAGE

keep an eye for. You should report th

ortness of breath) that you can

Title

61. Ideas? Key words?

Signs and sympt

- Chest pain;
- Shortness of b
- Leg swelling;
- Feeling faint or dizzy;
- Increased tiredness;
- Fast or irregular heartbeat.

Introduction/welcome to page

62. What do you think about the introduction/welcome?
63. What else should be included?
64. Should we add a summary/purpose of page/what will be included on the page?

Signs and symptoms of CVD risk to look out for include:

65. Are there any missing that should be included?
66. Are these clear?
67. How much information about each sign/symptom should be included here?
68. All information appears on page, or click link for more information if you want it?

Information & S

Home > Information

TITLE of PAGE:

Introduction/welcome to page

70. What do you think about the introduction/welcome?
71. What else should be included?
72. Should we add a summary/purpose of page/what will be included on the page?

INTRODUCTION/WELCOME TO PAGE

team can help you in many ways.

Title

69. Ideas? Key words?

ted or managed. Your health care

Who might be involved in your risk management? Who can you reach out to for assistance?

78. Any missing?
79. Or
80. Sh vider?
81. All
82. Should we include a list of specific providers according to areas (e.g., southern Adelaide, etc.)
83. What do you think about including information about referral requirements for each health care provider type?
84. What do you think about including information about private vs public?

Specific considerations for this page (engagement enhancers):

84. How can we help patients to get the assistance they need from their health care team? e.g., Question list?

Who might be in

- Cancer specia
- Cardiologist;
- Pharmacist;
- Nurse;
- General pract
- Allied Health professional (e.g., dietitian, exercise physiologist)
- Pharmacist.

How your healthcare team might assist you to manage and monitor your risk:

73. Anything missing?
74. Should any be removed?
75. Order?
76. How much information about each management type should be included here?
77. All information appears on page, or click link for more information if you want it?

Information & Support

Home > Information & Support > CVD risk man

Title

86. Ideas? Key words?

General tips for how you can be involved in your own healthcare

93. Any missing?

94. Order? Wording?

95. What do you think about including their specific roles or link to specific problems that could be addressed by each health care provider?

96. All information appears on page, or click for more information if you want it?

89. Should we add a summary/purpose of page/what will be included on the page?

- Setting healt

What can you do to manage your CVD risk?

90. Any missing?

91. Order? Wording?

92. All information appears on page, or click for more information if you want it?

General tips for

- Ask questions
- Seek a second
- Work with you
- Monitor for health changes and report to your health care team;
- Involve your friends and family in your care, bring them to appointments, tell them about your goals.
- Follow your treatment and monitoring plan carefully (e.g., book appointments when they are due, take your medication

Specific considerations for this page (engagement enhancers):

97. How can we help patients to get self-management support they need from their health care team? e.g., Question list that is printable? FAQs?

98. How can we best facilitate goal-setting? Printable page? Suggested goals with space for user to enter their own?

Feedback & Questions

Home > Feedback & Questions

99. What do you think about this page? Is it useful?
100. Wording?

If you have any questions or comments about this website, please email us at ***@flinders.edu.au or send us a message using the form below.

Name

Email address

Please type your message here

Submit message