Reproductive health after cancer in childhood, adolescence, or young adulthood: Unmet informational needs of female survivors and recommendations for optimal care

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Reproductive health after cancer in childhood, adolescence, or young adulthood: Unmet informational needs of female survivors and recommendations for optimal care

By

Angela Polanco

PhD

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Reproductive health after cancer in childhood, adolescence, or young adulthood: Unmet informational needs of female survivors and recommendations for optimal care

Angela Polanco

A thesis submitted in partial fulfilment of the University's requirements for the Degree of Doctor of Philosophy

May 2021

Ethical Approval

Certificate of Ethical Approval – PICCS1

Certificate of Ethical Approval

Applicant:

Angela Polanco

Project Title:

Pregnancy after malignancy in childhood: Communication and information needs of female survivors and recommendations for optimal care

This is to certify that the above named applicant has completed the Coventry University Ethical Approval process and their project has been confirmed and approved as Medium Risk

Date of approval:

03 April 2019

Project Reference Number:

P87230

Certificate of Ethical Approval – PICCS2

Certificate of Ethical Approval

Applicant:

Angela Polanco

Project Title:

Pregnancy Information for Childhood Cancer Survivors 2 (PICCS2)

This is to certify that the above named applicant has completed the Coventry University Ethical Approval process and their project has been confirmed and approved as High Risk

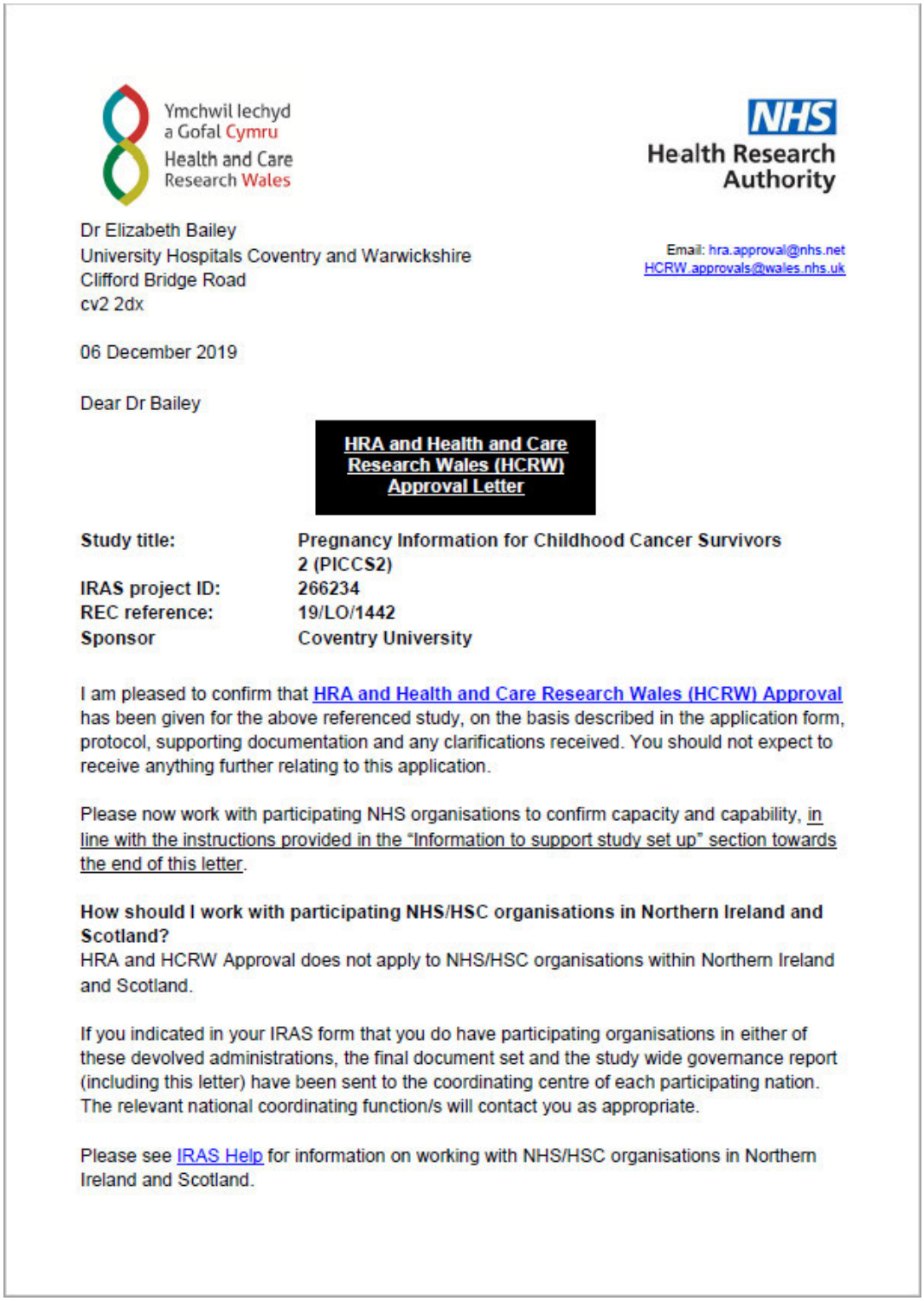
Date of approval:

23 July 2019

Project Reference Number:

P93106

HRA and Health and Care Research Wales (HCRW) Approval Letter



Ymchwil Iechyd a Gofal Cymru
Health and Care Research Wales

NHS
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06 December 2019

Dear Dr Bailey

HRA and Health and Care Research Wales (HCRW) Approval Letter

Study title:	**Pregnancy Information for Childhood Cancer Survivors 2 (PICCS2)**
IRAS project ID:	**266234**
REC reference:	**19/LO/1442**
Sponsor	**Coventry University**

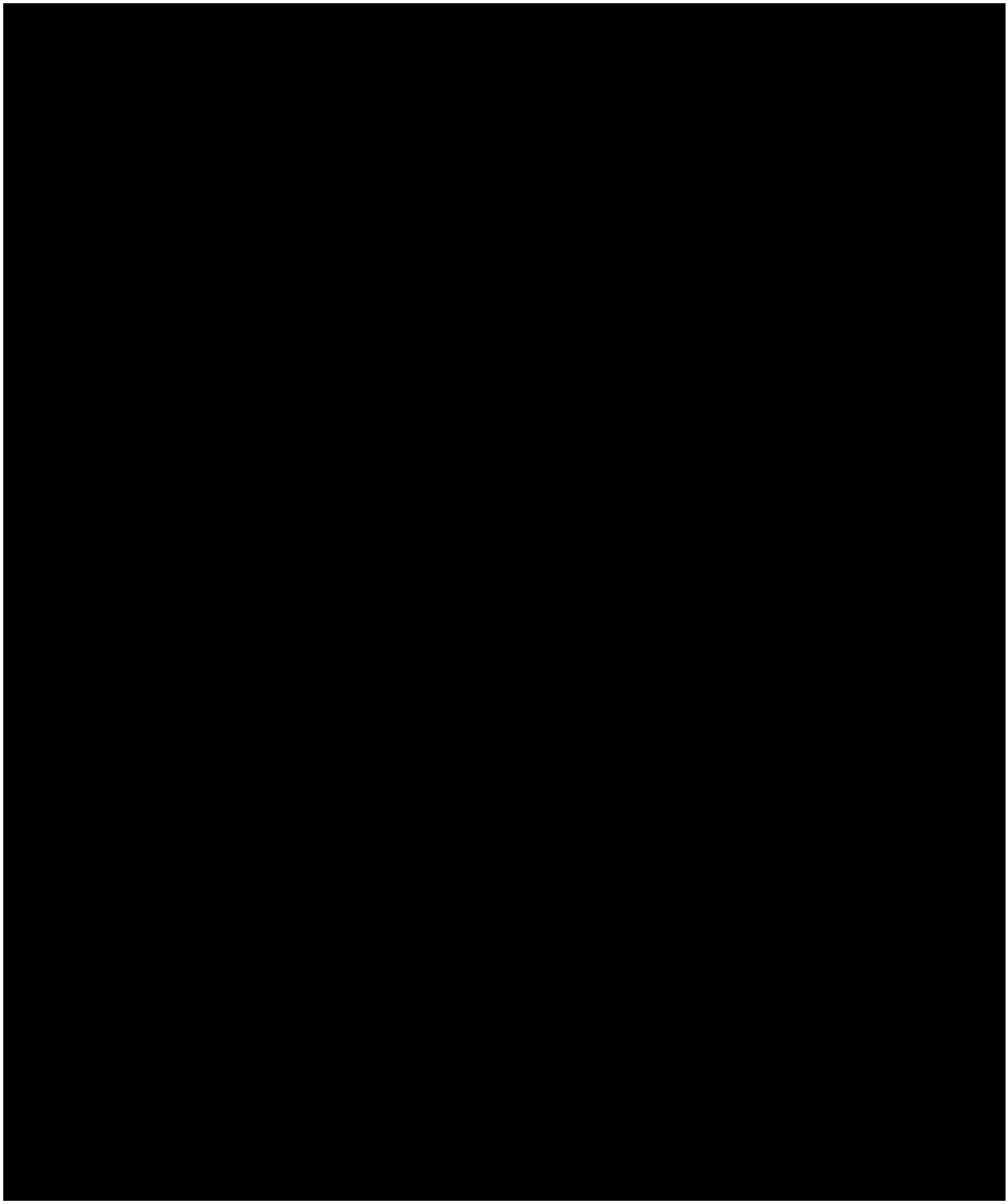
I am pleased to confirm that HRA and Health and Care Research Wales (HCRW) Approval has been given for the above referenced study, on the basis described in the application form, protocol, supporting documentation and any clarifications received. You should not expect to receive anything further relating to this application.

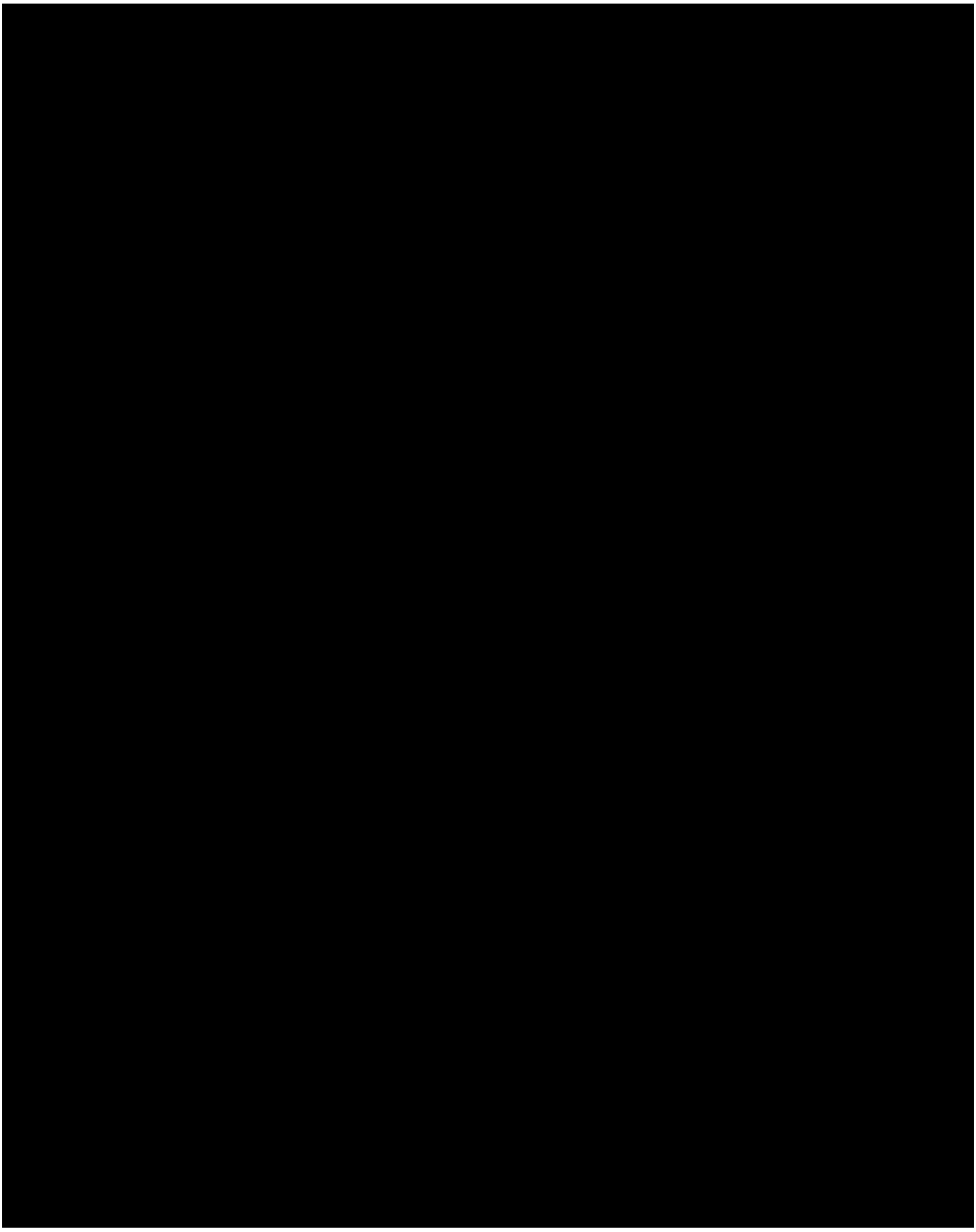
Please now work with participating NHS organisations to confirm capacity and capability, in line with the instructions provided in the "Information to support study set up" section towards the end of this letter.

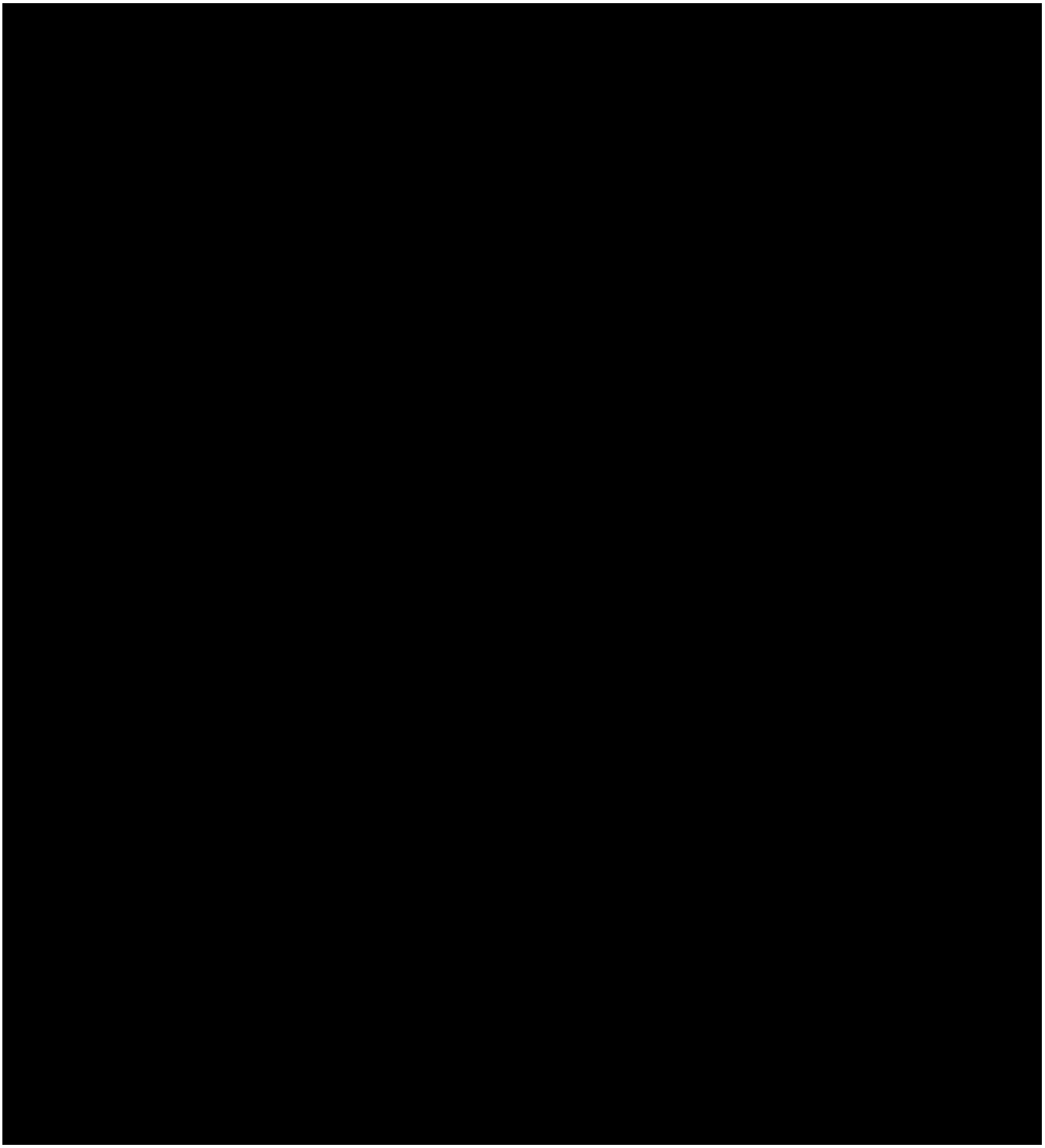
How should I work with participating NHS/HSC organisations in Northern Ireland and Scotland?
HRA and HCRW Approval does not apply to NHS/HSC organisations within Northern Ireland and Scotland.

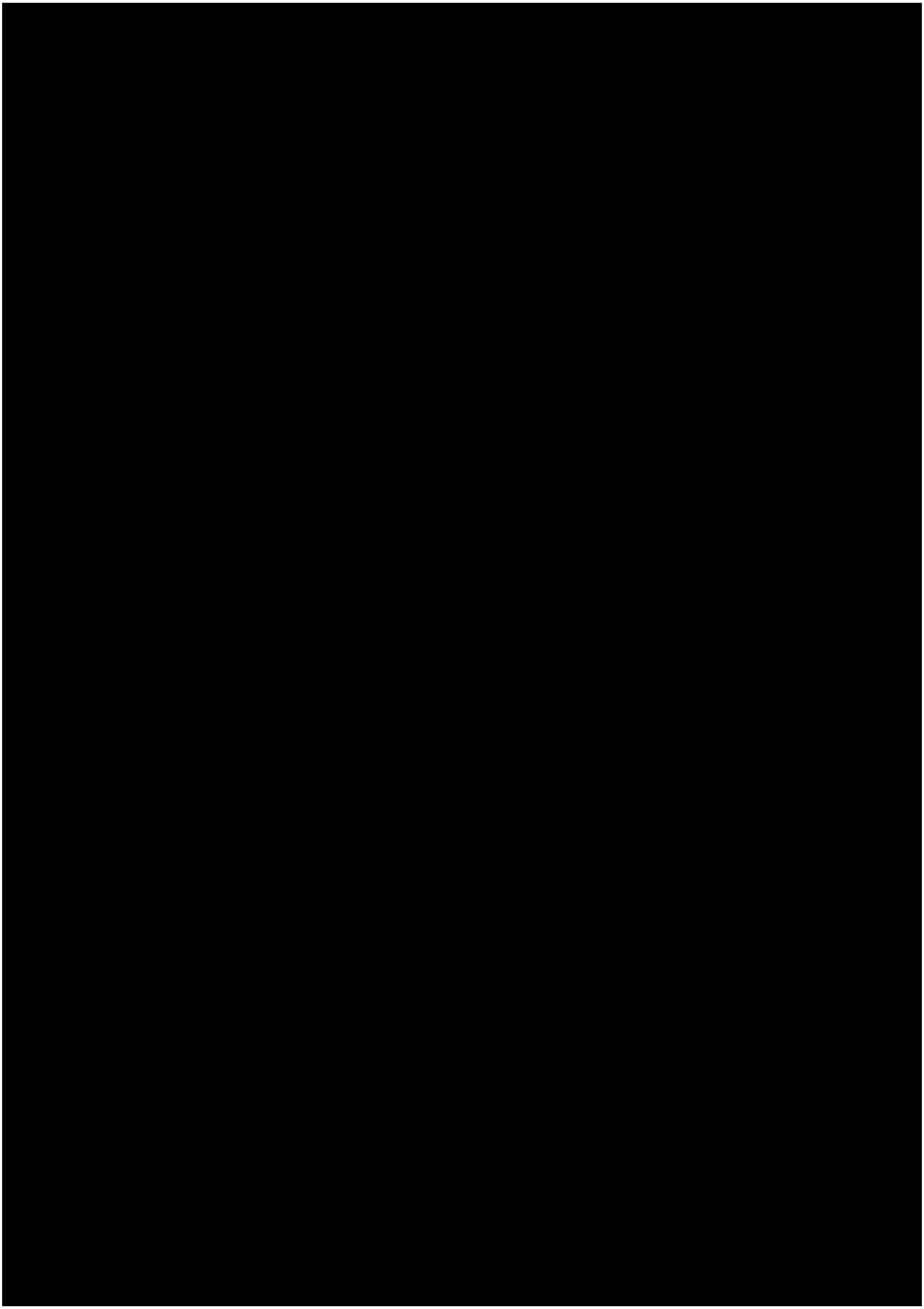
If you indicated in your IRAS form that you do have participating organisations in either of these devolved administrations, the final document set and the study wide governance report (including this letter) have been sent to the coordinating centre of each participating nation. The relevant national coordinating function/s will contact you as appropriate.

Please see IRAS Help for information on working with NHS/HSC organisations in Northern Ireland and Scotland.









Contents

Abstract

Background

The survival rate for childhood, adolescent, and young adult (CAYA) cancers is now approximately 92% (0-14 years). CAYA cancer survivors are at high risk of life-long, chronic health conditions and side-effects from treatments (late effects). Unmet informational needs about future health risks are linked to high levels of psychological distress in CAYA cancer survivors. Female CAYA cancer survivors in particular, have reported that communication of future fertility and reproductive health risks is inadequate and one of the most significant unmet informational needs.

Methods

Pregnancy Information for Childhood Cancer Survivors Studies (PICCS1 and PICCS2) explored the evidence base for the who, what, when, and in what detail, surrounding the optimal communication of late effects with female CAYA cancer survivors. PICCS1 consisted of three-parts; a systematic review, two online questionnaires, and eight semi-structured telephone interviews. PICCS2 then featured a three-round modified Delphi technique to produce an expert guidance document for Health Care Professionals (HCPs). The document outlined recommendations for the communication of future fertility and reproductive health risks with female CAYA cancer survivors. PICCS2 recruited 19 stakeholders from professional, survivor, and parent backgrounds. An embedded patient and public involvement and engagement strategy was used throughout both studies.

Findings

PICCS1 (systematic review) reported 15 studies revealing the themes ‘Future fertility’, ‘Partnership’, ‘Awareness’ and ‘Timing, format and delivery of late effects information’. Late effects informational need was the most significant unmet need for CAYA cancer survivors, with female CAYA with cancer reporting significant unmet needs for future fertility and reproductive health risk information. PICCS1 (questionnaires) found that although HCPs were confident to discuss future fertility risks, they lacked confidence in discussing future pregnancy risks with female CAYA cancer survivors. HCPs preferred verbal communication of risks, at diagnosis or at the end of active treatment. However, survivors and parents reported that in practice, there was a wide variation in the timing of risk communication. PICCS1 (interviews) explored the themes; ‘Emerging practice’, ‘Who, what, when?’, ‘Which late effect risks’, ‘Honest and transparent communication’, and ‘Long-term distress’. The findings revealed a strong link between unmet informational late effect needs and psychological distress. PICCS2 subsequently produced expert recommendations for the optimal communication of risk (specifically future fertility and reproductive health risks) with female CAYA cancer survivors.

Conclusion

Communication of future fertility and reproductive health risks for CAYA with cancer is an important unmet informational need for families. An individualised, age-appropriate communication plan is recommended to avoid psychological distress and risk of miscommunication. Risk based communication dependant on level and type of treatment received is needed, delivered alongside a flexible, age-appropriate approach. PICCS2 addresses this need and provides HCPs with evidence-based guidance for the communication of future fertility and reproductive health risks with female CAYA cancer survivors. However, the guidance requires broader investigation of applicability and impact before wider clinical adoption. Likewise the impact of COVID-19 upon communication preferences and delivery of CAYA cancer survivorship health services merits further consideration.

Glossary and abbreviations

The following terms and abbreviations have been used in this document.

Term or abbreviation	Explanation
ACCELERATE	ACCELERATE is a collaborative research platform created in 2015 by The European Society for Paediatric Oncology (SIOP Europe), ITCC (Innovative Therapies for Children with Cancer in Europe) and CDDF within the ENCCA project (European Network for Cancer research in Children and Adolescents)
ASPIRE	Action to Support Practices Implementing Research Evidence
AYA	Adolescent and young adult
BCCSS	British Childhood Cancer Survivorship Study
CASP	Critical Appraisal Skills Programme
CAYA	Children, adolescents, and young adult
CCLG	Children's Cancer and Leukaemia Group
CCS	Childhood cancer survivor
CCSS	Childhood Cancer Survivorship Study
CI	Confidence interval
COVID-19	On February 11, 2020, the World Health Organization announced an official name for the disease that is causing the 2019 novel coronavirus outbreak, first identified in Wuhan, China. The name of this disease is coronavirus disease 2019, abbreviated as COVID-19. In COVID-19, 'CO' stands for 'corona', 'VI' for 'virus', and 'D' for disease
CRD	Centre for Research and Dissemination
CREDES	Conducting and REporting of DElphi Studies
CRUK	Cancer Research United Kingdom
CTYA	Children, teens, and young adults
DNA	Deoxyribonucleic acid is a molecule composed of two polynucleotide chains that coil around each other to form a double helix carrying genetic instructions for the development, functioning, growth and reproduction of all known organisms and many viruses
GDPR	General Data Protection Regulation

Term or abbreviation	Explanation
GP	General Practitioner
Gy	Gray (Gy) is the unit used to measure the total amount of radiation that the patient is exposed to
HCP	Health Care Professional
HEE	Health Education England
HR	Hazard ratio
HRA	Health Research Authority
ICCC	International Classification of Childhood Cancer
IGHG	The International Late Effects of Childhood Cancer Guideline Harmonization Group
IMRT	Intensity-modulated radiation therapy
INVOLVE	INVOLVE is a national advisory group that supports greater public involvement in NHS, public health, and social care research. The NIHR Dissemination Centre supports NIHR objectives for dissemination of high-quality evidence
IPA	Interpretative phenomenological analysis
IRAS	Integrated Research Application System
ITCC	Innovative Therapies for Children with Cancer academic Consortium
JLA	James Lind Alliance
LTFU	Long term follow-up
MBRRACE	Mothers and Babies: Reducing Risk through Audits and Confidential Enquiries across the UK
MDT	Multi-disciplinary Team
MeSH	Medical Subject Headings
MMAT	Mixed methods appraisal tool
MRC	Medical Research Council
NCRI	National Cancer Research Institute
NCSI	National Cancer Survivorship Initiative
NGT	Nominal Group Technique
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NIHR	National Institute of Health Research

Term or abbreviation	Explanation
NMC	Nursing and Midwifery Council
NVivo	NVivo is a qualitative data analysis (QDA) computer software package produced by QSR International. It has been designed for qualitative researchers working with rich text-based and/or multimedia information, where deep levels of analysis on small or large volumes of data are required
ONS	Office for National Statistics
OR	Odds ratio
PANCARE	Pan-European Network for Care of Survivors after Childhood Cancer
PCT	Primary Treatment Centre
PICCS	Pregnancy Information for Childhood Cancer Survivors
PICO	Population, Intervention, Comparison group, Outcome
PICOS	Population, Intervention, Comparison group, Outcome, Study
PO	Primary outcome
POSCU	Paediatric oncology shared care unit
PPIE	Patient and public involvement and engagement
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PROSPERO	The International Prospective Register of Systematic Reviews
PSP	Priority Setting Partnerships
RAND	RAND, a research organisation, developed the Delphi method in the 1950s, originally to forecast the impact of technology on warfare. The method entails a group of experts who anonymously reply to questionnaires and subsequently receive feedback in the form of a statistical representation of the 'group response,' after which the process repeats itself
RCT	Randomised control trial
RR	Risk ratio
SIGN	The Scottish Intercollegiate Guidelines Network
SO	Secondary outcome
SPIDER	Sample, Phenomenon of Interest, Design, Evaluation, Research
SPSS	SPSS Statistics is a software package used for interactive, or batched, statistical analysis

Term or abbreviation	Explanation
UK	United Kingdom
USA	United States of America
WHO	World Health Organisation

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Acknowledgements

I would like to take this opportunity to thank everyone who has taken the time to offer advice, support and guidance during the past few years. This journey has definitely had some bumps along the road (i.e., a world-wide pandemic!), however it has provided me with the opportunity to gain valuable experience, learn new techniques, reflect upon what drives me as a researcher, and ultimately finish something that started as a small idea over coffee, more than 7 years ago. My passion for research, ongoing academic learning and teaching others will always stay with me and I am very honoured to have been given the opportunity to do this.

Firstly, I would like to thank my supervisory team, especially my director of studies, Dr Elizabeth Bailey who has been a constant source of reassurance and a true inspirational figure for me to aspire to. To Professor Jane Coad, for your wealth of experience and knowledge, and for your small nudges in the right direction when I needed them. Professor Debra Bick for your calm, reassuring and valued experience and Mr Neil Ranasinghe, who has been my life coach, friend, editor in chief, and PPIE expert all rolled into one. I would have not been able to finish this without you and your constant advice and support continues to help me navigate the various challenges that I come up against both professionally and personally. I have no words that can repay you but thank you! Also to the infamous Dr Bob Phillips for being my ongoing mentor, cheerleader and sounding board at numerous random hours in the day.

A huge thank you to my family and friends who have supported me throughout this process, especially in the past few months. My wonderful husband who has quite simply taken the reins over the past year and has afforded me the time, patience and understanding when I needed it the most.

Most of all I would like to acknowledge my beautiful daughter Bethany. Her strength, bravery, her need to help others, is what drives me each and every day. Without her in my life, I would have never started this journey and I certainly would not have had the resilience or strength to keep going when things got tough. I promise to keep making a difference in your name, however small. This thesis is dedicated to her and all the children, teenagers and young people with cancer. Tomorrow should be promised, slowly we will help to change that.

Chapter One – Introduction

1.1 Rationale of the thesis

This thesis built upon the researchers previous work (HEE/NIHR funded master's programme) and the dissertation entitled – *Female Childhood Cancer Survivors and the impact of flank, abdominal or pelvic radiotherapy on live birth: A systematic review and meta-analysis (Polanco et al. 2021).* The findings of the dissertation demonstrated an increased risk for female childhood, adolescent, and young adult (CAYA) cancer survivors of miscarriage, premature labour, low birth-weight babies and stillbirth in future pregnancy and birth. This evidence aligned with previous publications by (van der Kooi et al. 2021, 2019, Reulen et al. 2017) and led to the identification of a gap in the knowledge, surrounding the most effective way to communicate future risks to survivors of childhood cancer.

Therefore, this thesis, aimed to examine in more detail the how, when, and in what detail, treatment-related health risks (in particular future fertility and reproductive health) should be communicated with female CAYA cancer survivors and their families. The two research studies, Pregnancy Information for Childhood Cancer Survivors study 1 and 2 (PICCS1 and PICCS2) represents a two-year PhD award, and produced an evidence-based set of recommendations for health care professionals (HCPs), to optimise their communication of future fertility and reproductive health risks with female CAYA cancer survivors.

To achieve the aims of PICCS1 and PICCS2 (Table 1), current clinical practice

examples of future health risk communication from the United Kingdom (UK) were explored. This was then compared to the existing published evidence and combined with data from the lived experiences of CAYA cancer survivors, parents[1], and HCPs. Lived experience data illustrated a wide range of future health risk (late effects) communication examples and highlighted the unmet informational needs of female CAYA cancer survivors, in particular unmet informational needs relating to future fertility and reproductive health risks.

An overarching mixed-methods approach was used in the study design, drawing from the realist method of enquiry. This method aimed to explore and evaluate the 'when, by whom and in what circumstances' of the issue, alongside the contextual factors of the CAYA cancer survivor population. A critical realist perspective in the design of PICCS1 and PICCS2 allowed for detailed consideration of the scientific evidence alongside the patient voice, which included listening to their experiences, values and beliefs. This provided the basis for the overarching research questions of the thesis.

PICCS1 and PICCS2 used a collaborative, multi-stakeholder design with independent oversight. A patient and public involvement and engagement (PPIE) representative was integrated into all stages of the research design, delivery, and dissemination process of the studies. The PPIE representative (NR) was able to contribute to all three levels of the PPIE involvement and engagement hierarchy (Figure 1) as defined by The National Institute of Health and Research (NIHR) (NIHR 2021). This included significant contributions to the

[1] In this thesis the term "parents" will be used to define parents and carers of children, adolescents, and young adults with cancer.

development of the initial research question, protocol design, recruitment plan, facilitation and oversight of the studies, and data analysis and dissemination of the studies (see section 3.4 Patient and public involvement and engagement (PPIE).

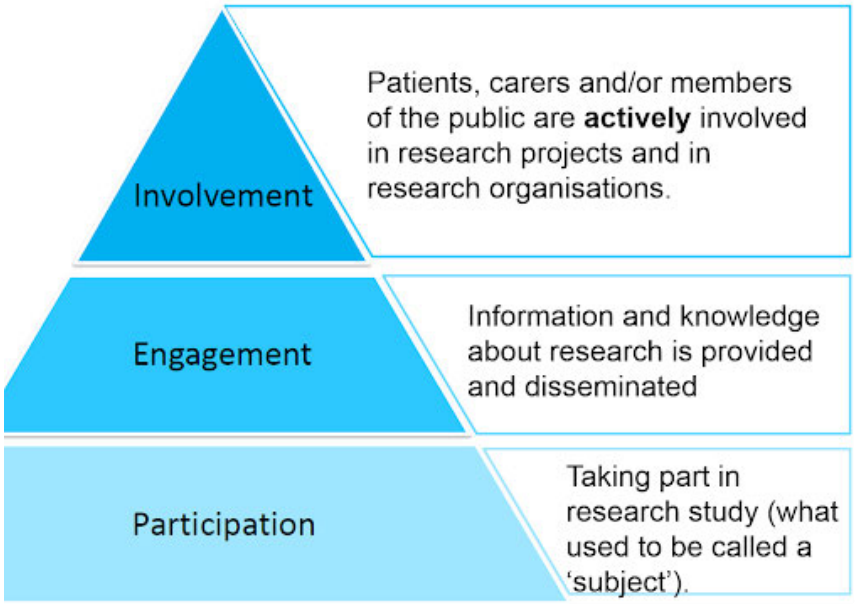

Figure 1 - PPIE triangle of involvement (NIHR 2021)

A noteworthy consideration to the completion of this thesis and the PhD award was the COVID-19 world-wide pandemic. The literature search and primary study of PICCS1 were undertaken before the outbreak. Subsequent elements of PICCS1 and PICCS2 and the synthesis of findings were undertaken during the pandemic, leading to a three-month extension to the two-year time frame due to the researcher being clinically redeployed for three months.

1.2 Research Aims

The research aims for studies PICCS1 and PICCS2 are identified in Table 1.

Table 1 - Aims of PICCS1 and PICCS2

Study	Aim
PICCS1	Critically review the available evidence for the communication of **all** late effects risk to CAYA cancer survivors and their families Explore if there is an optimal time for CAYA cancer survivors and their families to be told about the risk of late effects Investigate, using multi-stakeholder viewpoints, who is best placed to communicate late effects risk information to CAYA cancer survivors and their families
PICCS2	Understand the level of detail that female CAYA cancer survivors require in the communication of future fertility and reproductive health late effects risk Using the findings from PICCS1, to co-produce clinical recommendations for the optimal communication of future fertility and reproductive health late effects risk for female CAYA cancer survivors

Study one (PICCS1) compromised three parts:

- A systematic review of the existing literature
- A cross-sectional study of HCPs, female CAYA cancer survivors and their parents (using an online questionnaire)
- Primary data collection from eight semi-structured interviews of female CAYA cancer survivors, parents, and HCPs.

PICCS1 aimed to capture data about how late effects risk information was currently communicated in the UK, using a combined published evidence/real-life perspective model of analysis.

Study two (PICCS2) used a modified Delphi consensus technique to consider

the gaps in the research identified from PICCS1 and provide a set of recommendations to address the unmet informational needs of female CAYA cancer survivors. The focus of the recommendations was optimal communication of future fertility and reproductive health risks, as this was identified as a key unmet informational need of female CAYA cancer survivors and parents in PICCS1. PICCS2 recruited an expert panel of 20 participants from a range of multi-disciplinary backgrounds including parents, female CAYA cancer survivors and HCPs. Panellists participated in a three-stage design process to produce the evidence-based guidance document. Although the PICCS2 guidance was aimed at HCPs, there is scope for further development of the guidance more applicable to the wider CAYA cancer survivor community and future iterations reflective of new or updated research.

1.3 Formulation of the research questions

Recommendations from published literature highlighted the need to address unmet informational needs of CAYA cancer survivors (van der Kooi et al. 2021, Haupt et al. 2018). The researcher, having previously conducted a systematic review investigating the risks of pregnancy and birth for female CAYA cancer survivors, used this prior knowledge and gap in the research to formulate the research questions and the design of PICCS1 and PICCS2 (Table 2).

Table 2 – Overall research questions (PICCS1 and PICCS2)

Research questions
What are the unmet informational needs of female CAYA cancer survivors regarding their risk of future fertility and reproductive health late effects[2]?
What recommendations can be introduced into cancer survivorship care?

The composition of the chapters in this thesis is illustrated below (Figure 2).

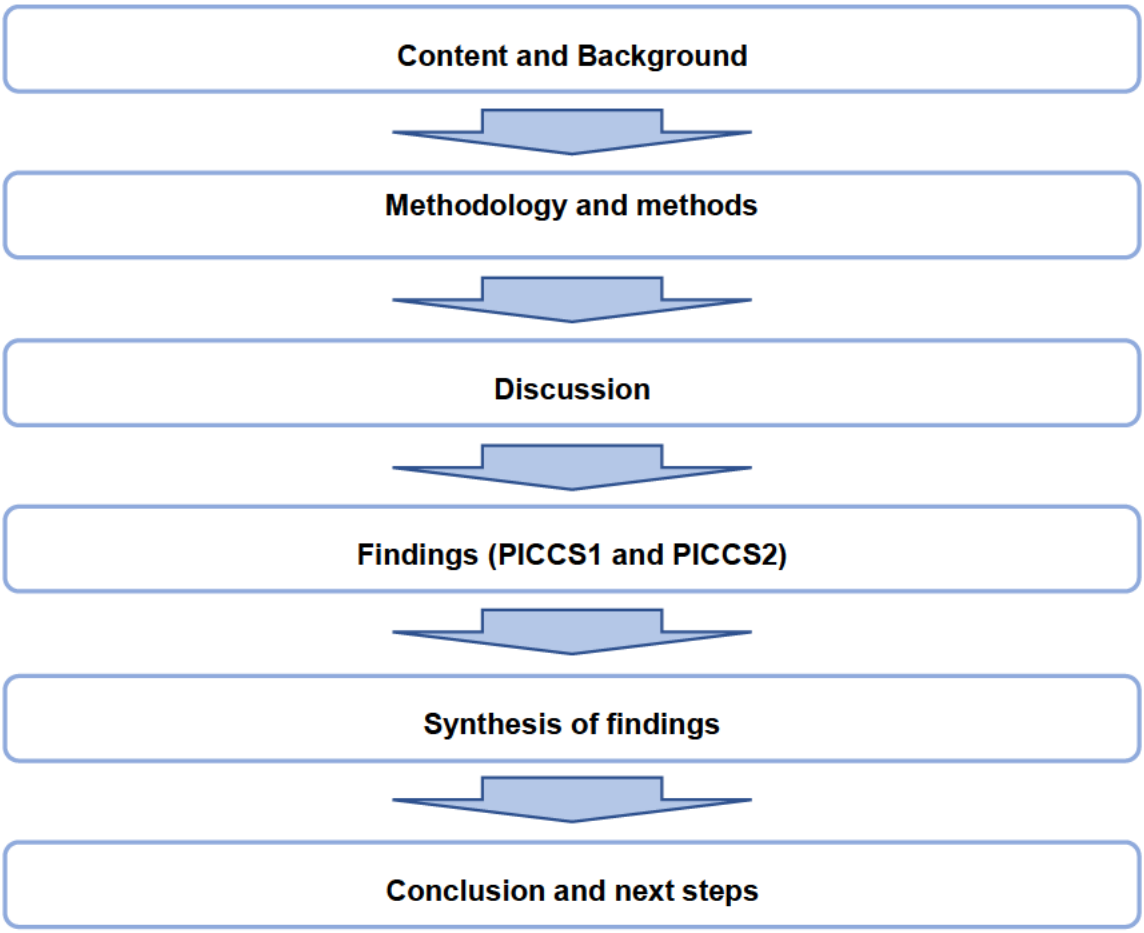

Figure 2 - Structure of the thesis

The scope of the research problem, background to the topic, and contextual

[2] Late effects refers to the effects of cancer treatments upon the health and well-being of the survivor and can be present from treatment completion until adulthood and beyond.

exploration of CAYA cancer survivorship and future fertility and reproductive health risks will now be explored in Chapter Two – Context and background.

Chapter Two – Context and background

Chapter Two is comprised of two parts, to provide context surrounding CAYA cancers, and subsequently, to explore the impact of late effects caused by cancer treatments upon future health outcomes.

Part one includes a critical analysis of the current reproductive health service structure in the UK and how services have adapted to accommodate needs of CAYA cancer survivors. Part two focuses on the delivery and organisation of cancer survivorship care in the UK, with a definition of risk, and how best to communicate risk within a clinical healthcare setting. This chapter provides the necessary context and clarity for Chapter Three – Methodology.

2.1 Part 1 – Children, adolescents, and young adults with cancer

The survival rate for children, adolescents, and young adults (CAYA) affected by cancer is now approximately 92% (Cancer Research UK (CRUK) 2021a). Children, adolescents, and young adults (CAYA) with cancer is a term often interchangeable with acronyms such as children, teens, and young adults (CTYA), adolescents and young adults (AYA) and childhood cancer survivors (CCS). For the purposes of this thesis, the abbreviation CAYA (Children, adolescents, and young adults) will be used throughout.

CAYA cancers are classified in the UK by cancer type, using the International Classification of Childhood Cancer (ICCC) (Steliarova-Foucher et al. 2005). There are over 76 subtypes of CAYA cancer. The ICCC categorises childhood

cancers into 12 diagnostic groups (CRUK 2021a). The most common CAYA cancers in the UK (per year) are leukaemia's (three in ten cases), brain, spinal, other central nervous system, and intracranial tumours (two in ten cases), and lymphomas (one in ten cases) (Office for National Statistics (ONS) 2021) (Figure 3).

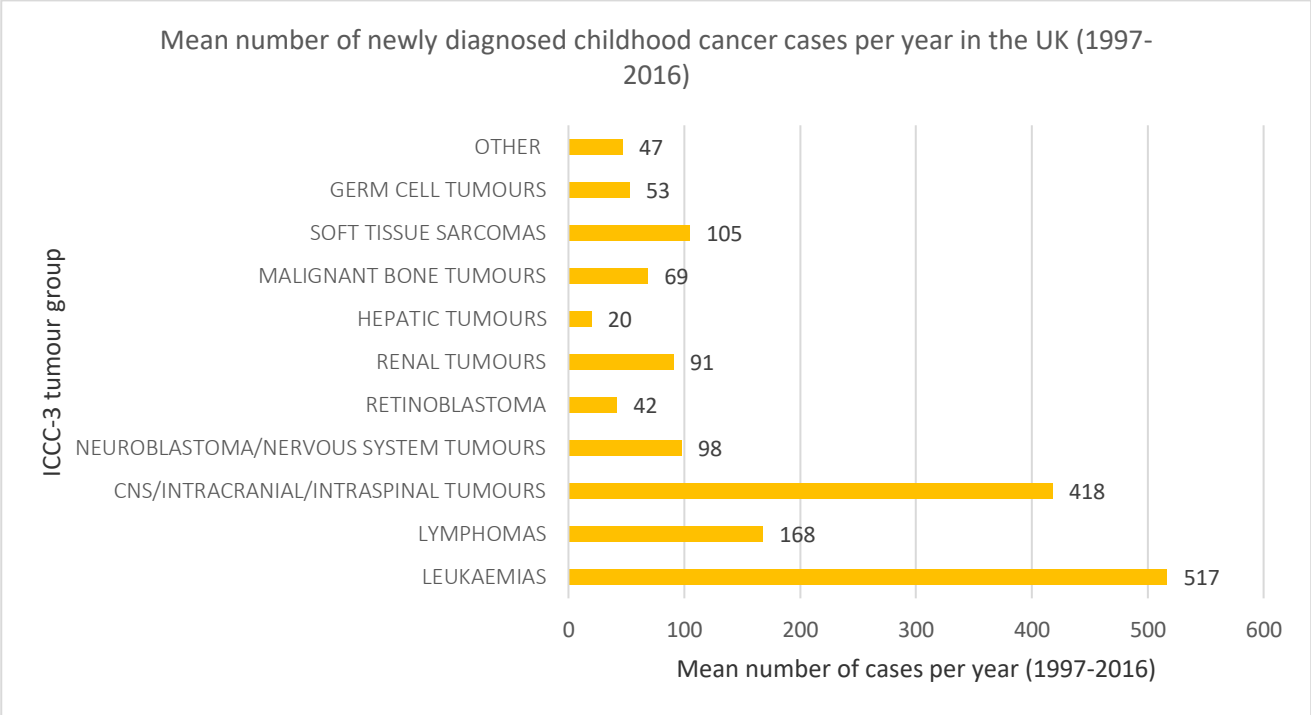

Figure 3 - Mean number of newly diagnosed cancer cases per year registered among children under 15 years of age and resident in the UK, 1997-2016, grouped according to 'International Classification of Childhood Cancer, Third Edition' (ICCC-3). (Reproduced from National Cancer Registration and Analysis Service for England (Public Health England 2021).

Many children in England, around nine in ten (92%), survive their disease for one year or more after diagnosis (2011-15) (CRUK 2021a). More than eight in ten (84%) now survive their disease for five years or more (2011-15), with approximately eight in ten (80%) surviving for ten years or more (2006-10) (CRUK 2021a) (Figure 4).

Survival rates (1,5- and 10-year) (%) for children with cancer in England (aged 0-25 years) 1971-2010

Figure 4 - One-, Five- and Ten-Year Actuarial Survival (%), Children (Aged 0-14), Great Britain (CRUK 2021a)

Survival following a cancer diagnosis, is a term used to describe a duration of five years or more following the end of active treatment (post-treatment) (Children's Cancer and Leukaemia Group (CCLG) 2021a). CCLG (2021a) estimated that there could be more than 40,000 people in the UK who have survived at least five years after developing cancer as a child. It is also estimated that there are over 500,000 CAYA cancer survivors within Europe who have survived more than five years (Haupt et al. 2018). The actual number of CAYA cancer survivors in the UK and Europe is difficult to predict as there is yet to be a prevalence study to accurately measure the number of CAYA cancer survivors within the population (ONS 2019). A lack of available data limits research capability to investigate population-based outcomes, in particular for long-term morbidity and mortality rates of survivors. This further limits the capability of health care services to plan for future health care needs of this

population due to a lack of data.

Childhood, adolescent, and young adult cancers are biologically different from adult cancers as tumours are often heterogeneous in their cellular makeup and contain multiple genetic proliferations and histological sub-types (Children with Cancer UK 2021). The site of the tumour, its origin, and how the cancer reacts to treatments, makes CAYA cancers distinctly different from adult cancers and makes standardising treatments difficult for clinicians and researchers (Children with Cancer UK 2021).

In addition, the causes of CAYA cancers are largely unknown. Many do not run-in families and are the result of malfunctioning cells at the embryonal stage of fetal development (CRUK 2021b). CAYA cancers are not linked to lifestyle causes such as smoking or obesity, nor thought to be caused by environmental factors such as x-ray exposure (CRUK 2021b). However, genetic predisposition (e.g., genome abnormalities) found within the germline Deoxyribonucleic acid (DNA) (DNA passed down from the parents) has been linked to an increased risk of developing some CAYA cancers (Kratz et al. 2021). DNA sequencing of CAYA cancers is now taking place in the UK as standard practice, through the expansion of the Genomics England 100,000 Genomes Project (Genomics England 2018). This may provide more knowledge surrounding the causes of CAYA cancers and lead to improved screening and surveillance procedures.

Within Europe, the move towards molecular level analysis and treatment of CAYA cancers rather than simply treating by cancer type or age, has been driven forward by The Innovative Therapies for Children with Cancer Academic Consortium (ITCC) and the ACCELERATE platform (see glossary).

ACCELERATE uses a collaborative stakeholder platform to facilitate early-phase trials for CAYA cancers with poor outcomes, with a focus on trials that target what drives the tumour to grow and resist treatment, rather than using a standardised treatment for a specific tumour type (ITCC 2021).

The range in age of CAYA cancers (0-24 years of age) is also a difficult factor when considering dosages of treatments. Adult and CAYA cancer treatments react differently based on the age, size of the patient and the way that the body processes the medicine (pharmacokinetics). The pharmacokinetics of cancer treatments, i.e., the processes of absorption, distribution, metabolism and excretion are all affected by changes in growth and development of the patient (Anderson 2002). This proves difficult to predict risk of late effects and requires HCPs to have a precise knowledge of pharmacokinetics in children to consider long-term risks versus benefit of cure for CAYAs with cancer (Anderson 2002). Despite this, notable increases in survival rates for CAYA with cancer due to a better understanding of mechanisms that drive CAYA cancers has led to a move towards less-toxic treatments for cancers with good prognosis rates (such as low-grade retinoblastoma and Wilms tumours) (Pritchard-Jones et al. 2013). This has enabled some CAYA with cancer, to receive more personalised, age-appropriate treatments, reducing the risk of long-term effects (Pritchard-Jones et al. 2013).

2.1.1 Mortality trends of CAYA cancer survivors

Despite high survival rates, cancer remains the leading cause of death by disease for children and adolescents worldwide (World Health Organisation

(WHO) 2021a). Significant advancements in survival have been made since the 1970s, with mortality rates for cancers in children (girls and boys combined) decreasing by 69% in the UK between the 1970s and 2018, and a reduction of 21% in the UK in the last decade (2006-2018) (Public Health England 2021) (Figure 5). However, CAYA cancers do carry an increased long-term mortality rate of 18.1% (95% CI, 17.3 to 18.9) at age 30 years from diagnosis, when compared to the general population (Armstrong et al. 2009).

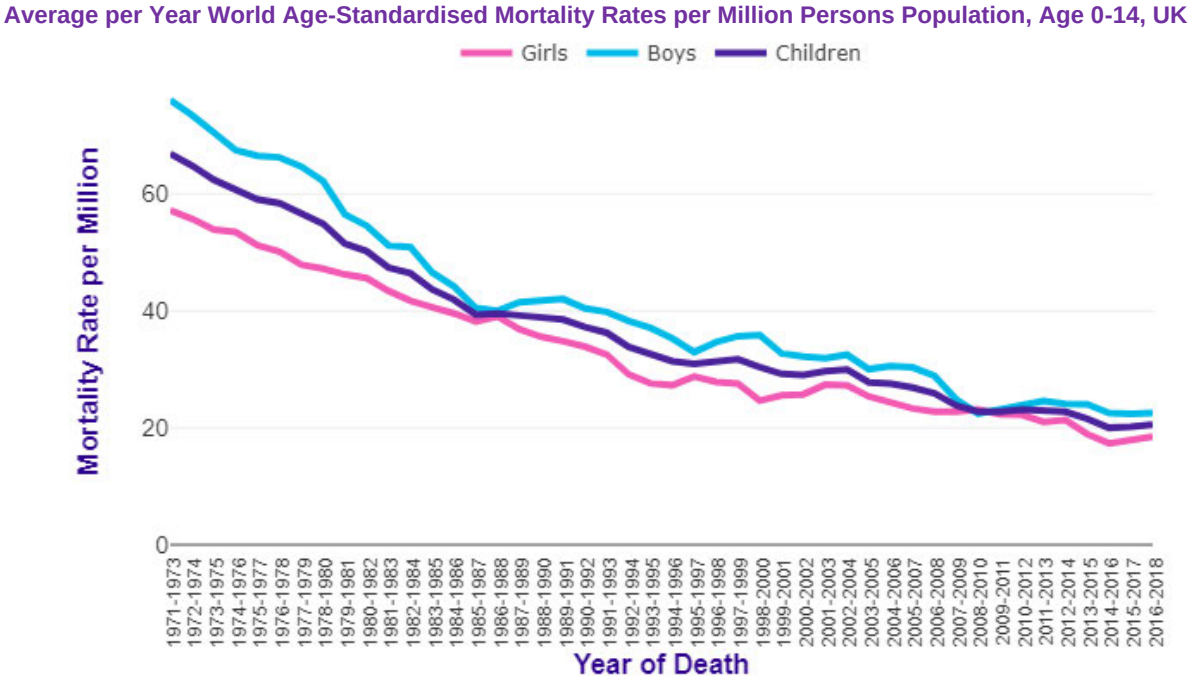

Figure 5 - Decline in average per Year World Age-Standardised Mortality Rates per Million Persons Population, Age 0-14, England 1971-2018 (Public Health England 2021).

The urgent need for more data surrounding very long-term outcomes of CAYA cancer survivors on a population level was highlighted by (Suh et al. 2020) in their study of 5,804 CAYA cancer survivors from the Childhood Cancer Survivor Study Cohort (CCSS) in the United States of America (USA). They reported an

increased risk of CAYA cancer survivors in developing severe, disabling, life-threatening, or fatal health conditions when compared to their siblings of the same age (HR 4·2 [95% CI 3·7–4·8]) (Suh et al. 2020). CAYA cancer survivors were also found to be at an increased risk of developing cardiac, endocrine, and musculoskeletal conditions in later life HR 5·6 [4·9–6·3]) (Suh et al. 2020). These findings replicate similar, large child, adolescent, and young adult cancer survivor cohort studies by Armstrong et al. (2009) and Fidler-Benaoudia et al. (2021).

Armstrong et al. (2009) in their cohort study of 20,483 survivors (taken from CCSS[3] cohort data), analysed the causes of mortality from 2,821 deaths of CAYA cancer survivors up to 2002. They reported a higher-than-average long-term mortality rate of CAYA cancer survivors who were >30 years from diagnosis when compared to sibling controls (Armstrong et al. 2009). They revealed a trend over time of mortality rates moving from recurrence of disease as a leading attributable cause, to treatment-related late effects (Armstrong et al. 2009). Fidler-Benaoudia et al. (2021) conducted an analysis of mortality rates comparing the CCSS and The British Childhood Cancer Survivorship Study[4] (BCCSS) cohorts. Analyses included a comparison of mortality rates, long-term morbidity, educational attainment, secondary cancer diagnoses and lifestyle variables (Fidler-Benaoudia et al. 2021). The BCCSS cohort

[3] The Childhood Cancer Survivor Study (CCSS) represents a cohort of 38,036 childhood cancer survivors diagnosed between 1970 and 1999 and >5000 sibling control comparators

[4] The British Childhood Cancer Survivor Study (BCCSS) is a UK population-based study of survivors of childhood cancer (cohort of 17981 diagnosed with childhood cancer between 1940 and 1991, surviving >5 years).

demonstrated a higher long-term mortality rate of (6.9%; 95% CI: 6.5%-7.2%) than that of the CCSS cohort (4.8%; 95% CI: 4.6%-5.0%) with the mortality rates of CAYA cancer survivors found to be increased when compared to a sibling or population controls in either setting (Fidler-Benaoudia et al. 2021). These data illustrates that the CAYA cancer survivor populations are at a significant increased risk of mortality when compared to those without a history of CAYA cancer.

However, age of data from these studies is a key factor for consideration. The CCSS and the BCCSS CAYA cancer survivor cohorts were treated between the 1970s and 1990s, which is not representative of current population demographics or recent cancer treatment protocols (Haupt et al. 2018). A predictive study by Yeh et al. (2020) of female and male CAYA cancer survivors, aimed to use hypothetical modelling in order to predict the life expectancy of CAYA cancer survivors by using more recent data from the CCSS cohort between 1970 and 1999. They compared survival rates of male and female survivors with acute lymphoblastic leukaemia against a control group without cancer (Yeh et al. 2020). Their findings showed that CAYA cancer survivors had an improved life expectancy when treated with newer treatment protocols, compared to those treated with traditional chemotherapy alone (Yeh et al. 2020). This finding aligns with the notable increase in survival rates over time as seen in data from the Office of National Statistics (ONS) (2021). However, the study does not provide data for modality of treatment and associated life expectancy rates when compared to older treatment protocols. The limited data on treatment modality did suggest a link between CAYA cancer

survivors who had received radiotherapy and a shorter life expectancy than those in the control group (Yeh et al. 2020). However, this finding might be incidental as cancers that require radiotherapy as well as chemotherapy are usually of a higher stage, and more aggressive than those treated with chemotherapy alone. The need for further longitudinal and prospective data collection of CAYA cancer survivors, reflective of modern treatment protocols, and with linkage to national health registries has been recommended by (Vassal et al. 2015).

2.1.2 What are late effects?

Late effects (also known as long-term effects) are often caused by the toxic treatments needed to cure the cancer. Treatments include chemotherapy, radiotherapy, immunotherapy and surgery and can be delivered alone or in a combination of therapies over a period of time (Pritchard-Jones et al. 2013). Once a CAYA with cancer is classified as being in remission (free from cancer cells in the body), clinical care moves to a schedule of surveillance monitoring for relapse of the cancer and to monitor for side-effects of treatment (late effects). This will usually continue for at least the next five years (CCLG 2021b). CAYA cancer survivors are at an increased risk of tumour reoccurrence within the first two years following cancer treatment and carry a lifetime future risk of developing a secondary cancer (Otth et al. 2021). However, the risk of future health problems following treatment can depend on the type of treatment received, how long it was given for, and the reaction that the CAYA had to the treatment (CCLG 2021b). Therefore long-term consequences of cancer

treatments can vary from person to person. Primary care providers, such as General Practitioners (GPs), often have little input into the care of CAYA with cancer until active treatment is complete and often receive little guidance regarding the level of risk for the survivor for long term complications (Signorelli et al. 2019b).

Late effects, or 'long-term effects' are a set of health conditions or ailments related to cancer treatments (Friend et al. 2018). They can occur at any point after treatment has finished, and throughout the lifetime of the survivor. The most common late effects affect the endocrine, cardiovascular and neurological systems (Friend et al. 2018). A CAYA cancer survivors' risk of late effects is dependent on the stage of their cancer, the site of the tumour, the intensity of the treatment received, and the age of the patient at the time (Friend et al. 2018). The most common treatments used to treat CAYA cancers have been linked with the following long-term or late effects (Table 3, adapted from Bottomley 2004):

Table 3 - Treatment-related late effects

Treatment	Late-effect
Cytotoxic drugs (chemotherapy)	Dose-related toxicity risks that result in organ dysfunction, infertility, and secondary cancers
Radiotherapy	Location and dose-related toxicity risks that result in secondary cancers, hormone and endocrine disorders, organ dysfunction, growth, and development disorders

Treatment	Late-effect
Surgery	Motor or neurological disorders or deficits, bone deformities and growth disorders. Treatments may include radical amputation, reconstructions and organ removal that carry significant long-term morbidity and mortality risks

The risk of late effects increases the more treatment that is given. Combination therapy (chemotherapy and radiotherapy) carries the highest risk of secondary cancers and fertility issues. Surgery alone or chemotherapy alone carries a lower risk of future complications, however, cannot be ruled out by HCPs (Friend et al. 2018).

Despite high survival rates and a reduction in treatment for low-risk cases, two-thirds of CAYA cancer survivors (around 60-90%) have at least one physical or psychological problem affecting their long-term health and well-being following treatment (Suh et al. 2020). One quarter of CAYA cancer survivors have reported experiencing a severe or life-threatening late-effect from cancer therapy (Armstrong et al. 2014). However, analysis of data by Armstrong et al. (2014) does not stratify CAYA cancer survivors by treatment type and sever late effects from treatment.

2.1.3 Fertility preservation

Fertility preservation is a rapidly advancing and emerging area within paediatric oncology services (Future Fertility Trust 2021). Fertility preservation consultations are now considered as routine practice in many primary treatment

centres, offering an opportunity for CAYA with cancer to avoid the consequences of permanent damage to reproductive organs and a hope for future childbearing (Future Fertility Trust 2021). Novel techniques such as oocyte cryopreservation, ovarian shielding during radiotherapy – where the ovaries are moved out of the radiotherapy field by covering them or by surgery – can be performed before or during active treatment for cancer (Future Fertility Trust 2021). However, in some cases a delay to treatment to offer these procedures may not be appropriate and will be a decision carefully balanced by the clinical team (Future Fertility Trust 2021).

Despite fertility preservation services being widely available within the UK, families have reported difficulties in accessing services with a lack of referral pathways and awareness of HCPs surrounding fertility preservation for paediatric patients (Panagiotopoulou, van Delft, and Stewart 2019). Equally, some fertility preservation procedures are still experimental, such as pre-menarche ovarian tissue harvesting and testicular tissue cryopreservation which makes the evidence unclear regarding potential future risks and success rates of these procedures (Mulder et al. 2021).

2.1.4 Unmet informational needs of CAYA cancer survivors

Unmet informational needs of CAYA cancer survivors (a need for further information, explanation and guidance of an issue) has been highlighted as an issue that directly affects long-term health outcomes and well-being (Vetsch et al. 2017a). Unmet informational needs about future fertility and reproductive health risks have also been reported to be one of the most important unmet

informational needs of female CAYA cancer survivors (Sandheinrich et al. 2018, Nieman et al. 2007). Similarly, unknown future fertility status and reproductive health risks have been linked to significant long-term psychological distress (higher rates of anxiety, depression, and post-traumatic stress disorder) in both female and male CAYA cancer survivor populations (Hendriks, Harju, and Michel 2021, Sandheinrich et al. 2018, Crawshaw et al. 2009).

In 2005, The National Institute of Clinical Excellence (NICE) QS55 Quality Standard document (NICE 2005), noted that the future fertility needs of cancer survivors was largely unmet and recommended that improvements to the provision of fertility preservation services for cancer survivors in the UK, including CAYA with cancer, be made (NICE 2005). Vetsch et al. (2017) in a mixed-method observational study of 485 CAYA survivors and parents, explored levels of psychological distress in CAYA cancer survivors and the link to unknown future fertility status. They reported that ambiguity surrounding future fertility status and risks led to a higher incidence of depression, anxiety, and a lower quality of life for CAYA cancer survivors than in general population controls (Vetsch et al. 2017).

The International Guideline Harmonisation Group (IGHG), who produce European Clinical Guidelines for the survivorship care of CAYA with cancer also emphasised the need to acknowledge the link between physical and psychological late effects and a poorer quality of life for the CAYA cancer survivor (van Dorp et al. 2018). They recommended that further research was needed to fully explore the long-term psychological impact of unmet informational needs (such as future fertility risks) for CAYA cancer survivors

(van Dorp et al. 2018).

2.1.5 Wider reproductive health and treatment-related risks

Reproductive health refers to the state of complete physical, mental, and social well-being, not solely the absence of disease or lack of fertility (WHO 2021b). The term relates to all matters of the reproductive system, its function, and processes (WHO 2021b). Good reproductive health is further defined as the ability to have a satisfying and safe sex life and the capability to reproduce and the freedom to decide if, when and how to do so (WHO 2021b). In the context of this thesis, the term reproductive health relates to the capability to reproduce naturally, i.e., to become pregnant and the ability to do so naturally for female CAYA cancer survivors.

Treatments for CAYA cancers affect the future reproductive health of CAYA with cancer by causing subfertility (Griffiths, Winship, and Hutt 2020). Inadvertent injury to the hypothalamic-pituitary axis (during surgery or chemotherapy/radiotherapy treatments), the ovaries, the uterus, and/or the vagina can result in 12% risk of precocious puberty (defined as puberty before the age of eight in girls and nine in boys), acute premature ovarian failure, early menopause, and permanent infertility due to ovarian follicle damage. Lehmann et al. (2019) in their cross-sectional study of 921 CAYA survivors from the CCSS cohort reported a primary ovarian insufficiency prevalence rate of 10.9% in female CAYA cancer survivors. The risk of future fertility late effects is also thought to be increased when cancer treatments are combined (e.g., chemotherapy and radiotherapy) (Griffiths, Winship, and Hutt 2020).

The future fertility and reproductive health of female CAYA cancer survivors extends beyond a definition of being fertile or being able to ovulate (Nilsson et al. 2020). However, the lack of published evidence surrounding safe toxicity thresholds of the uterus limits the ability to make accurate recommendations for care (Mulder et al. 2021). Larsen et al. (2004) reported a decreased uterine blood flow in female cancer survivors that were exposed to abdominal radiotherapy, with notable damage to the uterine musculature and vasculature. This type of damage has been linked to impaired uterine growth, lack of distensibility, an impaired endometrial function, endometrial and myometrial atrophy, and a decreased uterine elasticity (Larsen et al. 2004). Anatomical damage and inadequate growth of the uterus was also reported as a late effect of radiotherapy treatment by van der Kooi et al. (2019).

Late effects of treatment and associated risks for future pregnancy was investigated by Kalapurakal et al. (2004) who reported an increased risk of abnormal placental formation, abnormal conversion of spiral and distal uterine arteries and an increased risk of pregnancy complications such as placenta praevia, percreta or accreta, uterine rupture and early miscarriage for female CAYA cancer survivors treated with abdominal radiotherapy (Kalapurakal et al. 2004). Likewise, Reulen et al. (2017) in a retrospective cohort study of female CAYA cancer survivors from the BCCSS cohort highlighted future reproductive health and pregnancy risks such cervical insufficiency, premature birth and early/late miscarriage associated with abdominal radiotherapy treatment as a child. Van der Kooi et al. (2019) supported these findings in their study exploring the obstetric risks of female CAYA cancer survivors and reported an

increased risk of premature birth (birth <37 weeks) (RR 1.56; 95% CI 1.37-1.77), a low-birth-weight baby (<2.5kgs) (RR 1.47; 95% CI 1.24-1.73), postpartum haemorrhage (RR 1.18; 95% CI 1.02-1.36) and an even higher risk of premature labour when abdominal radiotherapy was received (premature labour RR 2.27; 95% CI 1.34-3.82) (van der Kooi et al. 2019).

Furthermore, in a previous publication by the author, Polanco et al. (2021) an increased odds of preterm birth (<37 weeks gestation) (OR 3.69 CI [2.82, 4.81] p= < 0.00001), miscarriage (OR 1.59 CI [1.37, 1.84] p=< 0.00001) and stillbirth (OR 1.72 [1.08, 2.74] p= 0.02) were reported for female CAYA cancer survivors treated with abdominal, flank or pelvic radiotherapy, when compared to non-childhood cancer controls. The vast amount of data linking adverse future fertility and reproductive health outcomes and cancer treatments as a CAYA demonstrates that it should be considered as an important topic in the communication of risk for late effects with families.

However, there are limitations to the generalisability of the study findings. For example, in a previous paper by van der Kooi et al. (2018) they reported no significant link between low-birth-weight babies and female CAYA cancer survivors, but in their 2019 paper using the same cohort, this was found to be of significance (van der Kooi et al. 2019). Similarly, Polanco et al. (2021) did not report an increased risk of low-birth-weight babies within their included data, whereas van der Kooi et al. (2019) reported this outcome as significant. This suggests that more research is needed. This includes further investigation into the cause of the adverse outcome, e.g., premature delivery and whether it was spontaneous or iatrogenic (caused by medical intervention). The analysis of this

variable within the data would be invaluable for clinicians when considering individual risk and/or additional pregnancy surveillance for female CAYA cancer survivors as it would indicate a structural growth risk or a placental insufficiency risk.

Similarly, the European guideline for the obstetric care of CAYA cancer survivors (van der Kooi et al. 2021) cannot be compared to the existing data accurately as the cohort includes CAYA cancer survivors diagnosed up until the age of 40 years. This limits comparability to other datasets that include the 0-24 years at diagnosis age range. Also, despite the guideline applying rigorous methods, and authored by a number of world-leading experts in this area, it fails to specify individual obstetric interventions or surveillance techniques that could be used by clinicians to help reduce adverse reproductive health outcomes. The issue of communication of future risk to families is also omitted.

Van Santen et al. (2020) aimed to provide guidance for HCPs involved in the ongoing care of CAYA cancer survivors, with the recommendation that CAYA cancer survivors at risk for gonadal dysfunction should be screened and referred to a (paediatric) endocrinologist, andrologist, gynaecologist, and/or fertility specialist with in-depth experience in CAYA cancers to discuss their options further. However, Mulder et al. (2021) contradicted this recommendation in their guideline “Communication and ethical considerations for fertility preservation for patients with childhood, adolescent, and young adult cancer: recommendations from the PanCareLIFE Consortium and the International Late Effects of Childhood Cancer Guideline Harmonization Group”. They recommended that the person who should be involved in communication of late

effects is dependent upon the HCPs knowledge, the patient's stage of cancer, and local access to services rather than a referral to a particular discipline of HCP (Mulder et al. 2021).

Another important consideration for late effects of cancer treatment and linked future fertility and reproductive health risks for young females is the potential impact upon future reproductive or childbearing choices as an adult. This was explored by van Dijk et al. (2020) who revealed that the chance of becoming pregnant in a Dutch cohort of female CAYA cancer survivors, was significantly lower than in non-affected controls (OR 0.5, 95% CI 0.4–0.8). Similarly, the time it took for female CAYA cancer survivors to fall pregnant was also increased when compared to controls (1.1 times longer for CAYA cancer survivors - $p = 0.09$) (van Dijk et al. 2020). The study by van Dijk et al. (2020) reinforced previous findings by Chow et al. (2009) who reported significantly lower future pregnancy rates for female and male CAYA cancer survivors (male survivors HR 0.63, 95% [0.58-0.68] $p<0.0001$, female survivors HR 0.87 95% [0.81-0.94] $p<0.0001$) than in non-cancer affected controls.

Part two of this chapter will now consider the organisation and delivery of CAYA cancer services in the UK. This will include insights explaining how CAYA cancer survivors view health care provision in the UK and how fertility and reproductive health services currently fit within the paediatric oncology survivorship model of care.

2.2 Part 2 – Health care service delivery

2.2.1 CAYA survivorship care: UK model

CAYA diagnosed with cancer in the UK are treated in one of 20 specialist hospital centres across the UK and Ireland, known as Principal Treatment Centres (PCTs) (Figure 6). This model of care for children with cancer originated to facilitate rapid access to experienced and specialised HCPs and treatments throughout the UK (CCLG 2021c).

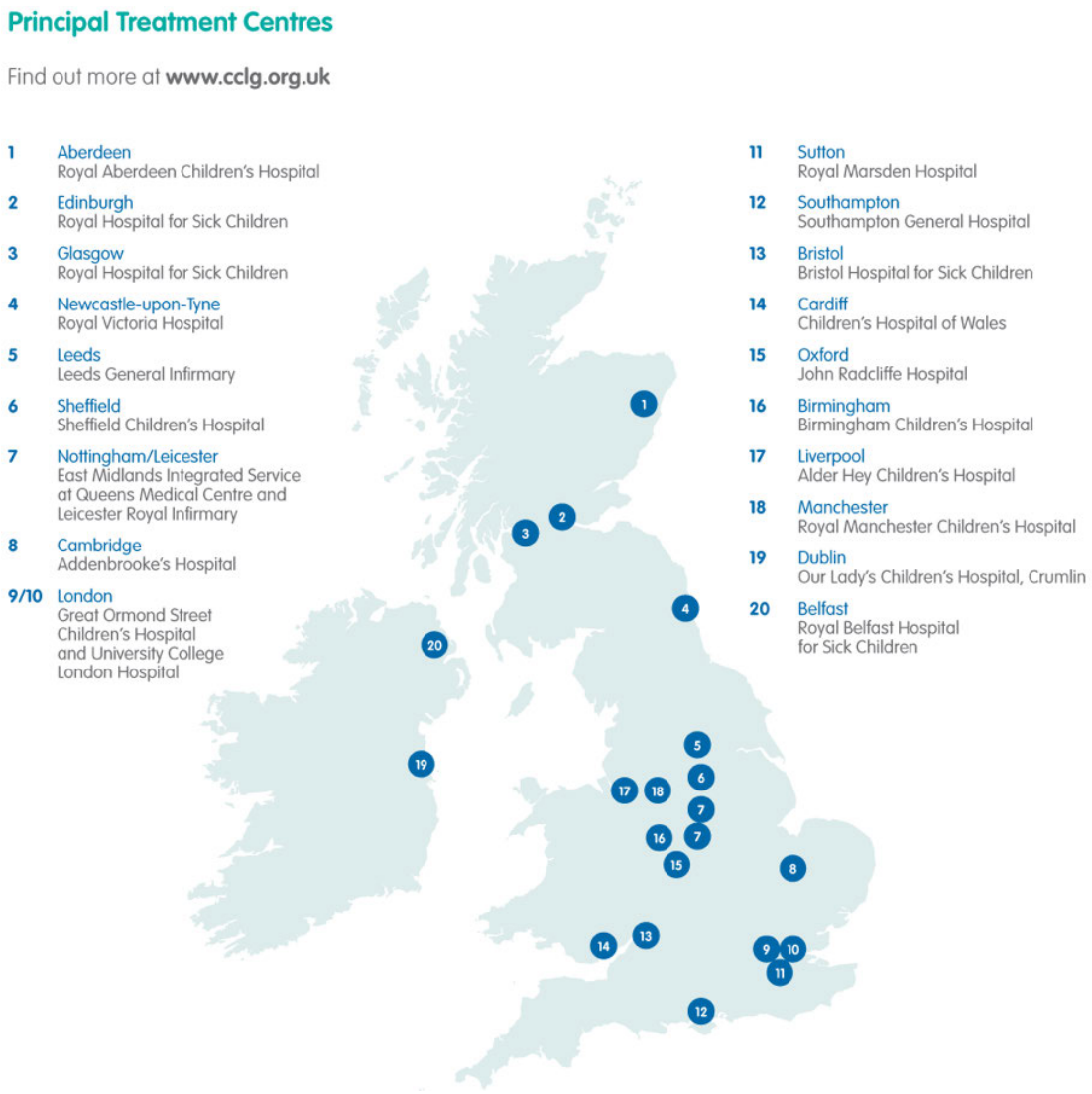

Figure 6 - Principal treatment centres in the UK (CCLG 2021c)

CAYA with cancer can also be treated at their local hospital, under the guidance of the nearest PCT. This allows the CAYA with cancer to be treated closer to home, with better access to local community support services (CCLG 2021c). The local hospitals that provide this service are called Paediatric Oncology Shared Care Units (POSCUs) (CCLG 2021c). PTCs and POSCUs collectively provide all chemotherapy, radiotherapy and other cancer treatments, specialist palliative care, ongoing support for CAYA living with and beyond cancer ('survivorship'), specialist therapies and rehabilitation.

After CAYA with cancer finish their treatment or reach an age where it is deemed more appropriate to monitor them within an adult setting, they will transition to the adult oncology survivorship service. This usually takes place around the age of 18 years, but varies greatly depending on the diagnosis, service availability and the professional relationship between the HCP and the family (CCLG 2021c). Many CAYA cancer survivors prefer to remain within paediatric oncology services for follow-up and into their adulthood due to the opinion that adult oncology settings do not meet their unique needs and primary care HCPs lack sufficient in-depth knowledge of their condition (Fidler et al. 2019, Haupt et al. 2018).

Furthermore, Knighting et al. (2020) discovered in their exploratory study of 126 CAYA cancer survivors from the CCSS cohort that a lack in the provision of information, a lack of interpersonal relationships with HCPs and logistical challenges prevented active engagement with long-term follow up services. Despite this, 80% of participants reported being satisfied with their long-term follow up care, which contradicts findings from 633 CAYA cancer survivors and parents from Australia and New Zealand who reported satisfaction with follow-up services of only 34%–56% (Signorelli et al. 2019a) and the findings of worldwide CAYA cancer registry review from (Fidler et al. 2019) who reported that the long-term follow-up of many CAYA cancer survivors, in particular those diagnosed as adolescents and young adults, remained sub-optimal. Signorelli et al. (2020) identified that CAYA cancer survivors were at high risk of service disengagement, with high levels of mistrust in HCPs from other disciplines that paediatric oncology. This led to an increased level of anxiety a greater fear of

recurrence (Signorelli et al. 2020).

2.2.2 Transition of care

The transition of care between paediatric and adult oncology services is described as a challenging and complex process (Signorelli et al. 2020). Fidler et al. (2019) suggested that a tailor-made model of care to meet all the physical and psychological needs of CAYA cancer survivors was needed. Signorelli et al. (2020) expanded upon this recommendation with a suggestion for a new model of care focused around ‘guardianship’. Nurses in particular, were recognised as a key part to addressing the ongoing needs of CAYA cancer survivors as they are ideally placed with the necessary skills and experience to enable CAYA cancer survivors with the self-management skills and empowerment that they need to use as they navigate the transition into adult oncology survivorship services (Signorelli et al. 2020).

The use of specialist nurses to support survivorship care delivery was discussed in an earlier publication by McInally and Cruickshank (2013) who proposed a flexible and multidisciplinary care model, reinforced by nursing expertise as standard. This care model aimed to keep CAYA cancer survivors engaged in long-term survivorship care for longer by providing them with a trusted outlet to discuss and explore worries and concerns that was not currently offered in the medically focused survivorship model of care (McInally and Cruickshank 2013).

Health care service disengagement and young people with chronic health

conditions is an issue that extends beyond paediatric oncology (Freyer 2010). Mulder et al. (2016) discussed the misconceptions connected with transition of health care between paediatric and adult care services. They emphasised that it is not simply a transfer of care from one doctor to another or a process of transfer to the adult equivalent of a service. Failure to transition effectively carried a risk of adverse future medical consequences such as poor mental health or late diagnosis of subsequent cancers (Mulder et al. 2016).

Adolescence and young adulthood have been described as a difficult and isolating time for CAYA cancer survivors, with fears of cancer recurrence and complications such as early menopause, reduced physical growth, cognitive/learning deficits and other factors which can affect their quality of life and the ability to lead a 'functional' or normal lifestyle (Walker et al. 2019).

Friend, Glaser, and Feltbower (2018) investigated if CAYA cancer survivors were at a greater risk of mental health problems when compared to their peers. In their systematic review, they reported that the majority of late effects data focused on physical late effects associated with high mortality such as stroke and heart disease. Psychological late effects of cancer treatment can result in higher levels of unemployment, difficulties forming and maintaining social and romantic relationships and carry a potential for increased levels of alcohol and substance misuse (Brinkman et al. 2018). The findings by Friend, Glaser and Feltbower (2018) suggest that transition of care from the paediatric to adult care services at this point in adolescence may also have psychological repercussions if not adequately managed. Likewise, the broad age-range of the CAYA with cancer population (0-24 years) provides a difficult challenge for

HCPs when attempting to meet individual needs in a service that is not designed to accommodate the diverse range of emotional, psychological and physical needs of CAYA cancer survivors as they transition into adulthood (Friend, Glaser and Feltbower 2018).

2.2.3 Behavioural change and adulthood

The psychological well-being of CAYA cancer survivors during adolescence and young adulthood is a pertinent issue to health care service delivery (Walker et al. 2019). They conducted 29 interviews with adolescent cancer survivors (aged 12-18 years) from the USA and reported a lack of evidence to effectively understand how CAYA cancer survivors emotionally frame, process or manage their mental health in the early days of cancer survivorship (Walker et al. 2019). A proportion of young people were also found to be completely unaware of any future health risks attributed to their previous cancer treatments (Walker et al. 2019). The study illustrates further the multitude of challenges faced by young people with cancer that spans a trajectory of domains including HCP-patient relationships, peer and family pressures or norms and ultimately a desire to ‘feel normal again’ or to fit into the expected version of normal that society expects (Walker et al. 2019).

Adolescence, between the ages of 16 and 25 years, has been described as a dynamic “time of transition” across multiple domains of emotional and physical development (Davies et al. 2020). Behavioural patterns during adolescence were also previously explored by Schwartz et al. (2011) who described adolescence and young adulthood as a key point in time to explore personal

identity and independence (Schwartz et al. 2011). A shift in the family dynamic during adolescence resulted in a desire for a greater independence, moving away from parental dependence, with a focus on peer relationships, romantic connections and an increased use of social media and the internet for valued advice and information (Schwartz et al. 2011). Increasing reliance of the adolescent and young adult age groups on digital devices and online communication is also an important factor when considering communication needs of this age group (Davies et al. 2020).

For young adults with a history of a chronic illness or a complex medical history (such as CAYA cancer survivors), the transition from childhood to adulthood is further complicated by their health-related experiences as a child. Their memories of cancer treatment can greatly affect their long-term psychological well-being, increasing the likelihood of traumatic memories being triggered by future health care episodes (Bitsko et al. 2016). Friedman, Freyer, and Levitt (2006) illustrated the need for HCPs to acknowledge that future hospital attendances or procedures may be a potential trigger for the young person, thus causing distress. Therefore, consideration of individual need, preferences for care and feelings of the survivor should be considered sensitively (Friedman, Freyer and Levitt 2006). Likewise, Schwartz et al. (2011) explored how traumatic memories are triggered in CAYA cancer survivors and likened the experience to post-traumatic stress disorder symptomology caused by previous medical procedures as a child. To avoid the potential for psychological distress or triggers, Schwartz et al. (2011) recommended a gradual transition of care into adult care services, with preparations taking place years before the

transition is made.

The psychological conflict experienced by CAYA cancer survivors in wanting to feel normal again, whilst acknowledging that they cannot return to a pre-cancer existence, was highlighted as a key finding by Walker et al. (2019). They linked this psychological conflict between being classed as ‘normal’ once in remission and the ongoing physical, psychological, and social challenges due to their cancer treatments with a greater likelihood of health care service avoidance in adulthood (Walker et al. 2019). Consideration of individual need, transition of care at the right age and timepoint for the individual and the family was recommended Smith, Link, and Effinger (2020) in their systematic review of 12 papers that presented data from adolescent cancer survivors aged 13-39 years. They revealed that cancer survivors wanted information about what was going to happen to them, in a controlled amount and at a time to suit them (Smith, Link, and Effinger 2020). However, a caveat to the findings of this review, which affects the generalisability of the findings, is the cohort data largely represents the younger adolescent population with nine out of 12 papers using data from participants aged <25 years (Smith, Link, and Effinger 2020).

In order to address the gaps within CAYA cancer survivorship service provision, strategic multi-level input, evaluation and analysis extending beyond the commissioning, organisational and delivery service level is needed (Smith, Link, and Effinger 2020). Akin to this recommendation is the adequate representation of the patient voice at the centre of any service improvement strategy (Smith et al. 2020). Consideration of the long-term physiological needs of CAYA cancer alongside the more recognised physiological surveillance methods should be a

standard of care for CAYA cancer survivors (Walker et al. 2019).

2.2.4 Gold standard CAYA cancer survivorship care

To achieve the best standard or often termed 'gold standard' of CAYA cancer survivorship care, commissioning of health care services is an integral part of the health care model (Feltbower et al. 2004). However, commissioning of health care services for CAYA with cancer has also been recognised as an extremely complex and challenging issue for health care services (Feltbower et al. 2004). In 2005, NICE published the guideline *'Improving outcomes in children and young people with cancer'* (CSG7, NICE 2005). The guideline accepted that improved survival rates for CAYA with cancer will result in a notable increase of CAYA cancer survivors within society (NICE 2005). This will subsequently present a challenge for health care service provision due to the lack of data surrounding long-term health outcomes of CAYA cancer survivors and real-time prevalence data for CAYA cancer survivors in the population (Fidler et al. 2019). NICE (2005) provided a set of outcomes for commissioning services for children and young people with cancer (Table 4).

Table 4 - NICE 2005 Guideline for improving outcomes in children and young people with cancer

NICE 2005 Main aims
Care should be coordinated across the whole NHS and be as close to home as possible
Multidisciplinary teams should provide cancer care
All children and young people should have a clearly defined key worker
Care should be appropriate for the child's or young person's age and type of cancer
Time in the operating theatre and a children's anaesthetist should be available when needed

Children and young people should be offered the chance to take part in research trials
Cancer networks should make sure there are enough specialist staff

Following the NICE guideline (NICE 2005), The Cancer Reform Strategy (formed in 2007 and developed by the National Cancer Survivorship Initiative (NCSI) and NHS England) also highlighted the need for a more holistic and equitable health care service for CAYA cancer survivors, offering better support, surveillance, and timely referrals to clinical services for any complications (NCSI 2013). They recognised the need for a CAYA cancer survivorship service that reduces demand on health care services, but that also encourages the promotion of self-management of long-term chronic disease based on individualised need (NCSI 2013). However, there is not a 'one size fits all' approach suitable for this population, due the ongoing physical, emotional, and social changes during childhood, adolescence, and young adulthood. This presents a unique challenge for health care commissioning services in the UK (Wright 2014).

The NICE guideline (NICE 2005) was reviewed in 2014, but no changes were made due to a lack of new evidence and no planned study publications within the proceeding five-years (NICE 2014). However, NICE did publish an additional quality standard (QS55) to accompany the guideline called '*NHS Cancer Services for Children and Young People'* (NICE 2014). NICE quality standards are designed to drive measurable quality improvements within an area of health or care. Evidence used in the QS55 standard was derived from additional resources such as the Scottish Intercollegiate Guidelines Network (SIGN) and their '*Long term follow up of survivors of childhood cancer: Clinical Guideline 132'* published in 2013 (Health Improvement Scotland 2013).

The '*QS55 standard for children and young people with cancer'* (NICE 2014) recommended health care service providers, HCPs, and commissioning services to adopt a collaborative approach to CAYA cancer care (NICE 2014). This approach recommended the involvement of a variety of multidisciplinary agencies and recommended a person-centred, integrated approach to CAYA cancer care services, responsive and tailor-made to individual need. However, notably the standard does not mention the inclusion of patients and their families in the reorganisation and improvement of care services but does promote the role of family members in the active decision-making processes for CAYA with cancer (NICE 2014).

Statement six and seven of the QS55 standard (NICE 2014) directly pertains to the role of the HCPs in ensuring that the needs of the CAYA cancer survivor and their families are met (Table 5).

Table 5 - NICE Quality Standards (NICE 2014)

NICE 2014 Quality Standard	Description
Statement 6	Children and young people who have been treated for cancer have an end-of-treatment summary and care plan that includes agreed follow-up and monitoring arrangements.
Statement 7	Children and young people with cancer are assessed for potential future fertility problems and advised about their options for fertility preservation before treatment is started.

Health care commissioning services were also offered the following commissioning guidance for the improvement of survivorship services (Table 6).

Table 6 - NICE Commissioning guidance for children and young people with cancer (NICE 2014)

Timepoint in treatment	Commissioning Guidance
Before treatment	Strategic clinical networks and CCGs should ensure: • Fertility preservation services are in place to assess CAYA with cancer for potential fertility problems before treatment • Appropriate advice given for available fertility preservation options Access to services is likely to be variable, however, knowledge of specialist fertility services aimed at the CAYA with cancer population should be encouraged. No significant cost is predicted due to low affected population numbers
End of treatment	Ensure services provide: • verbal and written information about the long-term risks of their cancer and treatment • arrangements for monitoring, identifying, and treating any potential problems as quickly as possible • an outline for the role of the GP and primary care services
End of treatment	Provide: • A high-quality aftercare program delivered locally with clinical expertise support to support the individual needs of the patient This recommendation may increase costs, but can reduce clinic attendances and provide increased capacity for services to cope with the predicted increase of survivors in the future

Despite NICE highlighting the need for an improved CAYA cancer survivorship care provision in the UK in 2005 and 2014 (NICE 2005, 2014) and in the NHS

Long Term Plan (NHS England 2019a), there are still areas of CAYA cancer survivorship care that need to be improved to meet the needs of survivors and their families (Hendriks, Harju, and Michel 2021). Similarly, CLIC Sargent, one of the leading childhood cancer charities in the UK, published a report in 2019, that evaluated CAYA cancer survivorship services in the UK (CLIC Sargent 2015). They identified that poorly managed survivorship care-plans and inequity in access to survivorship services have led to a devastating effect upon the level of care offered to CAYA with cancer in the UK (CLIC Sargent 2015).

The James Lind Alliance (JLA) is an example of an organisation in the UK that uses a collaborative stakeholder engagement model to address areas of need in healthcare, with the prioritisation of research questions (JLA 2021). They undertook a priority setting partnership project in 2019 for adolescents and young adults with cancer and reported one of their top-ten findings to be the need for an improved survivorship service to address the social, emotional, and physical health of survivors (JLA 2021). This finding is illustrative that the need to improve CAYA cancer survivorship care services is a priority for both health care delivery and commissioners and patients and their families. The NHS Long Term Plan (NHS England 2019a, chapter 3) also highlighted the need for any future service re-design plans to consider integration of novel health technologies (such as genome and tumour sequencing programmes). However, notably no deadline or expected implementation date has been provided to drive forward new initiatives or changes to current practice.

In Europe, a collaborative stakeholder group consisting of members from the European Network for Cancer research in Children and Adolescents, the

Clinical Research Council (composed of all the European Clinical Trial groups and national societies in paediatric haematology/oncology) and parents and survivors from the Childhood Cancer International European group, published a five-year strategy entitled "*The European Strategic Plan for children and adolescents with cancer"* (Vassal et al. 2015). They also placed an emphasis on developing a survivorship care model that incorporates a more holistic approach to survivorship care, inclusive of psycho-social support alongside surveillance.

2.2.5 The Survivorship Passport

A European initiative, named the *'Survivorship Passport'* (SurPass) (Haupt et al. 2018) was designed to address the need to improve survivorship care for CAYA with cancer by utilising a self-management model for managing future health. The initiative consisted of providing the survivor with a tool containing electronic health record data including a full clinical history of the patient, the original diagnosis, all treatments, and dosages received, and any follow-up or surveillance recommendations (Haupt et al. 2018). SurPass was launched in Italy in 2018, with the aim of disseminating the tool throughout Europe (Haupt et al. 2018). However, despite the tool being used widely within Italy, it was slow to be adopted in other European countries, with only Austria implementing the passport into their 5-year plan for paediatrics in 2015 (Haupt et al. 2018). In addition, despite the SurPass being available in a variety of multimedia formats and languages, countries such as Germany and Spain, are yet to recommend its use within their national cancer survivorship programmes (Haupt et al. 2018).

An explanation for the slow uptake of this tool could lie in the wide variation in

screening surveillance methods, follow-up programmes and availability of specialised clinical service on an individual country level (Haupt et al. 2018). Also, a link to the possible triggering of distressing memories as mentioned by Bitsko et al. (2016) was also discussed by Haupt et al. (2018) in the evaluation of the tool suggesting that it might inadvertently increase anxiety levels about side-effects or cancer reoccurrence in individuals who do not want to know that level of health information. Haupt et al. (2018) made the recommendation for further research exploring the communication of future health risks for CAYA cancer survivors, in order to reduce the psychological burden of their cancer history.

Additional worldwide examples of the SurPass have been demonstrated in the USA with their initiatives *'Passport to Care'* and the *'Care for CAYA'* protocol (Salchow et al. 2020). In the UK, The Survivorship Initiative in Scotland is the most recent example of a CAYA cancer survivorship care interventional tool that incorporates a risk-based scoring system with the promotion of open communication of future health risks between HCPs and survivors (Wallace, Thompson, and Anderson 2013). They also highlight the advantages of using an age-appropriate environment and the expert skills of nurse-led services to help deliver a survivorship service that meets the needs of survivors and families (Wallace, Thompson, and Anderson 2013).

2.2.6 The CAYA cancer survivor's viewpoint

At the centre of unmet informational needs is the CAYA cancer survivor and their families. Research has often been conducted on, about or on behalf of

participants rather than in collaboration with them (NIHR 2021). This culture of 'about us but not for us' has resulted in a lack of research designed to address the research priorities of participants and their families (Pii et al. 2019). Evidence of extensive Patient and Public Involvement and Engagement in research (PPIE) is now a mandatory element of research funding applications (e.g., Wellcome Trust, Medical Research Council (MRC). Good quality PPIE within research promotes a culture of collaboration and helps to prioritise future research shaped around patient need (Bate et al. 2016).

2.2.7 Communication of risk

Many younger CAYA cancer survivors (< 12 years old at diagnosis) are naturally reliant on their parents receiving information about their diagnosis, treatment, risk, and follow-up care, due to their age at the time of treatment (Lie, H C et al. 2015). However, many CAYA cancer survivors are unaware of their risk of late effects, and some are unaware of their previous cancer diagnosis as a child (Hess et al. 2011). In cases of very young children, all clinical information is communicated to the parents, which includes the provision of future health care information and late effect risks (CCLG 2021b). The CAYA cancer survivor diagnosed as a young child is therefore fully reliant on their parent/carer to pass on this information when they reach an age of maturity. Inaccuracies in the information or omission of key risks can lead to obtaining inaccurate, partial, or contradictory advice and may carry implications for future health choices and behaviours (Hess et al. 2011).

Clarke, Sheppard, and Eiser (2008) explored the communication of health

information between parents and their children in a qualitative exploratory study of 39 mothers of retinoblastoma survivors (USA). They revealed that parents shielded important health information from their child survivor, including information about future genetic risk, if they perceived that this could be stress-inducing for the child (Clarke, Sheppard and Eiser 2008). Although the study is limited to one disease area, it highlights that the issue of miscommunication or information shielding by parents is worthy of further investigation. Casillas et al. (2010) also reported that parents of childhood cancer survivors need help and support to effectively communicate future health risks to their child.

In contrast to the assumption that communication of future health risk information only happens between the parent and the HCP, The Teenage Cancer Trust (2019) in their survey of adolescents and young adults (AYAs) with cancer, reported that some young people preferred to take ownership of their diagnosis, care and clinical consultations at an early age. Some young people also reported that they preferred to receive information about late effects without their parent being present (Teenage Cancer Trust 2019). An assessment of individual competence, age and maturity was recommended by Lie et al. (2015) to address this variance in individual need and was particularly advised for discussions relating to future fertility and reproductive health.

Smith, Link and Effinger (2020) and Lie et al. (2015) explored the concept of a ‘reinformation’ session for CAYA with cancer to address unmet informational needs. The proposed intervention aimed to re-engage and re-educate families about key future health information, including the communication of late effects risk (Lie et al. 2015). Smith, Link, and Effinger (2020) suggested that a

'reinformation' approach prioritised the need for ongoing personal reflection of the CAYA with cancer, an assessment of their physiological and psychological needs and improved the overall awareness of the cancer diagnosis and treatments received. The 'reinformation' approach was also recommended as a method to alleviate reported parental pressures when communicating future health risk information to their child (Smith, Link and Effinger 2020).

2.2.8 Reproductive health and pregnancy

The UK adult population is increasingly representative of an older, medically complex demographic with increasing health care service needs (NHS England 2019a). Additionally, an increasing number of pregnant women in the UK now have a medical co-morbidity or mental health need (NHS England 2019b). Specific care pathways to optimise care and outcomes for women with complex health needs in pregnancy and birth (e.g., maternal diabetes, epilepsy, and cardiovascular disease) have helped to lower maternal morbidity and mortality rates (Maternal death report: Mothers and Babies: Reducing Risk through Audits and Confidential Enquiries across the UK (MBRRACE) 2019).

Data has illustrated that over 60% of CAYA cancer survivors also suffer from an additional long-term chronic health condition (Otth et al. 2021). The increasing number of CAYA cancer survivors within the UK population (although accurate estimates are unknown), suggests that CAYA cancer survivors as a cohort will be represented within the UK population within the next 10-20 years. Therefore, it can be hypothesised that more female CAYA cancer survivors will have a need to access maternity services for their pregnancy care. Women presenting

for maternity care with a medical history of CAYA cancer need to be adequately risk assessed and cared for by a multi-disciplinary team that are knowledgeable of her medical history, her associated risks and her own wishes for pregnancy and birth (Polanco et al. 2021).

Pregnancy has been identified as a key timepoint, where women routinely and voluntarily engage with health care services (NHS England 2019b). This could provide a unique opportunity for HCPs to re-engage women with a history of CAYA cancer back into health care services. A reinformation session as advised by Smith, Link, and Effinger (2020) of key late effects information and the assessment of any informational needs may help to re-engage those CAYA cancer survivors who may have been lost to follow-up or who have actively dis-engaged from survivorship services back into survivorship care (Signorelli et al. 2019a).

There is a depth of evidence to support a higher risk of adverse outcome during pregnancy and birth for female CAYA cancer survivors treated with radiotherapy to the abdomen (Polanco et al. 2021, van der Kooi et al. 2019, Reulen et al. 2017). MBRRACE (2019) also highlighted that HCPs need adequate knowledge surrounding the needs of women with a history of cancer, however, as yet there are currently no clinical guidelines for the management of obstetric care for female CAYA cancer survivors in the UK. A clear referral pathway for the female CAYA cancer survivor when they present for maternity care, with a rapid assessment of needs by an obstetric professional, would facilitate the evaluation for additional pregnancy surveillance and/or interventions and would allow the woman to be a part of the decision-making process. HCPs have a

professional responsibility to communicate potential health risks to patients before a treatment or procedure, as governed by the medical code of conduct and Duty of Candour (Nursing and Midwifery Council 2019). Therefore, HCPs caring for female CAYA cancer survivors during pregnancy and birth should be required to have sufficient knowledge to counsel women and their families about their individual health risks.

2.3 Summary

CAYA cancer survivors (aged between 0-24 years at diagnosis) are a rapidly growing population with complex and individualised health care needs (Suh et al. 2020). High survival rates for most CAYA with cancer (currently 92% overall) suggests an emerging population that will require a higher level of health care service need that adults without a history of cancer (Armstrong et al. 2014). Unmet informational needs of CAYA cancer survivors have been linked to significant adverse psychological outcomes (Vetsch et al. 2017). HCPs should be aware of the combined holistic needs of survivors in their care to provide an optimal survivorship care service (Hendriks, Harju, and Michel 2021). Communication of future health risks, in particular the communication of future fertility and reproductive health risks to female CAYA cancer survivors and their parents should be prioritised within any survivorship care service improvement strategy (Signorelli et al. 2019a).

The definition of fertility and wider reproductive health and the importance of future childbearing to the CAYA cancer survivor has been recommended for further investigation to explore the optimal communication method, timepoint for

delivery of information and individual preference of the survivor (Anazodo et al. 2019). Research exploring the communication and informational needs of CAYA and adult cancer survivors has largely been of qualitative enquiry, with a focus on outcomes reflective of physical late effects (e.g., conditions that affect the heart, bones, lungs etc.) (Brinkman et al. 2018). Likewise, the range in age of this population (0-24 years) carries a multitude of challenges and considerations, unique to each patient and their family situation. Innovative and patient-centred approaches that also consider the move towards digital-living and information seeking is needed to ensure that guidance reflects societal and medical advancements in line with patient need.

Exploration of the toxic treatment thresholds of reproductive organs, in particular of the uterus, is under-researched (Griffiths, Winship, and Hutt 2020). More data is needed to assist HCPs in the communication of risk for future health, which includes probable future pregnancy and birth/parenthood (Polanco et al. 2021). Likewise, there is limited evidence investigating HCP and CAYA cancer survivor/parent knowledge of future fertility and reproductive health risks, despite the strong association with adverse future fertility and reproductive health outcomes (Polanco et al. 2021).

The evidence suggests that there is an urgent need to re-design CAYA cancer survivorship care services to meet the unique and changing needs of CAYA cancer survivors (Signorelli et al. 2020, Haupt et al. 2018, Sandheinrich et al. 2018, Nieman et al. 2007). Health care authorities in the UK and Europe have encouraged a move towards a self-management model for survivorship healthcare (Brown et al. 2021, Mulder et al. 2021). However, if existing unmet

informational needs of CAYA cancer survivors and their families are not addressed, there is an increased risk of health care service disengagement and long-term psychological distress for existing CAYA cancer survivors (Suh et al. 2020). Equally, miscommunication or omission of key late effects information between the HCPs, parents and CAYA cancer survivors has been reported to be more likely to occur if the information is not communicated effectively in the first instance and if it is not presented in a way that can be recalled with accuracy and after a long period of time (Casillas et al. 2010).

In conclusion, future research to address unmet informational needs of CAYA cancer survivors and in particular surrounding future fertility/reproductive health outcomes is needed. There is also a need for a pre-emptive and strategic service re-design of CAYA cancer survivorship care services in the UK that is more inclusive of the patient voice (Henderson, Friedman, and Meadows 2010). Strategies to assist and support parents of CAYA cancer survivors in the delivery of key health information to their child is also needed (Smith, Link, and Effinger 2020).

The next chapter of this thesis will now consider the most appropriate research study design to address the unmet informational needs of CAYA cancer survivors, identified within the evidence. This will include a presentation of the philosophical reasoning of the researcher, the adopted methodology and research design for the two sequential studies, PICCS1 and PICCS2. PICCS1 and PICCS2 will in combination, address the overarching research questions of the thesis (Table 2).

Chapter Three – Methodology

This chapter outlines the philosophical reasoning, the approach and the justification of the research methods used in the study. It will examine the ontological viewpoint of the researcher, and the subsequent epistemological and axiological assumptions, that form the philosophical reasoning behind the research. Following this, Chapter Four will outline the methods used in PICCS1 and PICCS2, including justification and critical consideration of alternative methodological frameworks. This approach aims to demonstrate critical consideration and reflection upon key philosophical underpinnings used within this thesis and the implications upon the study findings and research design.

3.1 Methodological Underpinnings

Research can be defined as “an activity that involves finding out, in a more or less systematic way, things you did not know” (Walliman 2010). Integral to that process is the methodology that includes the identification and acknowledgement of a philosophical framework within which the research is conducted, often associated with a particular set of paradigmatic assumptions (Corry, Porter, and McKenna 2019). Furthermore, research studies should align with the methodological framework and philosophical underpinnings which best fits the objectives of the research and the research paradigm (Corry, Porter, and McKenna 2019).

It is important to be able to explain and understand, what drivers have shaped a research project and how this has informed the chosen methodological framework (Corry, Porter, and McKenna 2019). A key part to this explanation is

the understanding the human beliefs, values and/or external influencing factors that sit within or centrally underpin the work – known as the ontological viewpoint (Dudovskiy 2018). The personal beliefs of the researcher (i.e., the ontological viewpoint) is intrinsically linked to their understanding and belief of 'what is knowledge' within modern society. The understanding or belief of what knowledge is, where it comes from, and how we perceive it within the world, represents the epistemological standpoint of the researcher (Dudovskiy 2018).

The epistemological standpoint of the researcher guides and justifies the comprehension and acceptability of new/learned knowledge, thus forming the basis for what is accepted to be true or a reliable source of knowledge (Dudovskiy 2018). Together the beliefs and truths (i.e., ontological, and axiological views of the researcher) and the accepted definition of what is knowledge (i.e., epistemological standpoint), form the overarching philosophical 'framework' for a research study. The overarching philosophical framework is then used to design a research study and define and justify the methods used to capture and analyse data.

However, before an analysis of the adopted philosophical framework used for the research study can take place, it is important to explore in greater depth the theories that underpin the mechanisms of understanding and knowledge of the researcher. This will now be explored and defined below.

3.1.1 Axiology

Axiology is defined as the assessment of the researcher's values and their role

within the research process (Walliman 2011). Axiology refers to the aim of the research and proposes two questions; do you want to explain or predict the world, or do you want to simply understand it? These questions encourage the researcher the explore their definition of values within their research study design (Onwuegbuzie, Johnson, and Collins 2009). Personal acknowledgement of values and beliefs, and the potential impact upon the design of a research study are essential for the researcher, providing a mechanism for reflexivity and assisting in the reduction of bias within a study (Walliman 2010). Table 7 illustrates the values and beliefs (axiology) linked to the most common research philosophies.

Table 7 - Axiology and research philosophies (adapted from Dudovskiy 2018)

Philosophy	Axiology
Positivism	Research is not based on values; the researcher is independent of data and remains objective
Realism	Research is based on values, and is influenced by views, cultural experiences, and upbringings. These elements can affect the research findings
Interpretivism	Research is intertwined with values; the researcher is a part of the research and cannot be separated. This can lead to subjective application of the results
Pragmatism	Research is guided by values. The researcher adopts both objective and subjective points of view to interpret the findings of a study

The axiological beliefs and values applied to the design of the studies PICCS1 and PICCS2 align with a positivistic stance. However, the researcher accepts that there is an element of pragmatism to the applied research study design, reflective of the personal belief that 'one size does not fit all' within society. In

particular, the researcher aligns with the belief that research findings and wider knowledge should also be guided by the lived experience of participants to ensure compete representativeness of the chosen population. This is also a stance reflected in health care and reproductive health care research that places emphasis upon the individualised and tailor-made care provision based upon patient-reported needs (NHS England 2019a). Therefore, the researcher declares a pragmatistic philosophical approach to the axiology of the PICCS1 and PICCS2 research studies. The pragmatistic approach caters for both the objective point of view for collecting data and places equal importance upon the interpretive elements of the research design. This is defined further as *"The acceptance of knowledge that is based not only on evidence and facts, but reflective of beliefs, cultural dimensions, and additional external variables"* (Onwuegbuzie, Johnson, and Collins 2009).

3.1.2 Ontology

Ontology is defined as *"the science or study of being"* and defines the concept of 'what is reality' and 'what is the nature of existence' (Sniukas 2020). Ontology refers to a system of beliefs that can accommodate or be influenced by individual interpretation or personal influences (Sniukas 2020). Ontological assumptions help to guide researchers in their selection of a research paradigm that aligns with their philosophical reasonings and therefore guides their epistemological approach (Dudovskiy 2018). This also includes an effect upon the selection of research methods and use of specific data analysis/synthesis tools (Dudovskiy 2018). Ontological assumptions can reflect an objectivist or

subjectivist reasoning or set of beliefs and will now be explored in greater depth.

Objectivist and subjectivist philosophical dimensions are surmised to either describing knowledge of truth as 'being in the mind of each individual' (subjectivism) or being subject to a conceptual knowledge 'shaped by outside influences' (objectivism) (Dudovskiy 2018). Table 8, cited in Dudovskiy (2018) illustrates the differences between the two philosophical dimensions.

Table 8 - Dimensions of subjectivist and objectivist approaches in research (adapted from Dudovskiy 2018)

Comparative elements	Objectivist	Subjectivist
Philosophical thinking	Realism – the world exists and can be studied as it is	Idealism – the world exists but is observed differently by different people
Role of social science in research	Exploring universal laws of the society and the behaviour of people within it	Exploring how the world is interpreted by different people
What is social reality?	Society, groups, or organisation(s)	Individuals
Comprehension of social behaviours	Studying the type and nature of various relationships that allow the collective group to exist	Studying subjective 'different to different people' meanings that individuals use to base their actions
Definition of theory	A rational theory developed by researchers to explain human behaviour	Categories used by individuals to interpret their world and behaviours
Research design approach	Validation of assumptions by experimentation or quasi-experimentation	Examining relationships between individuals or outcomes to understand the consequences of actions

Comparative elements	Objectivist	Subjectivist
Methodology	The use of quantitative analysis and statistical methods	The analysis of behaviours, experiences and attitudes which define the individual interpretation of reality
Societal values	Society is managed by a set of general values, rules, and regulations to function	Society is based on values, held by individuals of power

The researcher, for the PICCS1 and PICCS2 studies, accepts a primarily objectivist standpoint relating to the personal belief of what is 'truth' or what is 'knowledge' in the world. This includes the consideration of expected societal norms and how this influences the definitions of 'truth' and 'knowledge'. The researcher adopts the perspective that truth, knowledge, and societal norms derive from evidence that has subject to a set of standards for data collection and analysis and the findings applied to a wider population or societal group. This belief reflects personal influences and cultural norms experienced by the researcher (military family background and upbringing) and is coupled with personal educational experiences and training (medical professional training as a midwife and clinical academic researcher). Societal expectations, i.e., that we live within a society that must follow rules and regulations in order to function also have influenced the thinking, reflection and understanding of the researcher when adopting a philosophical approach to the research studies PICCS1 and PICCS2.

The objectivist theory is represented within the design of PICCS1 and PICCS2 in the aim to investigate, understand, and then standardise expert knowledge

and recommendations for the communication of late effects information for female CAYA cancer survivors. Despite this, however, there is arguably a distinct influence of the subjectivist theory within the design of both PICCS1 and PICCS2. This is apparent in the use of a multi-methods or a mixed-methods approach using a combination of empirical evidence, primary data collection through telephone interviews and surveys and the use of the modified Delphi technique for the expert consensus recommendations in PICCS2.

Researchers often feel pressure to choose one or the other in relation to ontological theories or approaches, to provide an adequate justification of their philosophical approach (Corry, Porter, and McKenna 2019). However, it is pragmatic to consider the combination of several ontological theories within a philosophical framework (Walach 2020). This allows for a more in-depth examination of data, representative of the real-life perspective (Walach 2020). The researcher chose to combine the objectivist and subjectivist ontological theories with the use of a dual-paradigm approach. This was adopted to present a comprehensive reflection of how beliefs and values surrounding ‘what is knowledge’ within society have evolved to include the real-life experiences of the population to shape the evidence-base. This method also serves to address the criticisms of the objectivist view being too rigid or defined for application of the findings to a wider population group (generalisability) (Corry, Porter, and McKenna 2019).

Upon reflection, the professional background of the researcher (registered midwife) reflects a traditionally subjectivist domain. Midwifery research is saturated with examples of explorative, reflective, and story-telling processes

that are shaped by the experiences of women. This personal or lived-experience data is used to formulate patient-centred evidence-based recommendations and guidelines. The acceptance of which into clinical guidance reiterates the argument that accepted knowledge and evidence is not solely based upon statistical facts or observed phenomena. As a health care professional, the expectation is that clinical care is adapted to the individual patient on a case-by-case basis. The health care professional uses their autonomous, professional judgments to meet the needs of the patient, guided by the evidence and guidelines of their profession. This reflects an everyday example of the subjectivist theory within clinical practice. This example demonstrates the need for a cohesive approach combining both objectivist and subjectivist theoretical approaches to health care, to fully meet the needs of a patient group.

3.1.3 Philosophical reasoning

Philosophical reasoning is a principal factor within the overarching research philosophy. It relates to the thinking, reflection, and deliberation behind the active decisions taken in the design of a research study, or the logic behind a methodological choice (Denzin and Lincoln 2018). The three main forms of logic considered by the researcher within PICCS1 and PICCS2 are identified as deductive, inductive, and abductive.

Deductive reasoning in research is based upon a hypothesis of existing knowledge or data. A research study then is designed to validate or refute this hypothesis (Flick 2018:50). Deductive reasoning aims to generalise a single

outcome to a wider population underpinned by the assumption of causal relationships and that findings from a sole case will be replicable within a larger cohort (Flick 2018:50). The deductive approach is often favoured for research studies of quantitative design such as randomised controlled trials (RCTs) and for professional guideline development (Flemming et al. 2019).

Inductive reasoning illustrates a wider application of reasoning or the ‘casting of a net’ for information in a particular area. Then similarities, common themes and justifications are made within data (Flick 2018:49). Inductive reasoning reflects the lived-experience and considers what we as researchers can learn from it (Flick 2018:49). It can be argued that by including inductive reasoning to the research design, it adds the missing lived-experience element from a traditionally deductive approach. Furthermore, the objectivist, positivistic and deductive philosophical approach fails to acknowledge the role and values of the researcher, who must remain independent from the study delivery (Dudovskiy 2018). This limits reflexivity of the researcher and increases the risk of bias within the study design (Dudovskiy 2018).

An intermediary of the two approaches is abductive reasoning. Abductive reasoning aims to combine deductive and inductive reasoning and address the limitations in both approaches (Karlsen, Hillestad, and Dysvik 2021). Abductive reasoning mirrors the concept of a dual-paradigm approach, chosen by the researcher for the design of PICCS1 and PICCS2. Deductive reasoning can be criticised for lack of transparency in the selection of theory, whereby inductive reasoning has been criticised for having a high risk of over-saturation of data, resulting in no obvious theory or conclusion at the end of the process (Karlsen,

Hillestad, and Dysvik 2021). Therefore, abductive reasoning provides an opportunity to combine the methods and generate a best-prediction outcome using both numerical and cognitive methods of data synthesis (Karlsen, Hillestad, and Dysvik 2021). The use of abductive reasoning within nursing research was supported by (Karlsen, Hillestad, and Dysvik (2021) as an effective method for shedding new light on phenomena, providing a more in-depth understanding of the inquiry. However, despite the advantages of abductive reasoning, it is yet to be implemented on a wider scale within health care research (Karlsen, Hillestad, and Dysvik 2021).

Upon consideration of the deductive, inductive, and abductive reasoning approaches, the researcher aligns the studies PICCS1 and PICCS2 with the abductive reasoning paradigm. A combination of both deductive and inductive reasoning is reflected in the design of PICCS1 (systematic review and online questionnaires) and in the PICCS1 (semi-structured interviews). PICCS2, designed using a modified Delphi consensus technique, represents both a deductive and an inductive approach. The process of refinement by consensus but with the addition of free text and feedback, is conducive to both deductive and inductive reasoning. Therefore, the approach that best fits with the aims of PICCS1 and PICCS2, and that also reflects the dual-paradigm approach adopted by the researcher is abductive reasoning.

3.1.4 Epistemology

Epistemology in research represents the branch of philosophical understanding, within which the research study lies (Flick 2018:51). More specifically,

epistemology explores the sources of what we consider to be knowledge (Flick 2018:51). By explaining the epistemological approach to a study, it improves the transparency of the decision-making processes undertaken by the researcher (Flick 2018:51). A research study can be flexible and integrate a variety of different 'sources' of knowledge within a single study. Examples of which are provided below (Table 9).

Table 9 - Sources of knowledge in research (adapted from Dudovskiy 2018)

Source of knowledge	Description
1. Intuitive knowledge	Based on faith, beliefs etc. Human feelings play a greater role in intuitive knowledge compared to reliance on facts
2. Authoritarian knowledge	Relies on information that has been obtained from books, research papers, experts, e.g., systematic review in PICCS1
3. Logical knowledge	A creation of 'new' or 'novel' knowledge through the application of logical reasoning (PICCS2)
4. Empirical knowledge	Relies on objective facts that have been established and can be demonstrated, i.e., dissemination of findings (PICCS2 output)

The design of the research studies PICCS1 and PICCS2 incorporates a combination of the identified sources of knowledge. Intuitive knowledge is illustrated in the discussion surrounding the positionality and reflexivity of the researcher and the potential impact upon the research findings (see Chapter Seven – Discussion). Authoritarian knowledge is demonstrated in the systematic review and online questionnaires in PICCS1, with logical knowledge being captured within the primary data collection of the PICCS1 interviews and in the modified Delphi technique (expert consensus in PICCS2). Empirical knowledge is then reflected in the findings of PICCS1 and PICCS2, in the

synthesis of data, and in the production of the recommendations for the communication of future fertility and reproductive health risks for female CAYA cancer survivors.

Epistemology spans several sub-branches of philosophy including essentialism, progressivism, empiricism, idealism, realism, rationalism, constructivism etc. (Dudovskiy 2018). Once the researcher has considered their view surrounding acceptability of knowledge as a source, then this view is used to construct the overall research philosophy and methodology for the research study (Flick 2018:51). Table 10 (cited in Dudovskiy (2018), illustrates the different epistemological branches of philosophy and associated assumptions of knowledge source.

Table 10 - Research philosophy based on knowledge definitions (adapted from Dudovskiy 2018)

Research philosophy	What is knowledge?
Pragmatism	Observed phenomena and subjective meanings, dependent upon the research question. Practical and applied research which integrates different perspectives to help interpret data
Positivism	Observed phenomena provide credible data and facts. Deductive reasoning which applies causality and societal generalisations

Research philosophy	What is knowledge?
Realism	Observed phenomena help to provide credible data and facts, but gaps in feelings lead to inaccuracies of the knowledge (direct realism). Observed phenomena create credible data but include subjective feelings, open to misinterpretation (critical realism). Knowledge can be explained within a wider context or set of conditions
Interpretivism	Based on subjective meanings and varying social phenomena. There is a focus on the small details, the reality underneath data, subjective meanings, and actions that influence outcomes

The epistemological standpoint of the researcher in this thesis was guided by the ontological assumptions of knowledge and truth being represented by the objectivist paradigm but influenced and shaped by the subjectivist paradigm. In addition to this, the studies PICCS1 and PICCS2 represent abductive reasoning in their design with the researcher accepting a variety of sources to represent how 'knowledge' is defined. The use of a dual-paradigm approach to the design of research was supported by Crowther and Lancaster (2009) who argued that there are significant limitations to the objectivist paradigm and linked positivistic approach, including the rigidness of deductive methods used to construct a hypothesis as this limits the available data collection and analysis method choices for the study (Crowther and Lancaster 2009).

Upon reflection of the axiological, ontological, and epistemological viewpoints of the researcher, the selection of the most appropriate philosophical framework to use was the next stage in the process. Health care research frequently utilises a combination of paradigms, such as post-positivism and critical realism to

effectively answer and explore research questions that need a broader methodological framework (Broom and Willis 2013). Realism, a philosophical branch of epistemology, (see Table 10), offers a suitable framework for the proposed dual-paradigm approach and will now be examined further.

3.1.5 Philosophy of Realism

Realism, (a sub-branch of epistemological philosophy), offers a combination of the 'positivistic' assumption of observed phenomena or science (i.e., what we define to be 'knowledge') and places this assumption alongside the exploratory, subjective inquiry (McEvoy and Richards 2003). This allows for the inclusion, interpretation and influence of human nature and personal values upon the research findings (McEvoy and Richards 2003). Realism is used to explore the ontological perspective and investigate in more detail, the how, why, by whom, and to what extent/in what circumstances of a research question (McEvoy and Richards 2003). Realism uses an iterative approach to reach a conclusion or to discover a theory and is reflected in the design of PICCS2 and the modified Delphi technique.

Realism can be further defined into two sub-groups; direct and critical realism (Haigh et al. 2019). Direct realism reflects the view that 'what you see is what you get' in the research findings and can be described as a representation of the real world through a one-dimensional, human lens (Haigh et al. 2019). Critical realism, developed by Roy Bhaskar in 1978, states that the evidence we observe can come close to reality but is always a fallible, social, and subjective account of the real world (Sturgiss and Clark 2020). The logic or reasoning that

underpins critical realism was described by McEvoy and Richards (2003) as ‘retroduction’. Retroduction was defined as ‘a mode of analysis in which events are studied to discover what may have, must have, or could have caused them (McEvoy and Richards 2003). Figuratively, this is the process of asking why events have happened in the way they did. Retroduction outlines the basics of the observed phenomena and puts it alongside the lived experience. Then a deeper investigation of the underlying structures and mechanisms that influence or cause the phenomena are studied (McEvoy and Richards 2003).

Research questions investigating the how, and why, things are effective or ineffective are well placed to be answered by critical realism (Sturgiss and Clark 2020). Therefore, it can be hypothesised that critical realism is an approach suitable for many mixed-methods research studies due to the ability to capture insights from a wider landscape (the who, what, when and where). Critical realism as a framework provides criticality for the evaluation of methods and findings of a particular phenomenon or field of research (Sturgiss and Clarke 2020).

The choice of a philosophical framework and consideration of epistemological preference, axiological values and preferred ontological approach can be a complex decision for researchers (Dudovskiy 2018). The researcher has defined and justified the use of a dual-paradigm ontological approach for the design of PICCS1 and PICCS2. The dual-paradigm approach brings together the views and beliefs of the researcher (primarily an objectivist, positivistic standpoint) that accepts observed phenomena and/or ‘science’ to produce credible evidence or knowledge and combines this with the subjectivist,

pragmaticistic and inductive research philosophies. This demonstrates the value and importance that the researcher places on the inclusion of beliefs, lived-experience, and influential external factors within the evidence-based field of inquiry. Sturgiss and Clark (2020) describe this concept of a dual-paradigm approach to 'needing to consider the whole picture' within the research study.

Critical realism provides a platform from which to understand outcomes better – what works and what does not – in a variety of circumstances, rather than applying a set of pre-defined outcomes (Sturgiss and Clark 2020). The Medical Research Council (MRC) has acknowledged the advantages of using critical realism for the development of complex intervention guidelines (Fletcher et al. 2016). Fletcher et al. (2016) and Moore et al. (2015) suggested that critical realism is a superior method for evaluating how contextual influences affect interventions and what are the background elements to making an intervention work in clinical practice. Porter, McConnell, and Reid (2017) explored the concept of critical realism within the 'traditional' gold standard research design, the RCT. They argued that critical realism offered a bridge between the design limitations of the RCT and a pure realist evaluation by complimenting the findings of a study with a wider social context and individualised interpretation of the findings (Porter, McConnell, and Reid 2017). Recognition by national health research governing bodies such as the MRC, that critical realism is an accepted approach to interventional research studies, suggests that CAYA cancer survivorship research would also benefit from this additional critical lens. This allows for the consideration and evaluation of the underlying social contexts and external variables for a complex and heterogeneous population and would

provide greater translatability of the findings.

3.2 Mixed methods in research

Following the exploration of the underpinning philosophical framework, the choice of methods for a research study is considered (Onwuegbuzie, Johnson, and Collins 2009). Within health and social care research, a combination of qualitative and quantitative methods (mixed-methods) is widely advocated (Teddlie and Tashakkori 2011). However, the use of mixed-methods can be complex due to the merged nature or 'grey' ontological and epistemological approaches (Teddlie and Tashakkori 2011). A detailed rationale for methodological choice and transparency of the underlying research philosophy will help to address confusion or criticality of the methods used in a research study (Creswell 2003).

Quantitative methodology (positivistic) seeks to identify facts based on empirical observations (Ackroyd and Fleetwood 2004). The goal of positivistic research is to generalise findings based on the statistical relationships of the dataset (Ackroyd and Fleetwood 2004.) Sampling techniques are also used to eliminate potential bias in the study such as randomisation and blinding of participants (Ackroyd and Fleetwood 2004). Quantitative studies, such as clinical trials of investigational medicinal products (CTIMPs) are designed to test out theories or hypotheses and investigate causal mechanisms of success or failure when applied to a particular set of conditions (Mingers 2004). Quantitative research studies are often considered robust, replicable and a best-practice example in many health research disciplines such as medicine (Broom and Willis 2013).

In comparison, qualitative methodology, traditionally based within the interpretivist paradigm, seeks to understand how the world is socially constructed and understood (Broom and Willis 2013). Qualitative methodology can also aim to capture direct and in-direct interactions between the researcher and the participants (Broom and Willis 2013). Qualitative studies can include focus groups, unstructured interviews, and ethnographic case studies and recruitment is commonly reflective of purposive or theoretical sampling techniques (Strauss and Corbin 1998). However, due to this, cohorts may not be representative of the wider general population (Strauss and Corbin 1998). The key strength of using qualitative methods, from a critical realist perspective, is the open-ended or inductive design, allowing for the emergence of themes that occur naturally within a study (Haigh et al. 2019). Qualitative methods help to understand elements of complex concepts and relationships that are unlikely to be understood by using a pre-defined set of outcome measures (Haigh et al. 2019). Similarly, qualitative research is conducive to the reporting of the patient experience and voice, which are crucial elements to the improvement of clinical care (Davies et al. 2020).

The debate surrounding whether quantitative and qualitative methodology should be combined into mixed-methods falls between two methodological viewpoints or camps; namely the purists and the pragmatists (Teddlie and Tashakkori 2011). Methodological purists vote strongly in favour of a singular methodology and take the view that methods are not interchangeable and cannot be amalgamated (Broom and Willis 2013). Creswell (2003) supports this view and argues that the qualitative and qualitative paradigms are so radically

different that they cannot be reconciled. However, the methodological pragmatists accept the view of the purists, but they argue that researchers should use whatever methods are needed to obtain the most comprehensive findings, even if this involves switching between the two paradigms or combining the two (Teddlie and Tashakkori 2011, Onwuegbuzie, Johnson, and Collins 2009).

The view of the methodological pragmatists aligns with that of the researcher and is reflected in the mixed-methods design of PICCS1 and PICCS2. Mixed methods in a research study provides an outlet where the two research paradigms can complement each other and provide an overarching view of the problem to be explored. This view was supported by Creswell et al. (2003), who described mixed-methods as the ‘full-picture’ paradigm for research. However, as Perlesz and Lindsay (2003) reported, it is important to consider the risk of criticism when using mixed-methods, particularly in the justification and selection of methods for synthesis of data.

Both qualitative and quantitative data are traditionally used to describe and explore past events. However, findings from these studies can have limited generalisability or can fail to adequately predict future outcomes for patients and populations (Broom and Willis 2013). Critical realism can be beneficial in this instance as it seeks to understand the entire process, providing a considered and critical view of what is more or less likely to happen on a wider scale in the future (Haigh et al. 2019).

The critical realist philosophical framework used to underpin the studies PICCS1 and PICCS2 provides an opportunity for the deeper exploration of the

three key domains of reality – the empirical, the actual and the real.

The relationship between the three domains of reality and what was learned within PICCS1 was used to underpin and link to the methodological approach used for PICCS2. The modified Delphi technique used for PICCS2 algins with the critical realist philosophical framework and provides a platform for appraisal and dissemination of the empirical, the actual and the real evidence gained from PICCS1. The subsequent expert consensus and recommendation process is influenced and shaped by the values, beliefs, and experience of the panel members and reflects the dual-paradigm, critical realism philosophy.

3.3 Theoretical Reasoning for Modified Delphi technique

The Delphi technique is a method to achieve consensus through a process of iteration (Keeney, Hasson, and Mckenna 2010). Often criticised for a lack of theoretical underpinning due to its heterogeneous nature and variation in methods, the Delphi technique favours multiple paradigms – such as the positivistic – and assumes the position of the researcher to be that of an objective and uninvolved observer (Rowe and Wright 2001). The objectivist paradigm within the Delphi technique is reflected in the approach to data collection and in the application of a single statistical measure for defining consensus (Rowe and Wright 2001). The inclusion of experts for the panel assumes an ontological position of reality (where experts will agree) and also a deductive reasoning approach (seen in the rounds of the Delphi technique) adhering to the positivistic paradigm (Dudovskiy 2018). Despite this, the Delphi technique also can be described as a qualitative and explorative method

reflective of subjectivism (Dudovskiy 2018). Therefore, the Delphi technique can be difficult to define and justify as a methodological choice (Keeney, Hasson, and McKenna 2010).

The use of professionals and patients (CAYA cancer survivors and parents) in the design of PICCS2 also draws a resemblance to Eisner's theory of connoisseurship (Eisner 2017). Eisner first defined the term 'connoisseurship' in 1997 as an individual who has the experience and skills to understand the subtle, but also the not-so subtle aspects of a phenomena (Eisner 2017). This includes observations of behaviours that might normally be hidden to someone not classed as a connoisseur (Eisner 2017).

3.3.1 Reliability of the technique

One of the criticisms in selecting a Delphi technique for a research study is the omission of reliable measurement tools for the validation of data (Thangaratinam and Redman 2005). However, the Delphi technique is strongly advocated as a method for the investigation of phenomena with no definitive evidence available (Thangaratinam and Redman 2005). The Delphi technique is also recommended for studies where the output of the research relies upon the expert knowledge and experience of those that know the most (e.g., the expert panel) (Keeney, Hasson, and McKenna 2010). Rowe and Wright (2001) argue that the Delphi technique is a credible and reliable approach if there is evidence of a clear and concise decision trail. This includes a clear explanation of the methods, the scientific problem to be addressed, the selection process of the expert panel, the choice of data collection tools and a definition of the validation

criteria used for consensus (Rowe and Wright 2001).

The Delphi technique is a popular choice for health care research studies, particularly for guideline development to address a clinical problem (Keeney, Hasson, and McKenna 2010). Nagler et al. (2014) demonstrated in a systematic review of clinical practice guidelines for the diagnosis and treatment of hyponatremia; that the use of a consensus validation technique (such as the Delphi technique) improves the quality of healthcare by prioritising the most up to date evidenced-based care alongside examples of best-practice (Nagler et al. 2014). Early pivotal research from Linstone and Turoff (1975) and Murphy et al. (1998) who supported the use of the Delphi technique highlighted that the option of participant anonymity within the Delphi technique allows for more creative outcomes, adding richness to the dataset. Murphy et al. (1998) expanded this statement further and suggested that participant anonymity helped to address the risk of professional dominance, conflicts of interest and group conformity bias. Hallowell and Gambatese (2009) also recommended the Delphi technique to recruit a geographically dispersed, multi-disciplinary and multi-stakeholder participant panel, which can be difficult with other participant recruitment methods.

The researcher aimed to replicate the work of Hallowell and Gambatese (2009) in the recruitment of a wide range of stakeholders into the PICCS2 expert panel. This included HCPs, female CAYA cancer survivors, parents of female CAYA cancer survivors, and academics in the field of research. This collaborative approach aimed to provide a platform and voice to those that have direct experience of CAYA cancer, those that care for CAYA with cancer, and those

that undertake research around CAYA cancer survivor survivorship.

The use of patients and the public within the research process, has been strongly advocated in health care research to ensure that the focus of the research and any recommendations arising from the findings are patient-centred and based upon patient need (NIHR 2021). This is often termed as Patient and Public Involvement and Engagement (PPIE) or Patient and Public Involvement (PPI). This will now be discussed in more detail.

3.4 Patient and public involvement and engagement (PPIE)

3.4.1 The PPIE voice

The participation, involvement, and engagement of patients and members of the public (termed PPIE) affected by the phenomena or medical condition is considered a vital part of any research methodology (Holmes et al. 2019). PPIE has facilitated the incorporation of patient opinion, experience, and prioritisation of need into health research and clinical practice (Holmes et al. 2019). PPIE is a valuable tool for researchers to help shape health care services to fit patient needs and reinforces the ideology of making patients ‘partners’ in their care (NIHR 2021).

Adoption of a PPIE embedded research design helps to ensure that research studies demonstrate equality and diversity within their research and is a required element for grants and awards by research funding bodies such as the National Institute of Health Research (NIHR), MRC and Wellcome Trust

(Holmes et al. 2019).

Cancer research boasts over a 20-year history of active and meaningful involvement of cancer survivors, parents and people affected by cancer in their research applications, funding awards and in the evaluation and dissemination of their research findings (National Cancer Research Institute (NCRI) 2021). Collaboration and involvement by patients and the public, who are affected by the disease, has led to the prioritisation of late effects research in cancer survivorship and has highlighted the need for a research agenda that addresses both cure and the optimisation of long-term health outcomes and a good quality of life (Gibson et al. 2005).

A distinct challenge in the wider adoption of PPIE into other research disciplines is how to ensure the ongoing equality, diversity, and inclusion of those involved so that they feel their voice is heard and taken forward for change (NIHR 2021). The NIHR addressed this issue with a statement of requirement for researchers to demonstrate how they can show equality, diversity, and inclusion in their research proposals, including the provision of the steps taken to ensure a representative sample and a dissemination plan that is inclusive of the patient contribution (NIHR 2021).

It is possible to integrate PPIE into all levels of research from idea concept through to the delivery and dissemination of the findings (NIHR 2021). However, evidence of PPIE in the design of systematic reviews, early phase clinical trials and RCTs are still lacking (NIHR 2021). This suggests a need for further research to explore collaborative PPIE methodological designs. This approach is particularly suitable for clinical academic researchers seeking direct patient

benefit of their findings (i.e., from bench to bedside) as envisioned by the NIHR (NIHR 2021).

Within the PICCS1 and PICCS2 studies, a named PPIE representative (NR) was recruited and involved at all levels within the research design and delivery, including dissemination of the findings. The PPIE representative's personal background was a parent of a child that had cancer over 10 years ago. He was invited to take part by the researcher by email and was given the option to withdraw at any time if he wished to do so. The PPIE representative was proficiently trained in PPIE, having undertaken a wide variety of nationally recognised courses and open days, and had represented the patient and parent voice as a noted expert both on a national and international basis. He also possessed a sound research background with experience of being a part of a scientific research team in all aspects of research design and delivery prior to taking part in PICCS1 and PICCS2. This included the conduct of literature reviews, interviews, facilitation at focus groups and production of lay summaries for research findings. The PPIE representative agreed to and participated in the following ways as set out in Table 11 throughout the studies PICCS1 and PICCS2.

Table 11 - Role of the PPIE representative in PICCS1 and PICCS2

Role of the PPIE representative
Oversight of the overall conduct of the study, ensuring timelines were adhered to and aims and objectives of the study met
Provided feedback on the initial study protocol, selection of primary and secondary outcomes and systematic review protocol submitted to PROSPERO

Role of the PPIE representative
Active involvement in the systematic review process including selection of the included studies and assessment of the risk of bias and data extraction methods. Also provided oversight to the selection of themes from data
They were invited to facilitate round three of the modified Delphi technique (online web-based meeting)
They assisted with the writing of a lay summary of findings and the subsequent dissemination to participants, the public and other interested parties following completion of the study
They participated in the loop-feedback process of writing for publication and agreed to be a named author on the final publication of findings

3.4.2 Personal reflection of the PPIE voice

The researcher has a strong appreciation for PPIE within research and health care provision. The researcher declares a personal background of being a bereaved parent to a child that had cancer, and over a 10-year history of PPIE in childhood cancer research. The researcher has advocated the parent and patient voice both on a national and international level, through membership of boards, committees, and international research groups. This has included named authorship of scientific publications, as a nominated representative on steering committees and national cancer governing bodies, and as a lay person for large cancer research funding organisations. The researcher, therefore, holds the value and importance of PPIE in research in high regard and is fully conversant with the recommended practices and guidelines for active and valuable patient contribution within research.

The principles of PPIE set out by *INVOLVE*, a body of the NIHR (2012) have

been integrated throughout the PICCS1 and PICCS2 studies. PICCS1 has sought to include the patient and parent voice in the systematic review, online questionnaire, and telephone interviews. This approach is also reflected in the recruitment of female CAYA cancer survivors and their parents to PICCS2.

> *"The idea of bringing together clinicians, patients and carers to discuss research priorities seems obvious – why shouldn't all those affected have a chance to jointly discuss frustrations about the things we don't know, and aspirations for the future?"* ***(Irenie Ekkeshis, patient involved in the Sight Loss and Vision PSP (2018) (JLA 2021)***

3.5 Summary of research philosophy

The use of critical realism as an underpinning research philosophy for PICCS1 and PICCS2 combined the researcher's belief in science and evidence-based knowledge, but allowed for the further explanation, investigation and understanding of human factors. This resulted in a reflection upon the entire evidence base before any generalisation of findings to a wider population. The mixed-methods design of PICCS1 and PICCS2 aimed to understand the 'who, what, where, and how' behind the outcomes and permitted a deeper consideration and critical view of what might be likely to happen on a larger population-based level.

The use of the modified Delphi technique for PICCS2 aligns with the realist philosophical paradigm. The intended outcome of the expert consensus – a set of clinical recommendations – whilst positivistic and deductive in nature, also

represents the consideration and inclusion of feedback and opinion – reflecting a more subjectivist and inductive nature of inquiry. The inclusion of a wide range of stakeholders and the interwoven PPIE approach to both PICCS1 and PICCS2 demonstrates the value that the researcher places upon the need for a collaborative and patient-driven ethos in any research design, a concept of 'togetherness to produce excellence'.

A pictorial summary of the philosophical framework used for the design of PICCS1 and PICCS2 is below (Figure 7).

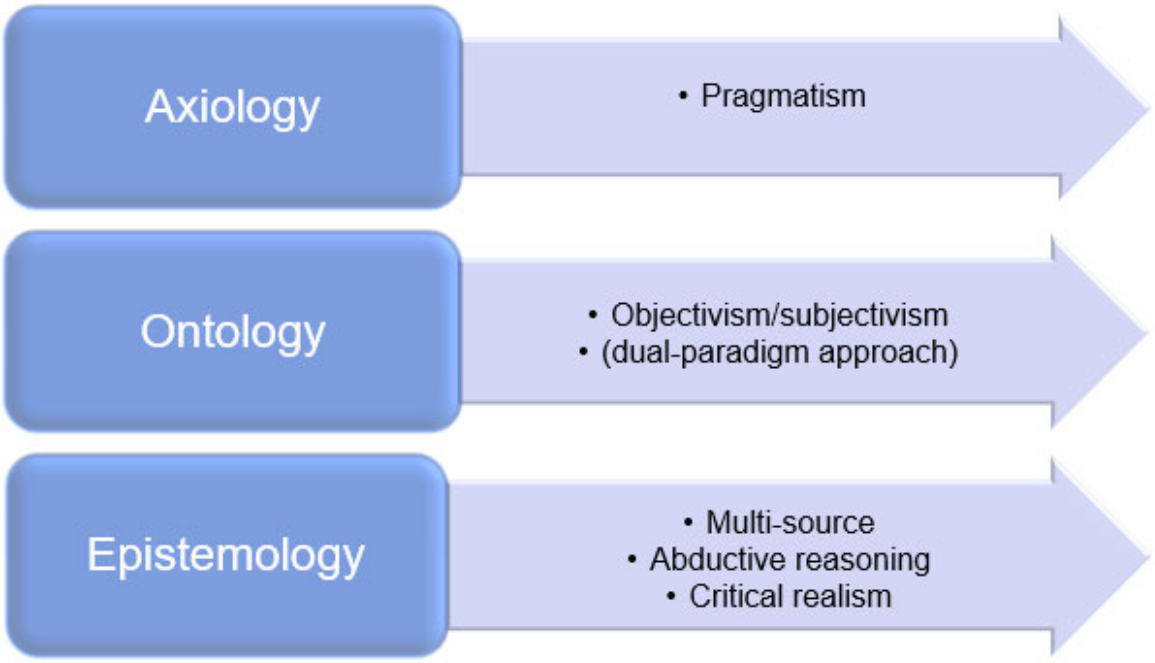

Figure 7 - Philosophical framework of the research

Presentation of the methods used for PICCS1 and PICCS2 now follows in Chapter Four – Methods. This includes an in-depth analysis and rationale for chosen method of synthesis used to collate the findings of both studies.

Chapter Four – Methods

This chapter will illustrate the methods used for the studies PICCS1 and PICCS2. The rationale, philosophical underpinning, and explanation of the methods will be presented in a sequential order, starting with the systematic review, and followed by the online questionnaires and semi-structured interviews that make up PICCS1. This will then be followed by the modified Delphi consensus technique in PICCS2.

The modified Delphi technique was chosen as a method to produce a set of expert consensus recommendations for the optimal communication of future fertility and reproductive health risks for female CAYA cancer survivors.

PICCS1 and PICCS2 have adopted an inductive approach by gathering data and then using the findings to inform and feed into the more deductive methodology used within PICCS2. Findings from PICCS1 were triangulated in order to inform the design of PICCS2 (see section 6.7 Triangulation of data (PICCS1).

4.1 Pregnancy Information for Childhood Cancer Survivors (PICCS1)

4.1.1 Rationale of the methods

The systematic review in PICCS1 was chosen as an appropriate method of inquiry to investigate current published literature in the area of unmet informational needs of CAYA cancer survivors. Background reading by the

researcher had indicated that there may be a lack of communication surrounding potential late effects such as risks for future pregnancies (Polanco et al. 2021). A systematic review methodology was selected over other review designs, such as a rapid review or a narrative review, due to the ability of systematic reviews to provide a replicable and rigorous selection process for included evidence with the ability to assess for risk of bias (Centre for Research and Dissemination (CRD) 2009). A systematic review design enabled the researcher to collate, critically appraise and synthesise all available published evidence with the use of a recognised evidence-based framework. PRISMA reporting guidelines and flow chart were used to achieve this (Moher, Tetzlaff and Altman 2009, Moher, Liberati and Tetzlaff 2009). This was not updated to reflect the new published guidance by Page et al. (2021) due to being already complete at the time of publication.

Following the findings of the systematic review, the researcher wanted to explore in more depth, the personal views surrounding the phenomena. To achieve this, two online questionnaires were designed to capture the lived experience of female CAYA cancer survivors/parents and HCPs in relation to communication of late effects. The questionnaires collected primary data about methods of communication reflecting the individual experiences of those that had received or delivered the information (Appendix 1 (CAYA cancer survivor/parent and Appendix 2 (HCPs). The use of online questionnaires was chosen as a means to capture the lived-experience of patients and has featured prominently as a method within health research in the last ten years (Blatch-Jones et al. 2020). The use of online questionnaires within nursing research has

also helped to facilitate rapid access to harder to reach patient groups, helping to understand barriers to recruitment (Blatch-Jones et al. 2020). The ethical approval process that is mandatory for any research involving contacting patients, is simplified when using online questionnaires. This serves as an advantage for researcher as it allows for rapid collection of a large amount of patient/professional data and accelerates the time it takes to analyse data and implement findings into clinical practice (Blatch-Jones et al. 2020).

However, data collection methods used in surveys or questionnaires are often criticised for their lack of a validated framework, the potential for contradictory findings, and a lack of valid and robust instruments used for data analysis (Blatch-Jones et al. 2020). Despite this, questionnaires have been reported to add important data needed to support or refute a hypothesis and also add a level of 'richness' to the findings that could not be otherwise achieved (Pettersen 2004). Questionnaires have also been encouraged as a method to gain a unique insight into the patient point of view and a deeper understanding of the meaning and implications of the proposed intervention or research question (Pettersen 2004).

The increasing popularity of online questionnaires presents academics with a challenge in how best to apply traditional survey research methodology and combine this with the behaviours and trends of modern internet use (Andrews, Nonnecke, and Preece 2003). There is a notable increase in the use of the internet and social media platforms to recruit research participants and the emergence of internet-mediated research (IMR) as a recognised research method suggests that online research methods are reliable and reputable

(Hewson 2014). IMR can be facilitated using a range of settings (e.g., email, chat rooms, web pages, social media platforms) and software packages such as *SurveyMonkey*, *Qualtrics*, and *Bristol Online Survey* (Hewson 2014). A noted disadvantage of this method, however, is the reliance on automated data collection and software programme-based analysis of findings. This can affect the validity of data and lends itself to sampling bias risk (Hewson 2014).

4.1.2 Relevance

The online questionnaires were designed in two formats: one for HCPs that contained more medicalised terminology that would be familiar to them and a CAYA cancer survivor/parent format with more lay terminology that had been approved by the PPIE representative (NR). Data were collected, analysed, and triangulated using the software *Qualtrics* and *SPSS* (for further details see PICCS1 questionnaire results).

The online questionnaires aimed to capture real-life data regarding experiences of late effects communication from both the CAYA cancer survivor/parent and professional contexts. Ethical approval was provided by Coventry University (P87230) as part of the PICCS1 study design. The inclusion of 'lived-experience' data to the PICCS1 study aimed to provide a deeper investigation to answer the research question and specific aims of PICCS1 (Table 12):

Table 12 - Aims for PICCS1 Questionnaires

Aims for PICCS1 Online Questionnaires
Explore if there is an optimal time for CAYA cancer survivors and their families to be told about the risk of late effects

Aims for PICCS1 Online Questionnaires
Investigate, using multi-stakeholder viewpoints, who is best placed to communicate late effects risk information to CAYA cancer survivors and their families

4.1.3 Questionnaire development and testing

Qualtrics was chosen as the software programme to host the online questionnaires. *Qualtrics* allowed for recruitment of a wide stakeholder cohort throughout the UK. Assistance to design the questionnaires was sought from software guidelines and statistical experts from Coventry University. This ensured that parameters/data categories were suitable for analysis as intended. The supervisory team provided critical oversight to the questionnaire design to ensure comprehensibility. A combination of descriptive statistics using ranking-order questions and free-text boxes were selected to capture data. Background demographic data was collected but maintained anonymity of participants. Internet Protocol (IP) addresses were collected as part of the function of *Qualtrics,* however, data were deleted following data extraction and not shared with anyone.

A *Qualtrics* recommended template design was used to create the questionnaires as a validated questionnaire design or tool did not exist for this patient population or this area of investigation. The questionnaires were piloted with the PPIE representative (NR) and a paediatric oncologist volunteer to ensure accuracy and legibility. Data were analysed using internal *Qualtrics* functions, *Microsoft Excel,* and *SPSS.* The findings of the questionnaires can be found in Chapter Six – Findings.

4.1.4 Recruitment strategy and follow-up

Female CAYA cancer survivors, their parents, and HCPs were recruited to take part in the online questionnaire via social media channels. Facebook, Twitter, LinkedIn, and existing personal CAYA with cancer networks. Participants were sent a link and then were asked to consent to the questionnaire. At completion, participants were asked to click a link, that directed them to a separate form if they wished to be contacted for the next part of the PICCS1 study (interviews).

A random selection of participants from a variety of backgrounds were recruited to the quasi-anonymised online questionnaires including:

- Female CAYA cancer survivors (aged ≥18 years old)
- Parents of female CAYA cancer survivors
- HCPs working in the field of paediatric oncology, haematology, radiotherapy, and long-term follow up

Questionnaire participants were informed that taking part was voluntary, that they had a right to pause, stop, or withdraw their data within a two-week timeframe after taking part and were given signposting information for support and advice with contact details for the researcher. Ethical approval for the PICCS1 questionnaires formed part of the application approved by Coventry University Ethics (P87230). As an additional step, participants were signposted their medical provider if they had additional medical or treatment queries.

4.1.5 Risk of bias

Risk of bias, including a consideration of the reflexivity and positionality of the researcher can be found in Chapter Three – Methodology. Researcher bias for recruitment and data analysis was considered and reflected upon at regular intervals, with oversight by the supervisory team and PPIE representative to ensure rigour and transparency in the study.

4.1.6 Data management

The software programme, *Qualtrics*, offered password protection and complied with General Data Protection Regulations (GDPR) (Data Protection Act 2018) (Department for Digital, Culture, Media & Sport and Home Office 2018). As *Qualtrics* temporarily stores IP addresses of participants as standard, data were defined as pseudo-anonymised. IP addresses were deleted immediately after data extraction and any reports or pictorial findings, i.e., word clouds, were stored on an encrypted device or *Microsoft SharePoint*.

4.2 PICCS1 Semi-structured interviews

4.2.1 Rationale and development

The use of interviews in health research is often reflective of the qualitative paradigm. The use of semi-structured interviews, as opposed to structured, provides researchers with greater control over the topic and structure of the interview schedule, however, still permits exploratory investigation on a deeper

level. This allows for individual experience data, feelings, attitudes, and behaviours to be captured. Semi-structured interviews provide flexibility for the researcher as the sequence of questions can vary with each participant and can be decided upon by the interviewer at the time of the interview. Semi-structured interviews are recommended for instances where the researcher already has a grasp of the subject area.

Semi-structured interviews were selected as the most suitable methodological design as they were to be used as a complementary element to PICCS1 and did not form the main dataset for analysis. Alternative methods such as Interpretative phenomenological analysis (IPA) or open-ended interviews, were not suitable due to the time demands of data collection and analysis. Semi-structured interviews facilitated a deductive approach to data collection with room for pauses, reflection of individual experiences and time to elaborate on responses if needed. Combined data from the systematic review, online questionnaires and the interviews would then be used illustrate the overall landscape for the communication of late effects information for female CAYA cancer survivors, with recommendations for future research to address unmet needs.

4.2.2 Recruitment strategy and follow-up

Participants were recruited after completing the optional online form following the PICCS1 online questionnaire. Participants provided their name, email address and agreed to be contacted to take part in the interview stage of PICCS1. A participant information sheet was then emailed to outline the

purpose, aims, and process of the PICCS1 interviews (Appendix 3a (CAYA cancer survivor/parent and Appendix 3b (HCPs). Signposting and contact details were given to each participant if they wanted to discuss anything relating to the study (e.g., professional organisations or directed to their GP or medical team). The participant was reminded that they had the right to withdraw, pause, or stop at any time both at the time of consent and before/during the interview.

A consideration of sample size for the interviews was undertaken with guidance from the existing literature. In quantitative research, adequate sample size is determined using a statistical power calculation, in qualitative research, the sample size traditionally refers to the concept of data saturation (Flick 2018:52). Morse (2000) defined saturation as “data adequacy” which means that saturation is reached when the collection of further data will not bring new relevant information and that themes from data are able to be assessed. Despite empirical research attempting to answer the question of ‘how big should a sample be’ for qualitative research, no one guideline exists. Guest, Namey, and Chen (2020) presented evidence to support that in the majority, data saturation could be achieved in the first six interviews with 80% to 92% of all concepts identified within the first ten interviews. Time constraints and financial limitations for honorarium (£10 shopping voucher) also guided the sample size allowance, which was capped at ten participants for this part of PICCS1. Four stakeholder categories were defined for the interview sample, which had to be met. These were CAYA cancer survivor, parent of a CAYA cancer survivor, health care professional (a doctor and a nurse) specialising in late effects. Eight participants were recruited to the interviews, who fulfilled the background

sample criteria. A larger sample size or more in-depth data collection/analysis would have been used if the focus of the PICCS1 study were to be interview data. As the interviews formulated an additional evidence base to add to published data and the online questionnaires, further recruitment and/or alterative analysis methods was not appropriate.

Once the consent form had been signed and received by email, the participants were contacted to select a date and time convenient for them for the interview. The interviews were conducted in a confidential setting (enclosed hospital meeting room with a fixed telephone line and only accessible with a pass). The participants were asked to verbally confirm their consent to take part before starting the interview. Interviews were audio-recorded, and participants were aware of and consented to this. The interviews were scheduled to take place over four weeks.

4.2.3 Data management

The PICCS1 interviews were conducted by telephone, using a private number in a room where no conversation or personal information could be overheard or seen. Telephone interviews were audio-recorded using an approved device from Coventry University and participants were made aware of the audio-recording before the start of the interview. Data were uploaded onto an encrypted device and then input into the software *Otter* (Otter AI 2021). A copy of the anonymised written transcripts were then held on *Microsoft SharePoint.*

Participants confirmed before taking part in the interviews that they had read the

patient information sheet and that they provided their consent to take part. Personal data collected at the point of consent were deleted after participation. Participants were again asked if they consented to take part before the start of the interview and were reminded that they could withdraw their data up until the point of data analysis. Data were stored securely for five years following completion of PICCS1, as specified in the ethics application. Participants were asked to consent for the use of pseudo-anonymised direct quotations in scientific publications and the PhD thesis.

The interviews were transcribed using *Otter* (Otter AI 2021). The application allows for auto-transcription of audio content using a voice-to-type function. This was extremely useful for time management and rapid data analysis. Despite this, manual transcription was also necessary as the application did not recognise specific terminology or audio that was quiet or muffled. To ensure accuracy, each participant transcript was checked by the researcher and transcribed verbatim, including expressions such as ‘um’ and ‘like’. Files from the audio-text transcription were extracted and uploaded to *Microsoft SharePoint* and then deleted on the application following transcription completion.

Following transcription, data were uploaded to the software *NVivo* (QSR International 2021) for thematic analysis. Thematic analysis was chosen as the most appropriate method to identify, analyse, organise, describe, and report themes found within the dataset. The theory of Boyatzis (Richard 1998) described thematic analysis as a translator for those speaking the languages of both qualitative and quantitative analysis. This theory enables researchers to

use different research methods to answer a research question and is comparative to the design and the structure of PICCS1. A more in-depth analysis of data, at this stage, would not be appropriate due to complementary element of data rather than compromising the main body of PICCS1. The aim of the findings for PICCS1 was to provide an overall landscape of the published and real-life experiences of CAYA cancer survivors/parents and HCPs.

Thematic analysis differs from alternative methods of analysis such as discourse analysis, IPA, or grounded theory (Braun and Clarke 2006). IPA and grounded theory seek to identify patterns within data but are bound by rigid theoretical processes (McLeod 2012). IPA is strongly aligned to phenomenological epistemology, which seeks to understand people's everyday experience of reality to gain an in-depth understanding of the phenomenon in question (McLeod, 2012). Grounded theory is multi-layered in approach, but seeks to produce a theory of the phenomena, that is grounded within data (McLeod, 2012). Grounded theory features procedures such as theoretical sampling and open coding that explores in great depth, the relationship of the findings to the phenomena or theory in question (Braun and Clarke 2006). This would not be suitable for PICCS1 as the mixed-methods data and summary of themes does not require such in-depth analysis. In contrast to IPA, grounded theory, narrative and discourse analysis, thematic analysis is not bound by theoretical procedures or frameworks and is adaptive to the field of study. Thematic analysis can, therefore, illustrate data from both the scientific or published 'reality' alongside the underlying patterns, which complements the methodological design of PICCS1.

The thematic analysis framework by Braun and Clarke (2006) was used for analysis of data. A cycle of consideration, based on the six-stage process for thematic analysis was used (Figure 8).

Figure 8 - Cycle of thematic analysis from Braun and Clarke (2006)

Data were read and then coded, with a colour coding system, to identify similarities or themes within the transcripts. Wider themes were then drafted, and transcripts then re-read to ensure data had not been omitted or missed in the coding stage.

Themes were then loosely described using quotations or words to illustrate the concept or definition of the draft theme. A mind-map was used to further explore the draft themes to help with the consideration of the meanings of the words, understanding relevance of data to the research topic, and comparison of the

theme to the original transcript data. This approach aimed to ensure accuracy in the representation of data, capturing personal experience, opinions, facts, and feelings of the participants.

The draft theme concepts, keywords and quotations were then focused down using a deductive, iterative approach to arrive at the selection of the final theme headings. These are explained and discussed in more detail in section 6.5.3 Thematic analysis – theme generation. A copy of the interview schedule for CAYA cancer survivors/parents is located in Appendix 4a and for HCPs, in Appendix 4b.

4.2.4 Risk of bias

The researcher had a mechanism for feedback, reflection, and personal support during the interview process by members of the supervisory team. This helped to ensure that the researcher remained objective, impartial, and professional and provided an outlet to discuss potentially sensitive content or traumatic memories/feelings related to CAYA cancer survival stories. The PPIE representative also reviewed a randomly selected, pseudo-anonymised interview transcript to ensure compliance with the interview process, ethics, and confidentiality. In addition to the strategies outlined to limit bias in the study, the interview schedule was approved by the supervisory team and the PPIE representative, with the supervisory team also considering final themes for appropriateness and comprehension.

Through personal reflection of positionality and reflexivity of the researcher,

PICCS1 was considered to be at low risk of bias. Despite this, the researcher acknowledges that the personal background of the researcher may have inadvertently affected the way that the topic is prioritised, perceived, and delivered. This also includes a risk of selection bias due to the professional/personal relationships with some of the participants of the study. The researcher also noted a 'hierarchical bias when conducting the interviews, particularly with well-respected HCPs. The researcher accepts that this may have affected the demeanour, language, and tone of some of the HCP interviews either sub-consciously or directly. This is therefore acknowledged as a limitation to the applicability of the findings from the PICCS1 interviews.

4.3 PICCS2 – Modified Delphi technique

4.3.1 Rationale of the method - Delphi

4.3.1.1 What is Delphi consensus?

Delphi, in its original meaning, was named after the Greek Oracle who could predict the future (Thangaratinam and Redman 2005). The technique has been used widely since the 1950s in military settings, education, and health care. The technique facilitates the achievement of consensus between using a process of iteration (Thangaratinam and Redman 2005). It provides a structured method of consultation by using a series of consensus rounds, interspersed by controlled feedback that aims to minimise the risk of bias (Keeney, Hassan, and McKenna 2010). The Delphi technique was originally developed by Dalkey and Helmer

(1963) outlining the fundamental elements of survey rounds, feedback of responses, opportunity to modify choices and anonymity of participants (Thangaratinam and Redman 2005).

The participants, or panel, traditionally consists of a selection of experts from the field of inquiry. Expert can be further defined as 'any individual with relevant knowledge and experience of a particular topic'. This provides the opportunity to include patients, carers, and those affected by an issue as well as professionals in the field (Thangaratinam and Redman 2005). The intended output of the Delphi technique is to produce a set of statements that have achieved the required level of expert consensus and that can be used for professional recommendations or guidelines.

The Delphi technique is a favoured method in research as it facilitates rapid impact and implementation of findings, avoiding prolonged delays in the delivery of a study and dissemination of findings (Keeney, Hassan, and McKenna 2010). The Delphi technique has been used widely in health care research as a recognised, concise, and reliable means of solving a clinical problem where limited or no previous evidence exists (Eubank et al. 2016). The Delphi technique has been advocated for the ability to allow open and active discussion of views, permitting changes in opinion and all taking place within a reasonable time frame for completion (Keeney, Hassan, and McKenna 2010). Therefore, the Delphi technique represents a practical and validated method for healthcare guidance development and is an appropriate choice of method for PICCS2.

4.3.1.2 Reliability of the method

Rowe and Wright (2001) explained that the Delphi technique can represent a highly structured method of consensus and can produce accurate and reliable findings when compared with other subjective/highly biased or poorly conducted research study methods. Rowe and Wright (2001) suggested that the Delphi technique can help to provide consensus in an area of uncertainty or when objective data proves unavailable. It can also provide anonymity, leading to more creative outcomes and a deep richness to data. Controlled feedback can be given to panellists, helping to eliminate issues such as professional dominance, conflict of interest, and group conformity, commonly associated with expert panel consensus. The Delphi technique can also facilitate the recruitment of a geographically dispersed and diverse group of panellists. This extends the scope of inference for conclusions and limits bias through the use of strategic questionnaire construction, the administration of controlled feedback and the careful analysis of group responses with independent facilitation (Rowe and Wright 2001).

The Delphi technique can be criticised for its timescale for delivery and the unclear methodological approaches of the researchers (Keeney, Hassan, and McKenna 2010). However, the Delphi technique offers an adaptive and replicable method that favours multiple research paradigms and aligns with the positivist standpoint (assuming the position of the researcher to be objective and uninvolved, a deliverer of the process rather than an active participant) (Thangaratinam and Redman 2005). The objectivist position in the Delphi technique is supported by a quantitative data collection and analysis approach

to achieve consensus. The inclusion of experts assumes an ontological position of realism (where experts agree) and the deductive approach between the rounds of consensus demonstrates a phenomena that adheres to the positivistic paradigm (Keeney, Hassan, and Mckenna 2010). Despite alliances to the quantitative paradigm, the Delphi technique can also be adapted to represent the qualitative, explorative paradigm. Therefore, the Delphi technique represents a method that is adaptive, flexible and which represents the dual-paradigm approach of the researcher to PICCS1 and PICCS2.

However, subjectivity of the researcher is also a criticism of the technique due to the ability of the facilitator to filter and edit statements between rounds (McMillan, King, and Tully 2016). Similarly, criticisms surrounding the lack of consistent reporting, definition of what is classed as a modified technique, transparency in the composition of the expert panel and the reporting of a complete set of findings have been highlighted (Banno, Tsujimoto, and Kataoka 2020). Insufficient or inconsistent reporting of findings impedes the applicability of a study and can lead to reporting bias (Jünger et al. 2017). To counteract this risk, a set of reporting guidelines were used for PICCS2 known as the Conducting and REporting of DElphi Studies guidelines (CREDES) (Jünger et al. 2017). The CREDES reporting guidelines (Jünger et al. 2017) were used to structure the reporting of the findings to participants and in the overall findings summary.

Co-design in research is a term now widely used and compared alongside the Delphi technique. However, the definition of co-design, its approved activities and methods for evaluation have rarely been reported in detail and requires a

clearer and more consistent explanation for use within research (Slattery, Saeri, and Bragge 2020). The Delphi technique is often confused as a method of co-design as they both align with the collaborative, PPIE ethos of involving patients, family members and experts in the design and approach to a research study (Slattery, Saeri and Bragge 2020). Co-design and the Delphi technique differ in their definitions as co-design is described as a set of activities used to create something new, or to gain insight on a particular issue. Alternatively, the Delphi technique is used to gain agreement based upon a validated consensus level. This agreement uses the existing evidence base to create expert recommendations with a group of stakeholders selected for their expertise in that area (Keeney, Hasson and McKenna 2010). Despite the differences, both approaches encourage a collaborative, patient-centred approach on to achieve an optimal outcome and should be encouraged within any research design.

4.3.1.3 Modified Delphi technique – process and limitations

The modified Delphi technique used for PICCS2, featured three-rounds of consensus. Rounds one and two were conducted via email communication and round three was planned to be a face-to-face meeting (later modified to a web-based meeting due to COVID-19). Once recruitment and consent were completed, a draft consultation document was sent to panellists by email. This draft document contained a summary of the evidence from PICCS1, a word document containing draft theme ideas and a set of example statements to be used in round one (Appendix 5). Panellists were asked to consider the documents and rank draft themes using a Likert scale of 1-9. Draft themes for

consensus represented areas of unmet need from the PICCS1 evidence and guided the formulation and context of the statements used within the Delphi rounds (Table 13).

Table 13 - Draft consensus themes PICCS2

Theme	Not important	Unsure of importance	Important
Communicating specific pregnancy and birth risks to female survivors and families	1 2 3	4 5 6	7 8 9
Identifying a key professional to communicate the information	1 2 3	4 5 6	7 8 9
Identifying the best time to communicate information	1 2 3	4 5 6	7 8 9
Creating a plan for communication of information that can be assessed and revised easily	1 2 3	4 5 6	7 8 9
Identifying terminology to use for communication that can be understood by all	1 2 3	4 5 6	7 8 9
Defining what is meant by future fertility (survivor and health care professionals view of the term)	1 2 3	4 5 6	7 8 9
Managing expectations for future fertility and pregnancy	1 2 3	4 5 6	7 8 9
Communicating risks to health care professionals from outside of paediatric oncology	1 2 3	4 5 6	7 8 9
How to assess if unmet need still exists and ways to address this within survivorship care	1 2 3	4 5 6	7 8 9

Theme	Not important	Unsure of importance	Important
Helping parents to communicate information to survivors	1 2 3	4 5 6	7 8 9

The modified 3-step Delphi approach used in PICCS2 recruited HCPs, female CAYA cancer survivors, and parents, and was adapted from the original technique by Dalkey and Helmer (1969). The introduction of a final face-to-face meeting (later amended to web-based) was not a component of the original Delphi method and reflected a modification known as the Ebel procedure that uses an Estimate-Talk-Estimate process (Eubank et al. 2016). Eubank et al. (2016) used a similar approach in their study with the structure of email (round one), face-to-face meeting (round two) and then email (round three), however the researcher wanted to maintain anonymity if possible before the collective discussion and therefore the email (round one), email (round two) and web meeting (round three) design was used to facilitate open interaction without any hierarchical bias between HCPs and CAYA cancer survivors/parents.

The Delphi technique is comparable to the Nominal Group Technique (NGT) often used for gathering group opinion. However, the NGT method asks panellists to generate ideas independently of each other, then ideas are culminated and discussed by the entire group. However, the researcher wanted to use a collaborative approach to consensus rather than silo working, therefore NGT was deemed not appropriate for PICCS2.

The use of the web-based meeting (round three) in PICCS2 allows novel interaction between professional and patient groups with the majority of the

decisions for consensus already taking place anonymously as panellists were blinded to the membership of the panel. Feedback and scores from each email round were anonymised before dissemination, with only the web-based meeting featuring names, professions, and faces/videos of panellists. This approach upholds the advantage of anonymity as recommended by Dalkey and Helmer (1963) and holds similarities with 'quasi-anonymity' (were people with expertise are mentioned by name and known to everybody from the beginning but questionnaire responses are anonymous).

4.3.2 Recruitment strategy PICCS2

4.3.2.1 Size of the panel

There are no set guidelines for the recommended sample size of an expert Delphi panel, but it is agreed that more members increase the reliability of the group judgments (Linstone and Turoff 1975). It has been suggested that an optimum number of panel members should be between 10 to 18, per area of expertise. However, this needs to take into consideration the time and financial budget of the study (Thangaratinam and Redman 2005). Likewise, the quality of the panel is viewed as more important than quantity, to enable focused, evidenced-based, and balanced discussions (Thangaratinam and Redman 2005).

A purposeful sample of 20 panel members for PICCS2 were recruited based on professional and personal experience factors. A snowball sampling approach was planned for, if recruitment was slow or lacked wider representation,

however this was not needed. Potential panellists were able to forward on invitations or suggest suitable candidates to take part if they were not able/did not want to take part. Panellists reflected HCPs from the field of late effects, paediatric oncology, obstetrics, midwifery, female CAYA cancer survivors and parents of female CAYA cancer survivors.

Panellists for PICCS2 were recruited by:

- A link, distributed via social media (Twitter, Facebook, LinkedIn) and an expression of interest form (*Qualtrics*) completed online and sent to the researcher
- Health care professionals were sent a personal invitation via NHS email and via non-NHS professional research group bodies (NCRI, PANCARE, CCLG professional membership groups). The invitation provided a link to the online expression of interest form that was emailed to the researcher
- CAYA cancer survivors/parents were invited via non-NHS based childhood cancer support groups (linked to registered charities and professional support groups) and via a printed leaflet containing the information about the online expression of interest form.

Recruitment for PICCS2 was unremarkable with 20 panellists from a variety of stakeholder backgrounds agreeing to take part. The methods for recruitment permitted the correct number of panellists needed for the study. However, the COVID-19 pandemic attributed to the loss of one panellist and made recruitment of the GP cohort more difficult. This could have been attributed to the fact that their profession was placed under a lot of strain, limiting availability.

The researcher acknowledged that this may result in under-representation of this stakeholder group.

A possible influence on recruitment was also a perceived reluctance of the researcher not wanting to trouble or follow-up with the invitations to the CAYA cancer survivor and parent group. This feeling can be attributed to the personal experience of having been a parent of child with cancer and understanding the emotional pressures of caring for a seriously ill child. The researcher also acknowledged a feeling of concern about possibly reminding the survivors of their past or worrying them about future late effects. Despite these concerns, the participants selected voiced no worries and were happy to be approached to take part. Ethical approval was also provided by Coventry University (P93106) to ensure the well-being of the researcher and participants throughout the study.

Following completion of the expression of interest form, a participant information sheet (Appendix 6) and consent form (Appendix 7) were sent via email to participants. The consent form contained permission for the taking of notes and the use of pseudo-anonymised direct quotations by the researcher in scientific publications and PhD thesis. The composition of the panel is detailed below (Table 14).

Table 14 - Stakeholder representation PICCS2

Stakeholder representation
Late effects (paediatric oncology)
Late effects (nurses)
Obstetrics

Stakeholder representation
Midwives
CAYA cancer survivors
CAYA cancer survivor parents
Paediatric Oncology/haematology
Radiotherapists
Academic researchers in the field of paediatric oncology survivorship
Nurses responsible for the care of CAYA with cancer and survivors
General Practitioners

The categorisation of the expert PICCS2 panel was chosen to ensure that the final statements or recommendations were created and approved by individuals with experience of the condition and that future recommendations will directly influence patient care in this field.

4.3.2.2 Consensus validation

Panellists were asked to review a series of statements and rank them in a pre-determined method. This enabled the formulation of statements that were deemed to have achieved or not achieved consensus validation. The statements were emailed to the Delphi panel members at each round, where they are asked to rank their agreement to statement options.

A popular choice for measuring consensus in health care surveys is a Likert scale. The Likert Scale is a well-recognised and universal standardised data collection tool which originated in 1932 (Likert 1932) and is now one of the most widely used tools for researching popular opinion, beliefs, attitudes, and

opinions (Trevelyan and Robinson 2015). The scale numerically ranks attitudes or opinions of participants in response to a question, reflective of the extent to which they agree or disagree with it (McMillan et al. 2016). However, data are dependent on the design of the scale, panellists free-text comments and previous subject knowledge (McMillan et al. 2016).

The scale, originating from the sematic differential technique developed by Charles Osgood in 1957 reflects three overarching categories ‘do not agree’, ‘unsure’ and ‘agree’ (Trevelyan and Robinson 2015). The scale can range from one up to 40, however, traditionally a 5-point or 7-point option is preferred (Trevelyan and Robinson 2015). The use of the 9-point scale in this study, was chosen as an option that allowed for deeper interpretation or exploration of the choices and a reduction in neutral responses, which carries a risk of consensus not being achieved. The 9-point scale is also validated by the RAND Corporation (a leading organisation of consensus methodology who developed Delphi) (RAND Corporation 2021).

The measurement scale and parameters chosen for PICCS2 were as follows:

- Not important (1-3)
- Unsure (4-6)
- Agree (7-9)

This classification reflects similar healthcare guideline development consensus models used in research (Taylor et al. 2016). The researcher was able provide a clear visual representation of the panel responses and was able to perform a quick 70% consensus rate calculation. Once the round was complete, each

statement findings were collated, anonymised, and analysed. Any statement option that achieved the pre-determined level of consensus was accepted for the next round. Statements that did not achieve the pre-defined 70% consensus rate were modified or removed. Then a findings summary was sent to participants. After a period of at least two weeks, round two then commenced. This back-and-forth process is continued for a specified number of rounds, until all statements have achieved consensus. If consensus cannot be achieved, then the panellists would need to agree to the early termination of the study (Taylor et al. 2016).

The reported lack of agreed standards for determining consensus level or recommended mathematical aggregation for the Delphi technique makes the selection of a consensus level difficult (Murphy et al. 1998). The heterogeneity of study designs and variations to the technique, result in a variety of definitions for consensus level. Jünger et al. (2017) suggested a rate of 75% is preferable, however, if the level of consensus is pre-determined, reported in advance and justified in the methods of a study, then the determinant level can be modified to suit the study. The consensus level set for this study was 70% which reflects other studies in the field of paediatric oncology guideline formulation (Murray et al. 2020).

4.3.2.3 Statistical analysis

Statistical analysis for PICCS2 included:

- Mean and 70% consensus calculations

- Freidman test (used to compare multiple statements)
- Wilcoxon signed rank test (used to compare two statements)

The statistical package *SPSS* and the software package *NVivo* (QSR International 2021) were used by the researcher. This allowed for reporting of the mean and the 70% consensus rate for each statement. The use of *NVivo* (QSR International 2021) allowed for the analysis of themes and free text. PICCS2 adopted a mixed-methods approach to data analysis, supporting the dual-paradigm, pragmatic approach to the overall study. The researcher accepted the knowledge that truth might be something that is not known yet, therefore, additional data (free text) and personal experience needs to also be considered in the synthesis of data. In the final findings of PICCS2, the statistical tests Freidman and Wilcoxon signed rank test were unable to be used due to the inability to apply collected data sets to the required parameters.

4.3.3 Study governance

4.3.3.1 Ethical approval

Ethical approval from Coventry University Ethics was given for PICCS2 (P93106) (See Certificate of Ethical Approval – PICCS2 on page 3). Following this, ethical approval was granted by the HRA following application to their IRAS portal (see Appendix 8 for full ethics documentation). This additional approval was needed due to the email correspondence with HCPs via NHS email. An amendment was submitted to the HRA on the 11th of November 2020 following the pause in recruitment due to COVID-19. This amendment was approved on

the 13th of November (see Appendix 8).

Participants received a participant information sheet and consent form, which included the option to inform their GP if they wished to. Appropriate signposting to professional organisations or medical professionals was made available to all participants, at any time throughout the study. This allowed for referrals to discuss any issues, feelings, or concerns that arose from the study or study content to be addressed in a timely manner. Links/contact details for approved organisations featured on the participant information sheet. The contact details of the researcher were also made available to participants.

Participants were aware that their participation was voluntary and that they could withdraw, remove consent, or decline to take part at any time. Participants were informed of the anonymisation process and consent was obtained to reveal their name, image, and professional/personal background in round three of PICCS2. Consent was also obtained for publication of their name for future scientific publication of findings as a member of the PICCS2 panel.

The researcher responsible for conducting the interviews was supported throughout the study by the supervisory team, which allowed for the opportunity to debrief, discuss, and reflect on the sensitive nature of the content of the study. This also helped to reduce any worries or stress associated with the project.

4.3.3.2 Dissemination

The overall findings for PICCS1 and PICCS2 were submitted as part of this PhD

thesis. Subsequently, dissemination of the findings was planned for in peer-reviewed journals, professional conferences, professional online forums, and amongst the international fertility and pregnancy (oncofertility) professional bodies. Outputs were also planned to be uploaded to *Research Gate, Research Fish,* and shared upon request with participants and/or groups with an interest in this area. Inclusive to this, a lay summary of the findings was planned to be shared with the CAYA cancer survivors and parent community via social media platforms and via charity organisations.

The systematic review (as part of PICCS1) protocol was published on PROSPERO, that enabled a record of initiation, amendments, and completion of the project. The study also has scope to be developed at the post-doctoral level by:

- A study to assess the acceptability of PICCS2 recommendations in UK health care
- A feasibility study to assess a high-risk clinical care pathway for pregnant female CAYA cancer survivors in the UK
- A randomised controlled trial comparing the provision of the PICCS2 guidance versus standard care to assess the impact of recommendations upon long-term outcomes

4.3.3.3 Costs and timelines

Costs associated with the study were minimal. Provisions for external funding were made but not used due to the COVID-19 pandemic that prohibited to face-

to-face meetings. This PhD was funded via a studentship award from Coventry University as part of the HEE/NIHR Legacy funding. PICCS2 adhered to a timeline to ensure that the delivery of the study was met within the timeframe and costs were adhered to. The participants of the PICCS1 interviews were given a £10 shopping voucher as expressed in the research protocol, as a gesture for taking part. This was funded using the yearly Postgraduate Fund allowance available to the researcher as part of the PhD award.

4.3.3.4 Data management

All documents, drafts, email correspondence, and data relating to PICCS2 were communicated as required using *Microsoft SharePoint* on Coventry University email. Communication between the participants and the main researcher was via secure email (NHS mail address and Coventry University email). Email communications were stored in an encrypted folder by the researcher and on an encrypted device (provided by the NHS). Email exchanges between participants during PICCS2 were performed using the Bcc method to ensure confidentiality and anonymity for the panel.

The web-based round three meeting was performed using *Microsoft Teams.* The meeting breakout sessions were recorded, and panellists consented to this prior to the meeting by email. Any recordings were deleted after two weeks, and any notes were stored securely on *Microsoft SharePoint.*

4.3.4 PICCS2 Round One

Panellists received the draft statements, themes and PICCS1 summary on March 17th, 2020. However, round one was delayed for three months due to clinical re-deployment of the researcher (COVID-19 pandemic). On June 29th, 2020, round one was able to be recommenced. Recruited participants were asked to re-confirm their ongoing consent for the study, with documents re-sent if needed. If they had already submitted a response to the draft documents or round one from March 2020, confirmation for the use of their responses for round one was received by email. Statements (phrased as questions at this stage) outlined the topics of time point for communication of information, format, and appropriate professional for communication delivery.

Panellists ranked each element of the questions (statements) using the Likert scale ranging from 1-9 below (Table 15).

Table 15 - Likert scale used for PICCS2

Not important			Unsure			Agree		
1	2	3	4	5	6	7	8	9

Free text for each statement was permitted and contact details for the researcher for any queries or support needed was provided. Participants were given two weeks for completion, with a reminder sent by email after one week. Once responses were received from all panellists, data input, anonymisation, statistical and thematic analysis were performed using a *Microsoft Excel* spreadsheet and the software programme *NVivo* (QSR International 2021).

A summary of the findings, the top-ranking option from each statement and those which had failed validation (did not achieve 70% consensus) were emailed to the panellists. A brief summary of the free-text responses (after a simplified thematic analysis exercise) and borderline options (those which fell into the 1% below the 70% cut-off for consensus) were also provided to panellists. They were asked to decide if borderline statements should be excluded, modified, or taken forward into round two. Statement responses were then revised and adapted based upon the feedback and ranking scores, for round two.

4.3.5 PICCS2 Round Two

Round two commenced on September 9th, 2020. Panellists were asked to confirm via email that they were happy to continue in the study and the revised statements were attached with guidance for completion. Statements were again ranked using the Likert scale of 1-9 and the option for free text was not allowed at this stage. The wording of some of the statements and options had been amended to incorporate feedback from panellists in round one. Panellists were given two weeks for completion, with a reminder sent by email after one week. Data analysis was completed following receipt of the responses and feedback then sent to panellists as with round one. Findings remained anonymous and were summarised with a table highlighting the options that had failed consensus and those which were ranked top. The panel was asked to send any queries or rebuttals within 14 days. The panel did not raise any queries to this round.

4.3.6 PICCS2 Round Three

Round three, originally planned as a face-to-face meeting, was conducted using the web-based platform, *Microsoft Teams*. This platform has been recognised as secure, confidential, and easy to access by NHS organisations in the UK and has been used extensively during the COVID-19 pandemic to allow professional interactions.

Following the 14 days allowed for feedback from round two, an online Doodle poll was sent to the panel members to select an appropriate date/time for the final round (round 3). A wide range of options were offered to cater to the variety of stakeholder responsibilities and needs. The date of the December 10th, 2020, was chosen, and invitations were sent via *Microsoft Teams* for the meeting (12 weeks after round two). The meeting lasted for one hour and was facilitated by the PPIE representative (NR), director of studies (EB).

Round three provided a unique opportunity for patient/professional virtual interaction and collaborative discussion. The panellists had consented to reveal their name, background, and image on the webcam before the meeting. If any panellist was not happy to do this, then provisions were made for an alias name and the webcam would be turned off. The breakout sessions were recorded to allow for replay and data analysis of the three groups. Participants were asked to consent to this prior to the meeting by email.

Facilitation of the meeting provided independent oversight of the process and permitted the use of breakout groups to keep the meeting to a minimum time. A summary of the evidence from PICCS1 and a round-up from the previous two

rounds of PICCS2 were presented via *Microsoft PowerPoint* by the researcher. The aim of the session and the planned output from the study was clarified as a clinical guidance document for the communication of future fertility and reproductive health late effects risk for female CAYA cancer survivors and their families. The dissemination plan for the findings of the study and plans for future scientific publication were then agreed with permission for identification in future publications agreed by all.

Following round three, panellists were sent a draft version of the final recommendations for agreement. The complete set of findings including any statements deemed not relevant or failed to achieve consensus during each round (1-3) are presented in Appendix 9.

4.3.7 PICCS2 - Risk of bias

A consideration of risk of bias for the selection of participants, the underpinning methodological approach, design, delivery, and formulation of the findings is presented below:

4.3.7.1 Selection and participation bias

The selection process for the panel in a Delphi technique can be criticised due to the quality, composition, and expertise of the panel members (Thangaratinam and Redman 2005). The quality of judgement from the expert panellists is paramount, therefore panellists need to represent all stakeholder groups and be selected with consideration of expertise and be reflective of the target patient

group. The expert panel for PICCS2 represented a wide-ranging stakeholder background including paediatric oncology, late effects, obstetrics, and midwifery, CAYA cancer survivors, and parents.

The definition of an expert in PICCS2, did not define an individual who was medically trained or an academic in cancer survivorship. The size of the panel was dependent on the acceptance of the invitation; however, a plan was made to recruit at least 20 participants from a selected group of backgrounds. There exists a risk of bias due to the personal background and professional familiarity of the experts used within the PICCS2 panel with the researcher. The researcher has worked in the PPIE field for over ten years and thus has met or communicated with many of the panel members previously. However, the rarity of the disease and the close-knit professional paediatric oncology community would make factor almost inevitable and unavoidable. Similarly, alternative methods of sampling such as random sampling would not have been appropriate for the study due to the need to represent a wide variety of stakeholder groups.

4.3.7.2 Group conformity bias

As identified by Rowe and Wright (2001), group conformity is a potential source of bias when using a Delphi technique. This is reflected by panellists choosing to agree with the rest of the group or ‘going along’ with everyone else. Durkheim (1982) also described this phenomenon as the theory of the collective unconscious (i.e., the bandwagon effect). Durkheim (1982) suggested that individuals are likely to unconsciously feel pressure to conform to the common

or standard beliefs within a group. The researcher aimed to address this with the selection of a validated agreement scale (Likert scale 1-9). The anonymity of participants was also a key feature of the design to limit hierarchical or professional pressure of conformity within the panellists.

4.3.7.3 Ranking bias

Bjarnason and Jonsson (2005) described the contrast effect, which occurs when the perception of a participant is enhanced or diminished, by the immediately preceding subject they last saw (being influenced by their last memory). This presents a risk of bias when individuals are asked to rate back-to-back statements as they have a memory of what they ranked previously. This risk was addressed by using an element of randomisation. The statements within each round were sent to participants in differing numerical order between to avoid subconscious preference for statements at the top of the table. This was not repeated in round three as the objective was to finalise all remaining statements.

4.3.7.4 Reporting bias

The participants received feedback in the form of statement rankings for each round. The top option from each statement and the options which failed to meet the consensus criteria were shared with the panel (and highlighted using colours). Panellists were given two weeks to reflect and feedback any queries for each round. A summary of the free text was provided to give context and explanations for any amendments to the statements provided. All final

statements including those that had failed to meet consensus were reported by the researcher (see Appendix 9).

4.3.7.5 Methodological bias

Inadequate survey measurement tools and poor data validation methods has been reported as a risk of bias when using the Delphi technique (Thangaratinam and Redman 2005). Likewise, poorly worded statements and lengthy timelines between rounds carries a risk of high attrition rates (Thangaratinam and Redman 2005). Downs and Black (1998) recognised this risk, warning that it creates a burden for both the facilitator and panellists. To avoid this, the researcher only conducted three rounds, and involved the panel in the decisions regarding timelines and selection of the draft themes. The measurement tool (Likert scale) is a widely recognised and validated survey tool and data analysis methods conformed to other studies of this kind. Regular contact between the panel with reminders and feedback also sought to maintain engagement with the study.

4.3.7.6 Dominance bias

The risk of dominance over other members of the panel has been reported in studies using the NGT methods (Eubank et al. 2016). Typically, one, very vocal group member attempts to exhibit control over the group, which can affect agreement of other panel members.

The structure PICCS2 allowed for anonymous email communication with

feedback for rounds one and two. The preservation of anonymity aims to eliminate dominance bias within the study (Trevelyan and Robinson 2015). Professional status, names, and ages were not shared with the panel and therefore they did not know who had submitted responses or scores for each statement round. The inclusion of feedback between rounds facilitated open and anonymous discussion for reasoning of scores and was overseen by the researcher. Through using methods like this, it has been shown to improve the decision-making ability of participants using a Delphi technique (Trevelyan and Robinson 2015).

The iterative nature of the Delphi technique involves a process of distribution, feedback, summary, and revision. This technique lends itself to focused consideration, revision and a high-level of discussion among panel members. However, it is important to consider how the methods chosen for PICCS1 and PICCS2 have linked, contrasted, and complemented each other and if the individual findings of the study elements can be combined. A consideration of triangulation of data will now be explored.

4.4 Triangulation

4.4.1 Methods of triangulation

The four main types of triangulation as proposed by Denzin (1978) offers characteristics that both enrich and critically analyse concepts, theories, and knowledge within a study. (Table 16).

Table 16 - Methods of triangulation (adapted from Denzin 1978)

Method of triangulation	Description
Data triangulation	Includes matters such as periods of time, space, and people
Investigator triangulation	Includes the use of several researchers in a study often with different theoretical theories
Theoretical triangulation	Encourages several theoretical philosophies to interpret the understanding of a phenomenon
Methodological triangulation	Promotes the use of several data collection methods such as interviews and observations within one study

The method of triangulation applicable to data obtained in PICCS1 and PICCS2 is methodological triangulation, or more specifically 'between-methods triangulation'. This choice was made as this type of triangulation offers the most appropriate method for the timeframe of a PhD award, the conduct of the overall study by one researcher and the aim to address a clinical problem rather than a philosophical theory. Methodological triangulation reflects the adopted dual-paradigm approach to the thesis.

Between-methods triangulation can combine data from several qualitative methods or a combination of qualitative and quantitative methods within a study (Flick 2018:10). The individual methods applied to the different elements of the studies help to maintain the individual philosophical underpinnings and logic of the research paradigm. Methodological triangulation maintains the individual method integrity and is widely advocated by methodologists such as (Karlsen, Hillestad, and Dysvik 2021). However, there is considerable scope for confusion, due to the complex ontological and epistemological issues (McEvoy

and Richards 2003). Likewise, triangulation may not be achieved with a uniform or consistent manner, limiting the replicability or transparency of the findings (Noble and Heale 2019).

Methodological triangulation aims to improve the credibility and validity of study findings from mixed-methods, multi-data sourced studies (Flick 2018:10). Credibility refers to trustworthiness and how believable a study is, and validity is concerned with the extent to which a study accurately reflects or evaluates the concept being investigated (Noble and Heale 2019). Triangulation has been described as the collation of more than one method (or source) of data within the study to provide an enhanced or richer understanding of the phenomena and confirmation of findings (Noble and Heale 2019).

The literal translation of triangulation comes from the ancient Greek ideology ‘synergy’, meaning working together, which theorises the concept of creating a ‘whole’ that is greater than the simple sum of its parts (Beneke, Schurink, and Roodt 2007). Flick (2018:10) also alluded to this notion of ‘collective enrichment of knowledge’ by stating that *“triangulation produces knowledge at different levels, which means it goes beyond the knowledge made possible by one approach”.*

Methodological triangulation was used in PICCS1 by combining qualitative and quantitative methods in order to enrich the knowledge base of the research problem. Data from PICCS1 were able to be triangulated, resulting in the identification of areas of unmet need. These findings were then used to structure the design and focus of PICCS2. The in-between methods of triangulation are illustrated below (Figure 9):

Figure 9 - Between-methods triangulation (taken from Flick 2018:10)

Methodological triangulation aligns with the critical realist perspective used within this thesis. The critical realist approach supports the assumption that there is a real social construct or reality, where findings can be applied. However, this reality is subject to a wider critical lens that encompasses human nature (McEvoy and Richards 2003). This theory also supports the adoption of a dual-paradigm approach as outlined in Chapter Three – Methodology, whereby the researcher draws upon the different participant perspectives (i.e., the CAYA cancer survivor/parent and HCP).

Triangulation within a research study, will typically result in three outcomes as described by (Heale and Forbes 2013).

1. Concordance - the findings may converge and lead to the same conclusions
2. Reconciliation - the findings may relate to different objects or phenomena but may be complementary to each other and used to supplement the individual findings

3. Dissonance - the findings may be divergent or contradictory

Convergence of the findings aims to increase validity through verification. Complementary findings can highlight different sides to the phenomenon and divergent findings can lead to new and better explanations of the phenomenon under investigation (Heale and Forbes 2013). The impact of triangulation upon the findings of PICCS1 will be considered in Chapter Six – Findings.

4.5 Conclusion

The critical realist philosophical framework has been used to guide the philosophical reasoning of the researcher in this thesis and has underpinned the methodological choice, data analysis and synthesis of data (including triangulation choice) in PICCS1 and PICCS2. Each element of the two studies offer a complimentary aspect of scientific evidence alongside the deeper exploration the key domains of reality, the empirical, the actual and the real.

Despite the elements of PICCS1 being performed in isolation, a sequential approach was used to ensure data integrity and to uphold the quality of the research paradigm. Data could not be combined or amalgamated as a whole due to the nature of how the data was collected, the participant background, independent variables (that cannot be adjusted in data), and the 'lived-voice' of participants. This type of data cannot be quantified or subjected to statistical tests or algorithms and thus prevents combined analysis.

However, methodological triangulation enabled the findings of PICCS1 to inform the design and focus of PICCS2 to address the unmet informational needs of

female CAYA cancer survivors. PICCS2 addressed the second of the overarching research questions to discover what recommendations can be carried forward into clinical practice to benefit female CAYA cancer survivors.

A modified Delphi consensus technique was selected for PICCS2, drawing upon the critical realist method of enquiry. This facilitated the exploration of the ‘when, by whom, and in what circumstances' involved in the communication of future fertility and reproductive health late effects risk for female CAYA cancer survivors. The adoption of a mixed-methods design based upon a critical realist philosophical underpinning helped to produce a set of expert recommendations that were guided by the published evidence and the values, beliefs, and experience of the panel members.

Following the exploration and reflection of the theoretical underpinnings and methods used within the research studies PICCS1 and PICCS2 the researcher will now present the findings from the individual study elements. This will compromise of findings from the systematic review, online questionnaires, and semi-structured interviews (PICCS1). This will be followed by the findings from the modified Delphi consensus technique (PICCS2).

Chapter Five – Systematic review of the literature

5.1 Introduction

This chapter shares a structured systematic review of the existing empirical knowledge surrounding the research topic. This allowed the researcher to consider, reflect, and critically analyse the methodological traditions, approaches, and previous published findings (Flick 2018:68). The systematic review represents the empirical domain of reality. It supports the critical realist philosophical approach to the thesis, that combines a framework of knowledge based on objective facts, alongside knowledge gained from a more subjective human enquiry (see Chapter Three – Methodology).

5.1.1 Unmet informational needs of CAYA cancer survivors

Vetsch et al. (2017) and Lie et al. (2015) reported that the communication of late effect risks to CAYA cancer survivors and their families is inadequate. This results in significant unmet informational needs. Priority areas for unmet informational need were reported as future fertility, risk of cancer reoccurrence and future heart health, following treatment for cancer (Cox et al. 2016).

The ideal format for communication of late effects risk information and when might be the optimal time point to discuss this with families, is under-researched (Cox et al. 2016). More research is needed to understand how CAYA with cancer and their families want to access and receive late effects information, for example, if they prefer digital or printed formats (Kunin-Batson et al. 2016).

Poplack et al. (2014) recommended further research that addresses the evolving individual needs of CAYA cancer survivors and advised HCPs to make sure that communication strategies are translatable to all (Poplack et al. 2014).

Interventional studies to address unmet informational needs are limited in the published literature (Devine et al. 2018). Devine et al. (2018) conducted a narrative review to assess digital interventions to address unmet informational needs of cancer survivors. They reported that unmet informational needs have significant impact upon the long-term psychological and physical well-being of survivors if left unaddressed (Devine et al. 2018). Likewise, Devine et al. (2018) linked unmet informational needs to a higher risk of detrimental long-term health behaviours (e.g., substance abuse, smoking and obesity) and poor self-management of chronic health conditions associated to cancer treatments (Devine et al. 2018).

Up to 60% of CAYA cancer survivors are reported to experience a long-term health condition directly attributable to prior cancer treatments (Edgar et al. 2012). This suggests that CAYA cancer survivors need to know and understand key future health information to help avoid long-term health risks and possible psychological distress from unmet informational needs (Brown et al. 2021)

5.1.2 Unmet informational needs of parents

Parents of CAYA cancer survivors have reported a need for help and support to deliver key late effects survivorship information to their child (Nieman et al. 2007). Parents of CAYA cancer survivors are often tasked with relaying key

future health information (due to treatments given in young childhood) and they want to make sure their child has the information they need to make informed choices for their future health and well-being (Nieman et al. 2007). Nieman et al. (2007), in their qualitative exploratory study of female CAYA cancer survivors and their parents, reported that parents often feel overwhelmed and find it difficult to cope with long-term prospects for their child at the time of diagnosis. The challenge of deciding what late effects information is most important to communicate to their child compared with deciding what information can be withheld until remission or later adulthood, has been described as a 'mine-field' by parents of CAYA cancer survivors (Greenzang, Dauti, and Mack 2018). Therefore, addressing unmet informational needs also extends to the parents of CAYA cancer survivors not just the survivors themselves.

5.2 Rationale for the review

To fully understand the concept of unmet informational need, its relationship with different methods of communication, and the impact upon the CAYA cancer survivor; a preliminary scoping review of the topic area was performed. Scoping reviews are described as an effective way to map the existing literature base and are particularly advantageous when a body of literature exhibits a heterogeneous nature, such as in CAYA cancer survivorship (Armstrong et al. 2011). Similarly, scoping reviews are reported to help identify appropriate parameters (i.e., define the targeted population, intervention, comparison, outcomes) and identifies common terminology, useful for searching academic databases (Armstrong et al. 2011).

After the scoping review, a systematic review was then performed to collate, critically-appraise, and synthesise the available published evidence according to a recognised and reportable framework (PRISMA). This method is recommended by the Centre for Reviews and Dissemination (CRD) (CRD 2009), particularly if the intended output of the findings will be taken forward for a possible intervention or change in practice.

A systematic review was chosen as the most appropriate method to address the research question, as it facilitated the synthesis of evidence, provided critical appraisal, and considered risk of bias in a replicable and robust way (Armstrong et al. 2011). Systematic review methodology provides a strong framework for the research inquiry. This helps to illustrate the current landscape, analyse the quality of existing research, and identify gaps in knowledge for future research (Armstrong et al. 2011).

The research question developed for this systematic review was distilled from the broader critical realist inquiry: when does communication happen; who does it; and what are the experiences of both professionals and patients when giving/receiving this information?

The PRISMA reporting guidelines and study flowchart (Moher, Tetzlaff and Altman 2009, Moher, Liberati and Tetzlaff 2009) are widely recognised tools used for conducting a systematic review in health research. The presentation of this chapter reflects the template recommended by Moher, Liberati, and Tetzlaff (2009), and features an explanation of review process, a full report of the research findings and use of the PRISMA flow chart, headings, and sub-headings (see Appendix 10). However, PRISMA recommends as part of the

checklist to include an abstract for the review and statement for the declaration of funding source. In this review, this has been omitted from the structure of this chapter to assist with flow and readability of the thesis. An overall abstract for both PICCS1 and PICCS2 can be found on page 14.

5.2.1 Prevalence and background – CAYA with cancer

The survival rate for CAYA with cancer is now approximately 92%, with the number of CAYA cancer survivors in the UK estimated to be around 35,000 and rising each year (Cancer Research UK 2021). Post-treatment, CAYA cancer survivors are reported to be at a high-risk of several chronic and treatment-related health conditions in adulthood, often called ‘late effects’ (Otth et al. 2021). The likelihood of suffering from late effects and the extent to which they might affect the everyday life of a CAYA cancer survivor in adulthood is often not known (CCLG 2021b). This is also largely dependent upon the type of cancer they had, where it was located, and the level of treatment they received (CCLG 2021b).

Late effects of treatment can arise during, shortly after or many years after treatment is complete and can affect organs such as the heart, lungs, and endocrine systems (CCLG 2021b). CAYA cancer survivors carry a higher rate of morbidity and mortality when compared to the general population, with 60-90% of CAYA cancer survivors affected by a long-term condition such as thyroid dysfunction, fertility issues and cardiovascular disease (Otth et al. 2021).

Long-term surveillance for cancer recurrence or relapse, and early detection of

physical problems are examples of physical focus of current survivorship health care services (Hjorth et al. 2015). A high level of surveillance is typically life-long and requires ongoing effective and accurate communication of information so that CAYA cancer survivors and their families are fully informed of their long-term health risks (Hjorth et al. 2015). Treatment for CAYA cancer and the psychological burden of this diagnosis as a child, adolescent or young adult was highlighted by Hendriks, Harju, and Michel (2021) and Vetsch et al. (2017) who called for survivorship care services to address the unmet informational needs of CAYA cancer survivors and consider the psychological as well as physical ongoing needs.

There is a reported need to improve the model of communication for future late effects risk, however there is a lack of translatable examples that are applicable to the UK NHS health systems. Hendriks, Harju, and Michel (2021) and Greenzang et al. (2020) agreed that a clearer definition of when and how late effects information should be communicated to families is needed and recommended further research into this area.

For this systematic review, to design a research question that targeted all available published literature around communication of late effects information – a scoping review of the literature was conducted prior to the full review. This will now be presented followed by the findings of the systematic review.

5.2.2 Preliminary scoping review

The scoping review was conducted using the framework by Arksey and

O'Malley (2005). This framework was chosen as it provided a clear, concise, and replicable method for the searching and reporting of findings that would be taken forward into the systematic review protocol and research question (Table 17).

Table 17 - Scoping review framework (Arksey and O'Malley 2005)

	Arksey and O'Malley framework (2005) **Scoping review – process stages**
1	Identifying the research question
2	Identifying relevant studies
3.	Study selection
4.	Charting the data
5.	Collating, summarising, and reporting the results
6.	Consultation (optional)

5.2.3 Findings from the scoping review

The databases CINHAL and MEDLINE were searched for academic journal articles from 2009-2019 (the last ten years), published in English and featuring the keywords below (Table 18).

Table 18 - Key word search - scoping review

Key word search
'childhood cancer'
'childhood cancer survivors'
AND 'late effects'
AND 'communication'
AND 'unmet needs'

The search returned 316,659 results. The first ten pages of the results were filtered for relevance by the researcher. Where abstracts and full text were available, these were read and considered for relevance to the topic area by the researcher. The findings from the scoping review reinforced the need for further investigation of this area. The findings confirmed that the proposed research question had not been answered previously, or that a systematic review did not already exist. Likewise, the scoping review identified the associated terminology needed for the database search, such as the inclusion of ‘neoplasm’ for cancer.

The scoping review revealed evidence to suggest that communication and informational needs of CAYA cancer survivors was an important topic to both parents and CAYA cancer survivors. Literature was published in this area primarily during the last ten to 15 years (Otth et al. 2021). Publications in this area represented a largely qualitative methodological approach, with examples such as an exploratory interview-based studies of CAYA cancer survivors (Nieman et al. 2007) and a physician-experience based qualitative cohort study (Michel et al. 2017). Two reviews, a narrative review and a systematic review by Vetsch et al. (2017) and Signorelli et al. (2017) investigated specific disease types and associated unmet informational needs and recommended the need for further research exploring the communication of future fertility status.

CAYA cancer survivors had reported confusion about their future fertility status after treatment and reported that by not knowing this information it led to a significant level of unmet informational need (McCarthy et al. 2013). This finding was supported by Devine et al. (2018) who recommended that HCPs needed

an increased awareness of late effect risks to prevent possible long-term psychological distress of CAYA cancer survivors.

The scoping review also emphasised the need to consider the use of the traditional mnemonic for constructing a research question, 'PICO' (Population, Intervention, Comparison group, Outcome) (Richardson et al. 1995). It was revealed that PICO would not align with the proposed search terms and although widely used in academia, its use would not have captured the desired depth or critical realist philosophical approach needed for PICCS1. The research question for the systematic review needed to represent the real-life experiences of the patients as well as the factual data, therefore an alternative mnemonic, 'SPIDER' (Sample, Phenomenon of Interest, Design, Evaluation, Research type), was used.

SPIDER is a recognised and validated method for research question construction that reflects a qualitative inquiry, developed by Cooke, Smith, and Booth (2012). Despite this, Methley et al. (2014) argued that SPIDER does not locate all the relevant papers when compared to PICO, however. The CRD (CRD 2009) suggested that an amalgamation of the two methods to form 'PICOS' can help to alleviate some of the restrictions of the original method. The definition of PICO, PICOS and SPIDER and a comparison of the mnemonics are provided in Figure 10.

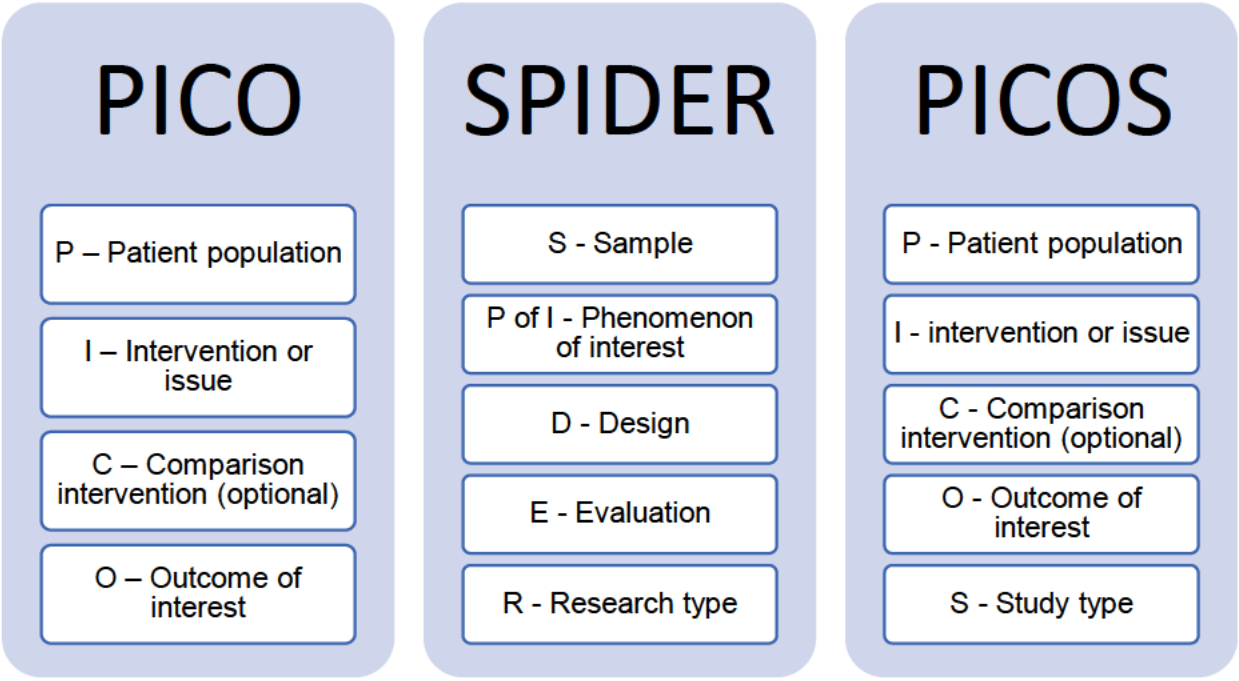

Figure 10 - Definition and comparison of the PICO, SPIDER and PICOS research mnemonics

All three variations were considered and reflected upon by the researcher. The use of SPIDER was chosen for the systematic review, as it was felt that it allowed for a wider inclusion of all medical and psychological databases and that it would therefore capture a wide variety of study types and data.

5.3 Objectives

The objective for the systematic review was to find, appraise and synthesise the published evidence for the communication of late effects information in CAYA cancer survivorship care. The aim of the review was to explore what currently happens in clinical practice from the CAYA cancer survivor/parent perspectives. This information would then be presented and used to highlight areas for improvement for both survivorship care service provision and future research.

5.3.1 Research question and outcomes

The SPIDER mnemonic (Table 19) was used to create the following research question:

1. What are the unmet informational needs of CAYA cancer survivors regarding their risk of late effects?

Table 19 - SPIDER formation of the research question

	Description
S	Childhood/teenage/young adult cancer survivors (and all deviations in spelling and pronunciation)
P of I	Communication (and all derivatives)
D	Guidance, recommendation
E	View, experience, attitude
R	Qualitative, mixed methods and quantitative studies (all types)

The research question traditionally drives the specified outcomes for the review. The primary outcome was identified by using evidence from the scoping review. This highlighted that unmet informational needs of CAYA cancer survivors about their risk of late effects was a key area of inquiry. The secondary outcomes for the review were designed to capture data from key variables of communication exchange and to identify future research questions (Table 20).

Table 20 - Outcomes for the review

Outcomes	Description
Primary outcome	Informational and communication needs

Outcomes	Description
Secondary outcomes	Perspective Professional who communicated information Age at diagnosis Time since diagnosis Method of communication Timing of communication

5.4 Methods

5.4.1 Protocol and registration

The protocol for the systematic review (part of the study PICCS1) was registered on PROSPERO with the registration number CRD42019145292[5]

The systematic review was regarded as 'review subject to change'. This defined that the review would take into consideration any new publications that met the inclusion criteria, up until November 2020. The literature search process would be replicated once after the main search, with search alerts activated on relevant databases to alert the researcher to new publications in the field.

Any new publications would be subjected to the same inclusion criteria and reported alongside the main findings of the review. This method was chosen to ensure the ongoing relevance of the evidence and applicability to clinical

[5] Available from https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42019145292. The protocol was registered on the 13th of August 2019, with an update submitted on the 19th of November 2019 (title edit) and 20th November 2020 (delays due to COVID-19 clinical re-deployment).

practice. This ‘continuous’ method of appraisal is supported by the Cochrane Collaborative in their handbook for the conduction of systematic reviews of interventions (Cochrane 2021a). This method is also recommended for reviews that intend to inform a service change or possible intervention (Higgins, Green, and Scholten 2008).

The systematic review protocol was updated three times during the course of PICCS1. Changes made to the entry on PROSPERO included:

- (1) Title edit to reflect wider nature of the inquiry (communication of all late effects)
- (1) To remove pregnancy late effects as the focus (inclusion and exclusion) and make the research question wider (all late effects communication). This decision was taken following consultation with the wider supervisory team and PPIE representative.
- (2) Correct grammar, terminology, and typos (e.g., < changed to >) and remove time requirement for end of cancer treatment from inclusion and exclusion criteria (following discussion with supervisory team)
- (3) To include details of the aggregate review date, change in selection for risk of bias tool used, and to update review to a completed status

5.4.2 Eligibility criteria

To effectively answer the research question; a decision was made by the researcher not to place a start date or year limit onto the review. This was

primarily due to the rarity of CAYA cancers, resulting in the likelihood that relevant data may be published more than ten years ago. It was considered important to ensure that all available evidence was considered for inclusion, which would be restricted by implementing a time frame. The literature search was limited to the English language, due to no translational resources available to the researcher. The studies were included for consideration if the dataset represented children, adolescents and young adults aged 0-24 years old (inclusive) at diagnosis of cancer. All study designs were considered, and studies were only included if the content of the study was directly relevant to the communication of late effects or unmet informational needs.

Further inclusion criteria included a requirement for the study to be published in a peer-reviewed journal (as it reflects a study assessed using a quality checking and standards procedure). If the population age at diagnosis was not stated, nor in a format where age at diagnosis could be extrapolated, the authors were contacted for further information. If data could not be obtained within four weeks, then studies were excluded from the review. If communication of information had been solely obtained through support groups, charities, or other online resources then the study was excluded. The reason for this was that the information would not be subjected to a peer-review quality checking process, nor reflective of the communication exchange between a HCP, the survivor, or their parent.

The full inclusion and exclusion criteria for the review is below (Table 21).

Table 21 - Eligibility criteria for studies

Inclusion	Exclusion
Sample of CAYA cancer survivors (diagnosed between 0-24 years inclusive) or parents of CAYA cancer survivors	CAYA cancer survivors >24 years old at diagnosis or not clear from data sample
Studies that have been peer-reviewed (all types)	Studies not published in peer-reviewed journals e.g., source from charity, website or other non-academic format
Studies relating to communication of late effects information in all formats	Studies that do not discuss communication of information to CAYA cancer survivors or parents
Studies in the English language	Studies not in the English language

5.4.3 Information sources

A search of MEDLINE, PUBMED, PsychINFO, CINAHL, Google Scholar, SCOPUS and ProQuest databases was performed for applicable studies up until 1st September 2019. An update to the review was conducted on the 1st of November 2020. The SPIDER mnemonic search terms were used to search the selected databases (example strategy applied to MEDLINE provided in Table 22).

Table 22 – Example search strategy (MeSH headings) for MEDLINE

MeSH heading	Description
S	"Childhood cancer surviv*" or "adult cancer surviv*" or cancer surviv*" or "childhood neoplasm surviv*" or "p?ediatric oncology surviv*" or "teenage cancer surviv*" or "young adult cancer surviv*" or "adolescent cancer surviv*" or "CAYA" or "CCS"
P of I	"communicat*" or "information" or "discussion*" or "consult*" or "advi*" or "decision making" or information sharing" or "translating" or "passing on"

MeSH heading	Description
	AND "long-term" or "risk*" or "health" or "outcome" or "effect*" or "complication*" or "disease" or "chronic" or "illness*"
D	"guideline" or "recommend*" or "questionnaire" or "survey" or "interview*" or "focus group" or "case stud*" or observ*" or "care" or "plan" or "review*"
E	"view*" or "experience*" or "attitude*" or "remember" or "awareness" or "belief" or "memor*" or perception*" or "thought*" or "know*" or "understand*"
R	"qualitative" OR "mixed method*" or "quantitative"

The choice of databases was considered to be extensive by the researcher, the supervisory team and the PPIE representative for the study (NR). Confirmation of appropriate databases for the search was also sought from the subject librarian of the academic host institution.

5.4.4 Search strategy

A search strategy was developed using the SPIDER search terms and then adapted to the chosen database syntax, i.e., medical subject headings (MeSH) were edited to the appropriate format. To ensure all eligible literature had been searched, the reference lists of included studies were scanned, and citations forward cited and back referenced.

5.4.5 Study selection

The study selection process for the systematic review used a six-step technique, featuring PPIE oversight and independent verification by the

supervisory team (Table 23).

Table 23 - Study selection process

Stage	Selection Process
Stage 1	Title and abstract screening against inclusion criteria (researcher 100% and PPIE representative reviewed a randomly selected 10% sample)
Stage 2	Full-text documents obtained in PDF form and uploaded to the appropriate reference manager (*RefWorks*) (100% researcher)
Stage 3	Full-text screening against the inclusion criteria (100% researcher)
Stage 4	Appraisal of final included studies (100% by researcher and verified by PPIE representative)
Stage 5	Risk of Bias and data extraction verification (PPIE representative appraised one randomly selected included study)
Stage 6	Final studies presentation of findings (verified by PPIE representative)

This six-stage technique with continuous PPIE oversight of the process was chosen as an exemplar process to demonstrate how to integrate PPIE into a review process. Consensus of inclusion was achieved with the input of the PPIE representative acting as an independent party in cases of arbitration (of which there were none). All screening decisions and findings were recorded using the PRISMA flow chart (Moher, Tetzlaff and Altman 2009) (Figure 11).

5.4.6 Data collection process

Data were extracted onto a *Microsoft Excel* spreadsheet using a modified Cochrane data collection template (modified by editing headings to fit data for the CAYA cancer population and disease categories). The original extraction template, developed by Cochrane in 2014 (Cochrane 2014) was used to

structure a summary table with modified headings. A *Microsoft Excel* spreadsheet was then produced that captured key demographics and main findings/themes from the included studies (Appendix 11). A risk of bias appraisal and extraction of the primary and secondary outcome data was then conducted and added to the summary table. Findings were then presented by using tabulated formats (summary table, risk of bias assessment and secondary outcome data) and thematic analysis (primary outcome data and narrative summary of included study characteristics).

Data collection and extraction were verified by the PPIE representative by providing him with one random full-text study. He was asked to appraise against the inclusion criteria and extract key data. This was then compared against the result from the researcher alongside the risk of bias assessment for the chosen study using the approved tool (Critical Appraisal Skills Programme (CASP) 2019). Any discrepancies found in the study selection and inclusion process were discussed and agreed between the researcher and the PPIE representative. The Director of Studies was available for arbitration but was not needed due to no conflicts within the process of selection and data validation.

5.4.7 Data items

Studies were included into the review with the following declarations:

- Any funding source (e.g., academic grant, pharmaceutical sponsored or charity)

- Use of any known abbreviations for the subject area (e.g., CAYA, AYA, CCS). A comprehensive list of abbreviations can be found in Glossary and abbreviations on page 16.

There were no other simplifications or assumptions made in the review.

5.4.8 Risk of bias

5.4.8.1 Study level

Risk of bias at the study level was considered using the CASP appraisal tool (CASP 2019). Alternative appraisal tools such as MMAT (Hong et al. 2018) and the Cochrane Risk of Bias Tool (RoB2) (Cochrane 2021b) were considered by the researcher. However, the MMAT tool (Hong et al. 2018), despite being well-recognised and validated for the appraisal of mixed-methods research studies, was not deemed suitable for studies which include quantitative methodology or reviews of the literature. As the inclusion criteria for the study allowed all types of study to be considered, this tool would not be appropriate for use. The Cochrane tool (RoB2) (Cochrane 2021b) was also deemed not suitable due to the high likelihood of qualitative studies and data being included.

The CASP tool (CASP 2019) is a widely recognised appraisal tool that offers templates for all types of study methodology. The CASP tool (CASP 2019) accommodates for the heterogeneous nature of the inclusion criteria and is a widely recognised and validated resource (CRD 2009). Therefore, it was chosen by the researcher in this review, but with acknowledgement of the

cautionary advice from Cochrane (Cochrane 2021a). This stated that the selection of an appropriate tool should be made very carefully due to the increased risk bias of the author in the selection of a tool to suit their optimal or desired outcomes (Cochrane 2021b). To mitigate the risk of bias in the selection of the appraisal tool, the CASP tool was approved by the PPIE representative and the supervisory team before application to the included studies.

5.4.9 Summary measures

Due to the heterogeneous nature of the included studies and the lack of comparable data, summary measurements and analysis such as meta-analysis or risk-ratio calculations could not be undertaken.

5.4.10 Synthesis of findings

5.4.10.1 Methodology of synthesis

The conduct of a narrative synthesis in research varies widely (Flick 2018). Historically there has been a lack of consensus as to the preferred process and the constituent elements of the approach (CRD 2009). Cochrane (2021a) advises that researchers attempt a narrative synthesis that includes investigation of the similarities, the differences, as well as the exploration of patterns within data from the selected studies. This includes examining links between study outcomes and any other factors related to the study design and conduct (Cochrane 2021a). This approach aligns with the critical realist philosophy by considering the impact of outside variables upon the study

findings.

Thematic analysis was chosen as the preferred method for the synthesis of data within the review. Popay et al. (2007) described thematic analysis as a means of organising and summarising the findings from a large, diverse body of research, whilst allowing the reflective portrayal of conclusions and ideas. This is in contrast to the traditional focus of simply a production of new knowledge (Popay et al. 2007). Braun and Clarke (2006) argued that thematic analysis is a vital part of the foundation for qualitative analysis as it provides core skills that are directly applicable to other analytical methods (such as ethnography and grounded theory).

5.4.10.2 Process of synthesis

Data for the summary table and primary and secondary outcomes for the review were extracted and inputted onto a *Microsoft Excel* spreadsheet. Data were then tabulated and presented. Additional findings from the included studies that could not be tabulated were described in narrative form and subjected to thematic analysis – using the framework by Braun and Clarke (2006) (see Figure 8).

Data of this kind were transcribed and inputted into a *Microsoft Word* text document with the six-phase process framework for thematic analysis by Braun and Clarke (2006) undertaken by the researcher. The document was then used to input data onto the software programme *NVivo* (QSR International 2021). *NVivo* was used to label data into draft codes, which were then colour coded

and grouped according to similarities and concept themes. Narrative findings were then sorted into final theme categories and presented within the findings section of this chapter (see section 5.5 Findings).

Following the six-stage process, draft theme concepts were further explored by the researcher using a mind map. A mind-map is a tool or diagram used to represent concepts, ideas, or tasks in a pictorial format. Terms are linked to and arranged radially around a central key word or concept (Burgess-Allen and Owen-Smith 2010). It is commonly used when rapid qualitative data analysis and synthesis is preferred and in studies that include a wide range of stakeholder experiences, such as PICCS1 and PICCS2.

However, a disadvantage to using the technique is the considerable risk of researcher bias. Human judgment plays a major part in the construction of the mind map, both in terms of the choice of words used to summarise participants' comments and ideas, and the choice of where to position those words on the map (Burgess-Allen and Owen-Smith 2010). Therefore, when creating the draft themes and the mind-map, the PPIE representative and the Director of studies appraised collected data to assist with the rigour of data synthesis process. This method permitted a wider reflection and thinking surrounding the relationships of data within and across the nominated themes. The process provided the researcher to present similarities within the data and compare findings with relevance to the research question.

Following the mind map, the draft themes were further refined into final themes and presented alongside tabulated data. This deductive process helped to demonstrate transparency in theme generation and allowed for the

consideration of all data into the findings of the review. The Director of Studies was asked to consider the final theme selection and summary table data as an additional level of transparency and objectivity to the review process. Alternative methodological approaches to data synthesis – i.e., narrative synthesis, meta-ethnography, and meta-synthesis – were considered for appropriateness by the researcher before the selection of thematic analysis. Alternative data analysis frameworks such as Miles and Huberman (Miles 1994) were also considered. The flexibility of the Miles and Huberman (Miles 1994) method works well when used for a wider collection of data and exploration of themes with independent validation. However, a more deductive approach was needed in the review, with a clear roadmap to link the process of the thematic generation to the findings. This method was thought to increase the replicability of the review and provide a sequential-type process that was used to inform and shape the development of the other elements to PICCS1 (online questionnaires and interviews).

5.4.10.3 Data management

Draft study documents, ethical approval for the review and all correspondence relating to the project, data and final thesis were held on *Microsoft SharePoint,* a secure online storage facility owned by Coventry University. Emails relating to the review were sent from a password-protected account. Ethical approval documents for PICCS1 and PICCS2 can be found in Appendix 11. References were uploaded from the database searches into *RefWorks*, a widely recognised and validated data management software programme for research.

5.4.10.4 Data handling

Data were transferred via exportation files into *Microsoft Excel* and used within the software programme, *NVivo* (QSR International 2021), used for coding and thematic analysis of the findings. Data input and analysis were conducted by the researcher with oversight of the selection of themes from the supervisory team once data had been analysed. The PPIE representative for the study was provided with an encrypted copy of the final review findings and theme and all data were stored electronically within *Microsoft SharePoint* on the Coventry University server as per ethical approval.

5.4.11 Risk of bias (across studies)

Risk of bias assessment at the review level (across studies) included the following assessments (Table 24).

Table 24 - Risk of bias across the studies

Type of bias	Description
Selection bias	Authorship representation (did one author dominate the field), where did the participants originate from, was it the same sample in each study?
Reporting bias	Outcome reporting considerations (did authors report negative outcomes or null hypothesis as well as main study findings), omitted findings or missing data
Methodological bias	Did the authors justify their design and approach, was there a saturation of qualitative or quantitative studies, does this impact the generalisability of the findings?

5.4.12 Additional analysis

There were no additional analyses performed within the review.

5.5 Findings

This section will present the findings of the review. Key findings, themes and individual study characteristics of the included studies are presented alongside the risk of bias assessment. Applicability of the findings and potential clinical impact (translatability) of the findings for CAYA cancer survivors and HCPs in charge of their care are also considered and discussed.

5.5.1 Study selection

A search of MEDLINE, PUBMED, PsychINFO, CINAHL, Google Scholar, SCOPUS, and ProQuest databases for published articles up until September 1st, 2019, was performed, followed by an update on the 1st of November 2020. Following the removal of duplicated studies, 143 were taken forward to the title HCP 'assessment of suitability' screen (used by the researcher for Google Scholar due to the magnitude of findings produced and the limited ability to apply appropriate filters). Titles of results from Google Scholar were scanned for relevance by the researcher and included into the title and abstract screening stage of the review if the keywords 'childhood cancer', 'communication' and 'late effects' were identified in the title or in the brief description of the study. The PRISMA flow diagram (Figure 11) illustrates the total amount of studies and reasons for exclusion.

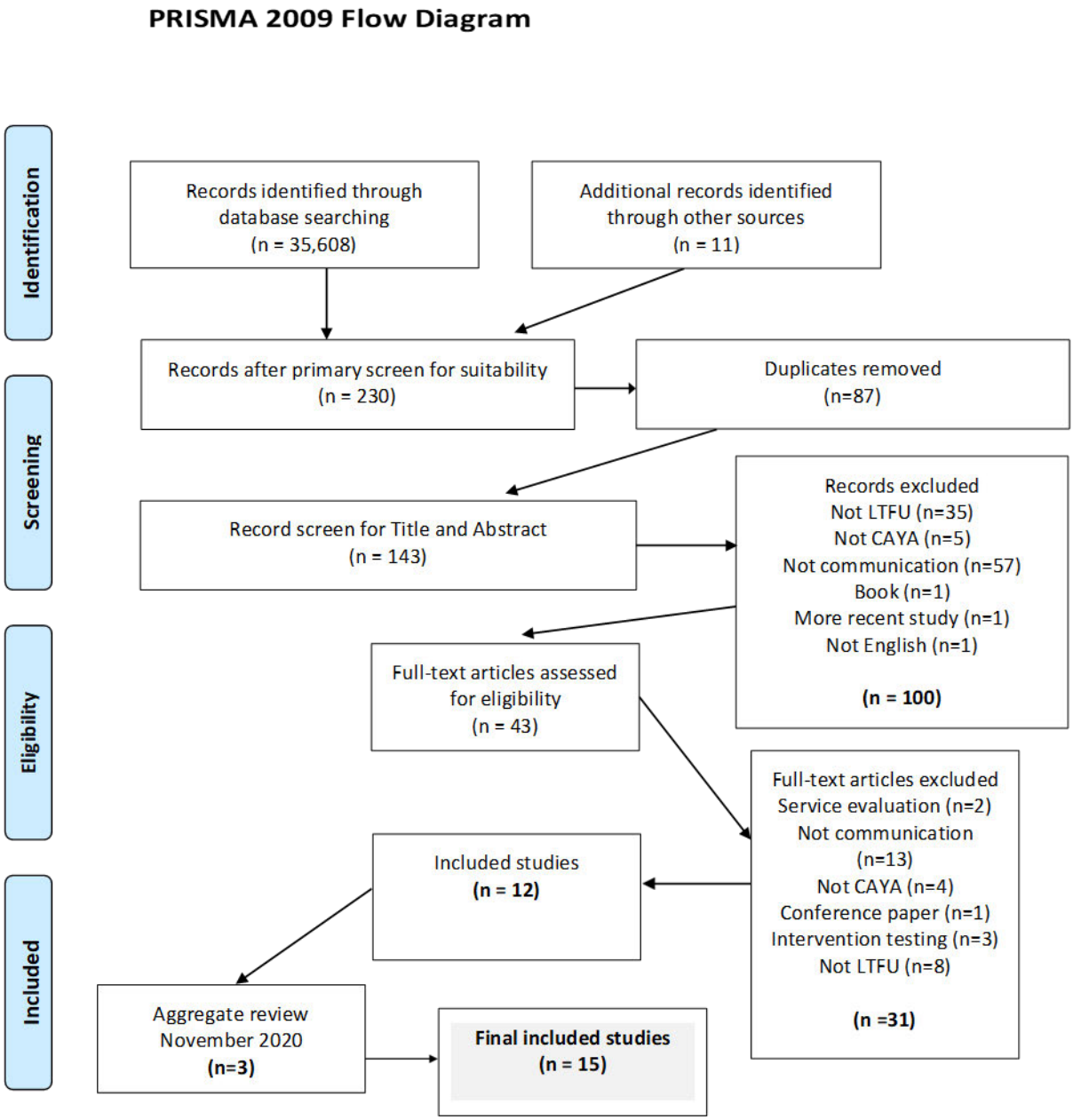

Figure 11 - PRISMA flow diagram

Following title and abstract screening, 43 studies were taken forward for full-text review. A random sample (ten percent) of the title and abstract studies were given to the PPIE representative and were agreed to fit the inclusion criteria. Following full-text appraisal of the studies, 12 were taken forward for data extraction and risk of bias assessment. The PPIE representative was provided

with one study from the 12 included and was asked to conduct an independent data extraction and risk of bias assessment. Following the aggregate review on the 20th of November 2020 another three studies were added. The final included studies for the review (15) are presented in Table 25.

Table 25 - Final included studies

Included studies
Brand, Fasciano, and Mack 2017
Cox et al. 2019
Crawshaw et al. 2009
Gianinazzi et al. 2014
Greenzang, Dauti, and Mack 2018
Greenzang et al. 2018
Hess et al. 2011
Keats et al. 2019
Lee et al. 2019
Lie et al. 2015
Signorelli et al. 2019b
Sisk et al. 2018
Vetsch et al. 2017
Wakefield et al. 2012
Wright et al. 2014

5.5.2 Study characteristics

5.5.2.1 Summary of included studies

Out of the 15 included studies, six were of qualitative (exploratory or content analysis) methodology, three were identified as mixed-methods and six were defined as quantitative. Five studies were funded by academic grants, four were

funded via charities, one did not disclose funding source and five were funded with a mixture of public grants and charity funding. No conflicts of interest were declared by any of the authors and 15 studies provided evidence of ethical approval. All studies were published in peer-reviewed journals and within the last 10 years and reported data from the UK (two), USA (six), Switzerland (one), Norway (two), Canada (one) and Australia and New Zealand (three). All studies used cancer registry data and medical records to provide descriptive statistics on diagnosis, age, treatment etc. Four studies provided control group data for comparison. Nine studies provided or acknowledged that socioeconomic data was collected and/or used for analysis. Five studies used questionnaires to obtain data, seven studies used interviews with survivors, parents and HCPs. Three studies reported using a mixture of interviews and questionnaire data.

All 15 studies reported on the primary outcome, communication or informational needs of CAYA cancer survivors/parents. Studies identified from before 2011 were found to be mainly published by the same research team with updated data. Therefore the most recent study data available was included. Data illustrating the primary and secondary outcomes from the included studies will now be presented using narrative for the primary outcome and a tabular format for the secondary outcome variables. This will be followed by a risk of bias assessment and critical discussion of the findings.

5.5.2.2 Risk of Bias (study level)

The risk of bias assessment for the included studies is reported below. All studies were examined for risk of bias using the appropriate CASP template for

the appropriate study type (CASP 2019).

Table 26 - Risk of bias assessment

Study name	Positive attributes	Negative attributes
Brand, Fasciano, and Mack 2017	Ethical approval acknowledgement No conflicts of interest declared Funding source revealed Detailed methods section	Possible leading research question Methods not justified by evidence The statement of findings was not concise Evidence of sampling and recruitment bias in the study population No follow-up support offered to participants
Cox et al. 2019	Consent method provided Ethical approval details given No conflicts of interest declared by authors Limitations acknowledged such as low response rate (39%) and generalisability for larger populations Sound data collection and synthesis process	No follow-up support offered to participants Ethics by hospital review board of lead researcher institution Declares first study to investigate needs individually, however reports needs results in categories

Study name	Positive attributes	Negative attributes
Crawshaw et al. 2009	Conflicts of interests declared Funding for study declared Underlying methodology justified and explained Low participation rate acknowledged	No evidence of ethical approval Limitations not discussed Risk of bias not discussed No mention of follow up for participants that took part in the study
Gianinazzi et al. 2014	Conflicts of interest declared Ethical approval provided Funding source declared Low response rate acknowledged by authors Risk of bias discussed in detail Validated response scales used Strong inclusion criteria and data analysis methods	Limited data for the comparator group No evidence of follow up or ongoing support for participants Risk of self-selection and small sample bias
Greenzang, Dauti, and Mack 2018	Funding source declared Conflicts of interest declared Incentives for participants declared Methods for data analysis were strong and replicable	Ethical approval related to review board approval from the hospital rather than a formal ethics committee Limited discussion of limitations No justification for methodological choice Authors acknowledged the small sample size, selectiveness, and limited application to the wider population No follow-up support offered to participants

Study name	Positive attributes	Negative attributes
Greenzang et al. 2018	Incentive for participation declared Patient involvement in the design of the questionnaire Medium sized sample Matched control group comparator data Methodological limitations acknowledged Statistical analysis of the data were appropriate and extensive	No justification given for methodological choice The same outcomes were not recorded for both population groups, limiting comparability and transferability of findings There was no mention of follow up or signposting for parents that took part No formal consent procedure disclosed Risk of sampling bias
Hess et al. 2011	Ethical approval given No conflicts of interests declared Limitations of results discussed The authors did consider future research gaps in this area.	Funding source not declared No justification for methodological choice Closed questions used, limiting data collection and analysis Participation bias was possible due to sample selection methods and there was no mention of follow up or referral for participants if distressed

Study name	Positive attributes	Negative attributes
Lee et al. 2019	Limitations acknowledged by authors No conflicts of interest declared Funding source provided Power calculations defined Methodology clear and replicable	No ethical approval mentioned SKQ created for this study and therefore not piloted or validated as a tool Small cross-sectional sample from a single site The sample only included non-CNS cancer survivors, limiting generalisability No follow-up for participants mentioned
Lie et al. 2015	Funding source declared No conflicts of interests declared Ethical approval given Limitations discussed for sample representation A low response rate noted by authors Good ethical considerations for participants and follow-up Clear aims and results	Sample bias due to prior study data showing 66% of the included population were not given late effects information No follow-up support offered to participants

Study name	Positive attributes	Negative attributes
Signorelli et al. 2019b	Ethical approval given COREQ guidelines for qualitative research adhered to Informed consent obtained Funding declared No conflicts of interests declared Interviews piloted Thematic analysis performed using framework Strategies to limit recall bias used Funding declared	Ethics provided by hospital board No mention of who was responsible for transcription and undertaking interviews Sample representative of CAYA cancer survivors engaged in LTFU No follow up for participants
Sisk et al. 2018	Good statistical analysis Limitations for sample size acknowledged Ethical approval given No conflicts of interest declared Funding source provided	No justification for methodological choice No comparator group data collected No follow up for participants Small review of data
Vetsch et al. 2017	Ethical approval given Funding source declared No conflicts of interest declared Good explanation of methods and statistical analysis Methodological limitations acknowledged Small sample size and risk of bias acknowledged	No mention of follow up or referral for participants if distressed after taking part Recall bias risk for parents reporting data Small sample size

Study name	Positive attributes	Negative attributes
Wakefield et al. 2012	Funding source declared No conflicts of interest declared Data analysis methods clear	Ethical approval for the study was detailed as hospital board approval only Data missing from abstract and only found within data tables No justification of methodology or positionality of the researcher No follow up or support mentioned for participants
Wright et al. 2014	Ethical approval given Funding source declared Conflicts of interest declared Link to additional study given Limitations of the data discussed Good evidence of triangulation of data Risk of sample bias noted by authors	Need to access additional paper for sampling and methodological detail No follow-up support offered to participants

5.5.2.3 Primary outcome

Keats et al. (2019) identified in their sample of HCPs, that five out of 6 participants noted a lack of, or insufficient knowledge about paediatric cancer treatments, potential late effects risk and recommended guidelines for surveillance for CAYA cancer survivors. Likewise, Signorelli et al. (2019b) identified that primary care-based HCPs also had unmet information needs regarding survivors' current/future health care outcomes. In particular, HCPs identified unmet informational needs about their patients' risk of developing late effects (94%), their recommended surveillance schedule (77%) and general childhood cancer survivorship information (76%). The unmet informational needs identified by Keats et al. (2019) and Signorelli et al. (2019b) highlight that CAYA cancer survivor and parent unmet informational needs are influenced and might stem from the unmet informational needs of HCPs. A lack of knowledge from HCPs may therefore result in increased levels of survivor and parent unmet informational needs.

Cox et al. (2019) reported a high prevalence of unmet emotional, care/support, and information needs among CAYA cancer survivors with 54% reporting unmet psycho-emotional needs. Concern about the ability to have children was associated with 27/77 unmet needs, however survivors all reported to having some information provided for future fertility outcomes. Vetsch et al. (2017) revealed that unmet informational needs were reported by 85% of CAYA cancer survivors and in 90.2% of parents of a CAYA with cancer, with a late effects informational need of 57.5% and 62.5% respectively. This suggests that the CAYA cancer survivor population have a high rate of unmet informational need

surrounding emotional support and quality of life measurements (a desire to lead a ‘normal’ life). Gianinazzi et al. (2014) also highlighted that information on late effects was generally lacking in survivorship care and required investigation.

Wright et al. (2014) had emphasised that young women survivors were more likely to receive incomplete late effects information, with many female survivors being unaware of their fertility status and no knowledge of from where to obtain this information. Crawshaw et al. (2009) had also alluded to the female/male divide in unmet informational needs by reporting that women are more likely to have higher unmet informational needs and a general lack of comprehension for wider late effects risk information. However, male survivors, who had reported fertility preservation decision making as a straightforward process and reported no unmet informational need for this area, did not associate fertility impairment as a potential side effect of their cancer treatment (Crawshaw et al. 2009). This suggests that there is a gap in the comprehension and understanding of information, which may not align with the perception of unmet informational needs.

Lie et al. (2015) reported that although some CAYA cancer survivors were ambivalent in their desire to receive late effects information, most did think late effects information was essential to know. Ambivalence was also discussed by Greenzang, Dauti and Mack (2018), who demonstrated that parents are sometimes unsure whether they would like to receive more sensitive or distressing types of information about their child’s future. Wright et al. (2014) discovered that young people were often not included in late effects

conversations and that the standard of information and manner of delivery was important to them. Wright et al. (2014) recommended that survivors should receive tailor-made information and honest and open communication between professionals and families. Gianinazzi et al. (2014) supported this recommendation as they reported 44% of participants wanted personalised information on late effects, with 71% rating it as an 'important' unmet need. Furthermore, Vetsch et al. (2017) also recommended a tailored late effects information plan for CAYA cancer survivors as treatment summaries are often not understood and contain too much jargon.

Interestingly, Lee et al. (2019) reported that among the survivors who were identified as increased risk for late effects, the rates of knowledge were lowest for physical issues such as stroke, weaker bones, and lung problems (60%) and were highest for highest for hearing problems, thyroid problems, heart problems, and fertility problems, with >50% of survivors classed as ‘at-risk’ possessing knowledge of these risks. However, Lie et al. (2015) identified that survivors had great difficulty in finding accurate information, with some only being told about late effects as they happened to them. Likewise, Crawshaw et al. (2009) revealed that participants felt there was an assumption by HCPs, that late effects risks (e.g., fertility matters) would be of little importance to the survivor and therefore HCPs avoided discussions about issues such as this. This could lead to a risk of under-reporting of informational need about fertility issues due to it not being raised by HCPs or survivors/parents in survivorship care.

Unmet informational needs were strongly linked with a rise in psychological

distress in the included studies. Cox et al. (2019) reported a high rate of psychological distress and lower quality of life scores in participants with unmet informational needs. Previous to this, Gianinazzi et al. (2014) also reported significantly higher depression scores ($p=0.005$) in CAYA cancer survivors with unmet informational needs than those of an unaffected population. Likewise, Vetsch et al. (2017) reported a link between a higher perceived risk of late effects ($p<0.001$) and a greater risk of anxiety and depression in survivors with unmet informational needs ($p<0.001$). Interestingly, Vetsch et al. (2017) reported a significant association between unmet informational need and being a parent ($p=0.001$).

Greenzang et al. (2018) discovered that parents were found to be less likely to understand future health risks when the child is at substantial risk, or when they consider the risks to be upsetting to the child. Alternatively, if the child is at minimal risk of complications, then parents were more knowledgeable of future risk and were accepting of the receipt of key health information (Greenzang, Dauti, and Mack 2018). Greenzang, Dauti and Mack (2018) reported that although many parents reported being satisfied with the quality and quantity of late effects information given to them, fertility information provision was reported as lacking. Wakefield et al. (2012) previously supported this finding with the discovery that parents of survivors lacked specific information about when and how to test their child's fertility, and about how to communicate with their child about the issue as they matured.

The link between a lack of trust in HCPs and health care avoidance was reported by Signorelli et al. (2019b) who revealed that survivors were reluctant

to access primary health care due to low levels of trust in the HCP. Survivors felt that the HCPs in primary care lacked the necessary breadth and depth of knowledge surrounding CAYA cancers and risk of late effects. The building of a strong relationship with the oncology team, primary care and the CAYA cancer survivor/parent was recommended as a key priority to increasing the level of trust and rapport with the multi-disciplinary clinical team (Signorelli et al. (2019b).

Evidence to support this recommendation was reported by Wakefield et al. (2012) who described instances where parents did not receive a formal treatment completion meeting and felt that there was a lack of general information post-treatment altogether. This finding also corresponds with Vetsch et al. (2017) who reported that survivors felt dissatisfaction with their follow up care ($p=0.003$) and made the association between unmet needs and lower overall health ($p=0.014$).

Overall, informational and communication needs of CAYA cancer survivors, parents and HCPs are reported in all of the included studies. Particular areas of unmet need are identified as psychosocial/emotional and future fertility needs (females more than males). There is evidence to support that CAYA cancer survivors perceive HCPs to lack the necessary knowledge to support and advise them in survivorship, leading to a lack of trust and subsequent health care avoidance in adulthood. The importance of specific informational needs from the perspective of the survivor, parent and HCP appear to be different for each group and would benefit from further investigation surrounding the effect upon unmet informational needs.

5.5.2.4 Secondary outcomes

The secondary outcomes of the review will now be presented using a table format for each included study. The secondary outcomes were defined as; Perspective (CAYA cancer survivor or parent), Professional who communicated the information, age at diagnosis, time since diagnosis, method of communication, and timing of communication.

Table 27 - Outcome synthesis – Secondary outcomes

Brand, Fasciano, and Mack 2017 - Secondary outcomes					
Perspective	**Professional**	**Age (at diagnosis)**	**Time (since diagnosis)**	**Method of communication**	**Timing of information**
Survivor	Health care provider	8.3 - 17.8 years	Not provided	Verbal	Not provided
				Young people wanted prognostic information and wanted to be direct participants in medical conversations. Participants valued open and honest communication	
	Many young people reported seeking information from other sources, including the internet and television			There was certain information they did not want to receive about their health status, and many had made their wishes about this known to their healthcare providers	
				Survivors felt confused or distressed by information from outside sources and wanted critical information provision in the medical setting	

Cox et al. 2016- Secondary outcomes					
Perspective	**Professional**	**Age (at diagnosis)**	**Time (since diagnosis)**	**Method of communication**	**Timing of information**
Survivor	Clinician	0 - 20 years	24- - 42 years	In a way that the survivor feels treated more like a person than a disease, having complaints heard and addressed	A communication style that encourages survivor dialogue and welcomes input can be incredibly useful in beginning, to address many of the unmet needs
				Clinicians should be proactive in asking all survivors about their level of anxiety/worry about cancer-related issues and to what extent multiple psycho-emotional needs are concerning	
				Clinicians should be prepared to refer for help. Open, highly supportive communication is essential	

Crawshaw et al. 2009 - Secondary outcomes					
Perspective	**Professional**	**Age (at diagnosis)**	**Time (since diagnosis)**	**Method of communication**	**Timing of information**
Survivor	Consultant oncologists with limited involvement from nurses	11 - 20 years	1 - 15 years	Strong support for conversations to be directed to patients and not through parents	Strong support for being told at around diagnosis was found regardless of gender, age, incapacity or availability of fertility preservation services.
				Family and HCP support needs to be proportionate to the impact of the future health risk	Participants reported having little choice about timing of fertility discussions

Gianinazzi et al. 2014 - Secondary outcomes					
Perspective	**Professional**	**Age (at diagnosis)**	**Time (since diagnosis)**	**Method of communication**	**Timing of information**
Survivor	Not provided	<21 years (8.9 mean)	>5 years (12.5 mean)	Most survivors received verbal information only (late effects verbal 68%, written 14%) Suggestion for official online resources	Not provided

Gianinazzi et al. 2014 - Secondary outcomes					
Perspective	**Professional**	**Age (at diagnosis)**	**Time (since diagnosis)**	**Method of communication**	**Timing of information**
Control group (non-responder survivor)	Not provided	mean 8.9 years	mean 12.8 years	Not provided	Not provided

Greenzang, Dauti, and Mack 2018 - Secondary outcomes					
Perspective	**Professional**	**Age (at diagnosis)**	**Time (since diagnosis)**	**Method of communication**	**Timing of information**
Parents	Not provided	0.2 - 15.7 years	3.6 - 10.5 months	Many parents satisfied with quality and quantity of information but fertility information lacking	Most parents wanted early and detailed information about their child's risk of late effects to make treatment decisions and to feel prepared for the future
				Parents also spoke of the importance of HCPs asking what they would like to know	7 parents preferred early information regarding late effects

Greenzang et al. 2018 - Secondary outcomes					
Perspective	**Professional**	**Age (at diagnosis)**	**Time (since diagnosis)**	**Method of communication**	**Timing of information**
Parents and physicians	Not provided	0 - 18 years	Diagnosis between 1 and 6 weeks from the date of first contact	Overall, 92% of parents felt it was extremely or very important to receive information with 86% of parents preferred receiving detailed information	Not provided

Hess et al. 2011 - Secondary outcomes					
Perspective	**Professional**	**Age (at diagnosis)**	**Time (since diagnosis)**	**Method of communication**	**Timing of information**
Survivor	Not provided	0 - 18 years	7 - 37 years	The treating paediatric or oncological department, family doctors, Internet/media, other childhood cancer survivors or own experience of health problems 15 patients (12%) confirmed that they had received a written summary, but in most cases, they had specifically asked for this	Not provided

Keats et al. 2019 - Secondary outcomes					
Perspective	**Professional**	**Age (at diagnosis)**	**Time (since diagnosis)**	**Method of communication**	**Timing of information**
Survivor, parent, family practitioner	Family doctor	3 - 15 years	Not provided	Preference for a more detailed follow-up care plan with a comprehensive timeline outlining what tests should be conducted and When	Not provided
				6/10 parents received a written summary 2/6 family practitioner received a treatment summary	
				Most patients prefer hard copy (written) information but would also like electronic- or web-based format—one that could be saved, accessed, and shared as needed.	
				Family practitioners commented that a web-based version would permit rapid and more efficient access to additional guidelines and supportive care resources	

Lee et al. (2019) - Secondary outcomes					
Perspective	**Professional**	**Age (at diagnosis)**	**Time (since diagnosis)**	**Method of communication**	**Timing of information**
Survivors, parents	Not provided (oncologist inferred)	14-21 years (mean 6.75 years, SD = 4.85)	>2years (mean = 9.85 years, SD = 4.35)	Personalised survivorship care plan as standard (written)	Not provided
				Verbal communication via HCP	
				Teach-back recommended as a method for information retention	
				Patient centred approaches recommended	
				Self-management leads to increased knowledge	

Lie et al. 2015 - Secondary outcomes					
Perspective	**Professional**	**Age (at diagnosis)**	**Time (since diagnosis)**	**Method of communication**	**Timing of information**
Survivor	Not provided	0 - 18 years	7 - 37 years	Information should be tailored, carefully timed, given "face-to-face" and in written format	HCPs should provide information through routine follow-ups. All participants agreed that young adulthood, e.g. the age of 25, was the best time to receive extensive information as they felt more mature, had "lived a little" and were more ready to appreciate the importance of the information
				Survivor's risk of late effects should not be trivialised as this could result in distrust in the clinician. Further, information should be given in a sensitive, honest manner, at a time when the survivor is ready for it	
				The clinician should not wait for the survivors to ask questions, but rather pro-actively volunteer the information	

Signorelli et al. 2019b - Secondary outcomes					
Perspective	**Professional**	**Age (at diagnosis)**	**Time (since diagnosis)**	**Method of communication**	**Timing of information**
Survivors, parents, primary health practitioners	Primary care practitioner	<16 years	5 - 41 years	67% HCPs recalled receiving letters from the survivor's treating oncologist about cancer history and current medical needs. 12% HCPs recall receiving a treatment summary or survivorship care plan	Not provided
				Verbal communication from primary health care professional	

Sisk et al. 2018 - Secondary outcomes					
Perspective	**Professional**	**Age (at diagnosis)**	**Time (since diagnosis)**	**Method of communication**	**Timing of information**
Parents	Not provided	3 - 18 years	12 - 39 years	Primary care professionals 'unaware' or have insufficient knowledge	Late effects information very or extremely important at diagnosis (94%), 4 months (91%), and 12 months (96%) Parents prefer to receive late effects information at diagnosis (85%),4 months (87%), and 12 months (83%)

Vetsch et al. 2017 - Secondary outcomes					
Perspective	**Professional**	**Age (at diagnosis)**	**Time (since diagnosis)**	**Method of communication**	**Timing of information**
Survivor and parent (if survivor too young)	Not provided	0 - 18 years	Survivor: 5 - 59 years	17% percent of survivors and 16% of parents received a treatment summary	The difference in information need between survivors

Vetsch et al. 2017 - Secondary outcomes					
Perspective	**Professional**	**Age (at diagnosis)**	**Time (since diagnosis)**	**Method of communication**	**Timing of information**
			Parent: 5 - 18 years	(written) only and 40.1% of survivors and 36.8% of parents received a combined treatment summary/survivorship care plan (written)	(medical) and parents (fertility) suggests a need to revisit discussions

Wakefield et al. 2012 - Secondary outcomes					
Perspective	**Professional**	**Age (at diagnosis)**	**Time (since diagnosis)**	**Method of communication**	**Timing of information**
Survivor, mothers, father, siblings	Treating oncologist, conference, internet, books, other family members, hospital newsletter	7 - 17 years (survivor)	1.9 - 27.7 months	The three most preferred interventions were: information booklet, online support and a question prompt sheet. However, parents rated the booklet highest, while survivors and their siblings gave their highest preference scores to online support	Information might be useful prior to treatment completion, and longer-term concerns might be more important after families have settled back into their normal lives
				Participants wanted more practical suggestions for coping post-treatment, and found disease-specific information lacking	

Wright et al. 2014 - Secondary outcomes					
Perspective	**Professional**	**Age (at diagnosis)**	**Time (since diagnosis)**	**Method of communication**	**Timing of information**
Survivor	Consultant, nurse specialist, or a	12 - 24 years	2 months - 4.5 years	Young women tended to receive incomplete information	Young men reported information

Wright et al. 2014 - Secondary outcomes					
Perspective	**Professional**	**Age (at diagnosis)**	**Time (since diagnosis)**	**Method of communication**	**Timing of information**
	combination of both			Standard 'package' of information about the illness, and the side effects of treatment	shared initially at the time of diagnosis, but continued throughout treatment

5.5.3 Synthesis of findings

5.5.3.1 Thematic analysis

Data from the included studies that could not be tabulated or analysed using statistics or quantitative methods (e.g., descriptive narrative, direct or indirect quotations and personal reflections of CAYA cancer survivors, parents, and HCPs) were synthesised using thematic analysis. Data of this type revealed a deeper insight into the thoughts, feelings, and opinions of CAYA cancer survivors, parents, and HCPs responsible for their care. Thematic analysis based upon the framework by Braun and Clarke (2006) was undertaken in order to fully understand, illustrate and report upon data so that the findings of the review upheld the power, emotion, and importance of the participant views within the studies.

Narrative data were imported to the software programme, *NVivo* (QSR International 2021) to assess data and production of theme categories. Similar thoughts or ideas were then colour coded by the researcher into the following

colour-coded categories.

Table 28 - Theme coding - Systematic review

Colour	Theme
Blue	Timing of information
Red	Type of information
Orange	Fertility
Purple	Medical late effects
Yellow	HCP awareness
Brown	CAYA attitudes to unmet informational need

Data were then explored and expanded into wider draft theme ideas by the researcher.

Table 29 - Draft themes from studies

Partnership
Survivors want to be direct participants in care
Parents need support to give advice
Health care professionals need more awareness
Joint decision making
Advocacy for survivor
Better control of health
Helps to reduce stress, anxiety, and depression
Female survivors tend to have more informational need than male survivors
Parents view vs. survivor view of informational need may be different.
How are risks of treatment communicated between professionals?
Patient's age is associated with the preferred style of patient-provider interaction
Younger patients expect a more consultative style with more shared decision making
Primary care HCPs want better communication with PTC's and more appropriate training

Timing of information
Communication around diagnosis welcomed
Survivors can 'cope' with it
There is a need to revisit and repeat late effects information
Consider parental input - framing of information, what is best?
Communication of risk does not diminish the hope of a cure
Fertility very important and should be discussed right away
Early discussions provide chance to process information

Information delivery
Should be open and honest
Should be responsive and intuitive
Balanced
Individualised
Personalised, continuous, adaptive
Pro-active communication, two-sided
In line with what the survivors think is important to them
Acknowledge difference in parents vs. the patient unmet informational needs
Do not make assumptions
Should be accessible for all
Not too much jargon or too much detail
Regular check-in advised
Consider ambiguity and how to work with this
Socioeconomic status does not impact the level of informational need
Be sensitive and considerate in language

Type of information
Accessible
Different formats
Not too much or too much jargon
Late effects informational needs particularly important

Type of information
Verbal delivery preferred with written back-up
Re-information session at a suitable time
Lay language to be used
Limit internet access to untrustworthy sources
Consider access for all demographics
Is it evidence-based?
Survivorship care plan as a concise method
Online information may be more rapid and easy to access

Source of information
Health care professional (oncologist) most likely
Need to consider the role of nurses
Trustworthiness?
Does it come from the experts? i.e., fertility specialists
Equality in accessibility
Trust in HCP particularly important
Does the HCP have the knowledge?
Verified source important to reduce fears

The draft theme categories were then considered, reviewed and re-focused by using a mind map (Figure 12). This method allowed for an overall consideration and reflection of data and was used to ensure that the theme categories were reflective of all extracted data. The mind map provided a more focused, visual representation of the themes and how they linked together. This process reflected step four and five of the Braun and Clarke (2006) thematic analysis framework (see Chapter Four – Methods).

Figure 12 demonstrates the mind map process, used by the researcher to

visually identify the theme terms and corresponding data used to expand on the concept. The mind-map was particularly useful for the identification of research questions and gaps within the area of late effects communication. These questions or gaps were then taken forward for deeper analysis within the final part of PICCS1 (Semi-structured interviews)

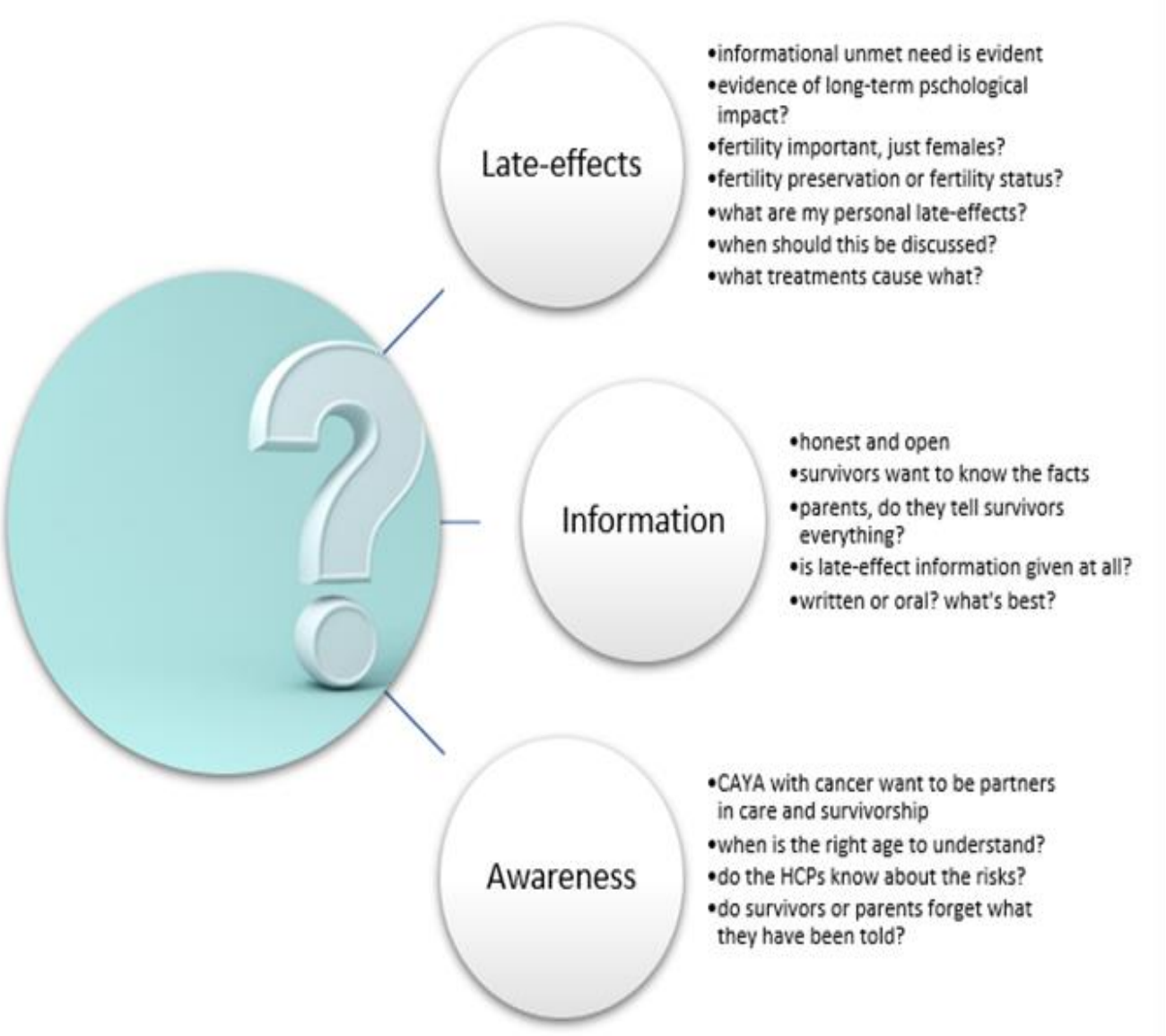

Figure 12 - Mind map - themes from systematic review

Following the creation of the mind map, the final theme selection was made by

the researcher. The researcher and the PPIE representative agreed, upon reflection, that fertility was a key theme from included data and needed an individual category as opposed to being part of the wider late effects' category. The data excerpts reflected that this was a prominent issue for CAYA cancer survivors and their parents, therefore it was added to the final theme list. Likewise, knowledge of the HCP and the influence on unmet informational needs of CAYA cancer survivors/parents and a lack of accurate toxicity data was linked to the long-term distress of CAYA cancer survivors. Therefore toxicity was incorporated within the wider theme of 'Future fertility' and HCP knowledge included into the theme 'Partnership'.

The final themes were agreed by the researcher and the PPIE representative as being representative of the concepts, experiences and unmet needs arising from data of the included studies. An illustration of the theme generation process from colour coding to final theme selection has been illustrated below (Figure 13).

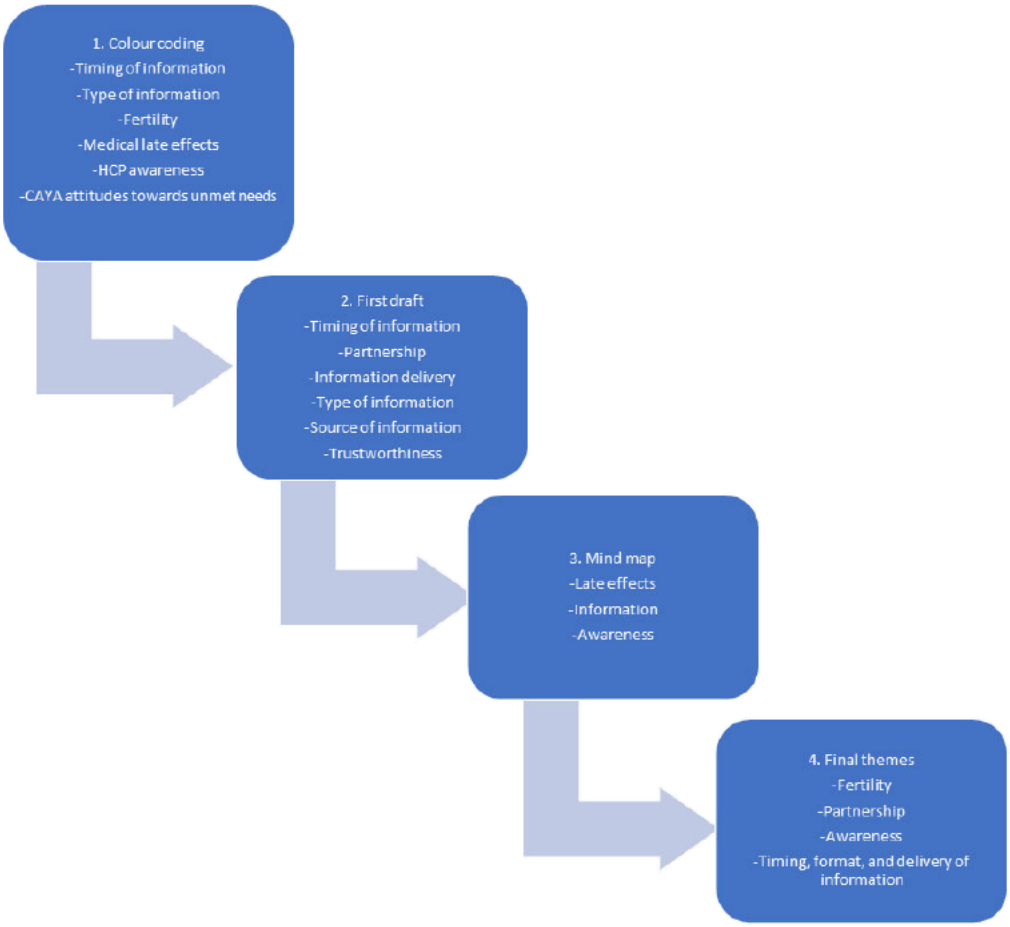

Figure 13 - Theme generation process

The final themes (Table 30) will now be explained, explored and data synthesised in greater detail using a narrative format for discussion.

Table 30 - Final themes – thematic analysis

Final themes
Future fertility
Partnership
Awareness
Timing, format, and delivery of information

5.5.3.2 Future fertility

Cancer treatment, aimed at curing disease, often involves treatments that can threaten future fertility due to their toxic effects on reproductive organs (Vetsch et al. 2017). Literature investigating the late effects of radiotherapy treatment experienced by female CAYA cancer survivors have discovered a high risk of premature ovarian failure and future pregnancy risks linked to damage caused by radiotherapy to the abdominal area by Polanco et al. (2021) and van de Loo et al. (2019). Further conclusive evidence surrounding safe toxicity thresholds of reproductive organs such as the uterus is lacking (Polanco et al. 2021). Irreparable damage to the uterus and ovaries has been suggested to occur at dosages as low as 2 Gray (Gy) (see glossary). However, the long-term implications of treatment delivered to reproductive organs requires urgent further investigation (van de Loo et al. 2019).

Loss of future fertility or ambiguity over personal future fertility status as a result of damage caused by cancer treatments has been reported to be a very important issue for young cancer survivors (Vetsch et al. 2017, Hess et al. 2011, Crawshaw et al. 2009). Crawshaw et al. (2009) reported that HCPs who initiated fertility preservation discussions with CAYA with cancer, lacked the ability to confirm potential success rates of procedures that are still experimental, such as ovarian transposition, ovarian shielding, and ovarian tissue transplantation. This left CAYA cancer survivors with an unknown future, despite them wanting to take proactive measures to protect their fertility from cancer treatments (Crawshaw et al. 2009). Crawshaw et al. (2009) illustrated that this lack of knowledge resulted in an unmet informational need and source

of ongoing ambiguity over potential future childbearing options. An unknown status for future fertility options and a lack of knowledge about long-term damage by HCPs was also highlighted as a key finding by Signorelli et al. (2019b) and Greenzang, Dauti, and Mack (2018).

Wright et al. (2014) reported that many teenage cancer survivors were unaware of their future fertility status, leading to a lack of knowledge about the impact of this issue upon young people and their long-term mental health. Wakefield et al. (2012) reported that fertility was the most common unmet informational need for both CAYA cancer survivors and parents. Vetsch et al. (2017) also suggested that it was not only the CAYA cancer survivor that was affected by this unmet need, as parents also reported future fertility to be one their top unmet informational needs with 62.5% of participants unsure of what information they had received. However, Lee et al. (2019) reported that in their study, CAYA cancer survivors reported fertility to be among the late effects where they possessed a high level of knowledge. This suggests that the generalisation of this claim needs further investigation.

Likewise, Crawshaw et al. (2009) highlighted that male CAYA cancer survivors may not have the same level of future fertility unmet informational needs as females. Female CAYA cancer survivors were reported to have higher levels of fertility informational needs and a need to revisit fertility preservation discussions in more detail than males (Crawshaw et al. 2009). This finding is also consistent with the wider literature suggesting that female CAYA cancer survivors have a higher rate of unmet informational need surrounding future fertility than males (Michel et al. 2021).

Despite evidence to demonstrate that a more detailed discussion about future fertility and damage caused by cancer treatments is needed with families, Wright et al. (2014) found that in their study of 40 interviews with young people with cancer, their parents, and their partners, five of the six younger teenagers, had received fertility information. However, satisfaction with the level of detail and delivery of this information was inconclusive (Wright et al. 2014). Also evidence that some young people were not aware of the possibility that fertility may return, suggests that communication needs to improve (Wright et al. 2014). Crawshaw et al. (2009), despite being an older study than Wright et al. (2014), suggested that the key to addressing future fertility unmet needs of CAYA cancer survivors lies in the investigation of the timing of the communication. Crawshaw et al. (2009) reported that CAYA cancer survivors want to be told about future fertility risk at diagnosis. Reports of assumptions made by HCPs that future fertility outcomes are not of importance to CAYA with cancer at diagnosis, can adversely affect the timing of this and affect the ability for fertility preservation and future childbearing options (Wright et al. 2014). In addition, Crawshaw et al. (2009) reported that CAYA cancer survivors felt that they were very capable at processing and coping with potentially distressing information about their future fertility status if they had an adequate support network of family and a trusted clinical care team.

5.5.3.3 Partnership

An open, honest and active partnership between the HCP, the CAYA cancer survivor, and the parent was described as a key element to the improvement of

CAYA cancer survivorship care in the included studies (Lee et al. 2019, Signorelli et al. 2019b, Greenzang et al. 2018, Brand, Fasciano, and Mack 2017). In a qualitative study of 16 CAYA cancer survivors, Brand, Fasciano, and Mack (2017) reported that survivors wanted to be considered as direct participants in their care and involved in all elements of their future health-care planning. Shared decision making, continuous information provision and an opportunity to revisit key information featured as key recommendations for an improved collaborative model of care (Brand, Fasciano and Mack 2017, Vetsch et al. 2017). Vetsch et al. (2017) highlighted that informational needs may change over time, therefore cannot be measured at one specific time point. This suggests that more research around timepoint for communication of information is needed.

The partnership, or relationship between the parent and the CAYA with cancer has been described as being deeply emotional and complex issue that varies widely across families, geographical areas and cultural groups (Bate et al. 2015). Parents of CAYA cancer survivors have reported a need for help, increased support, advice, and guidance for the communication of late effects risk to their child (Greenzang et al. 2018, Vetsch et al. 2017, Wright et al. 2014). Crawshaw et al. (2019) in their study of 38 CAYA cancer survivors, discovered that CAYA cancer survivors wanted conversations about late effects risk to be directed at them rather than their parents, echoing previous findings by Hess et al. (2011). Likewise, Brand, Fasciano, and Mack (2017) reported that some CAYA cancer survivors may choose to not receive certain information about their health status and may have made their wishes about this known to their

healthcare providers or parents beforehand. Therefore, asking the CAYA about their information preferences is recommended for both the parent and the HCP. The Teenage Cancer Trust also advocates the involvement of the CAYA with cancer in the conversation (if deemed medically and age appropriate) (Teenage Cancer Trust 2019). They recommended that transition of care to adult services should be improved, more should be done to collect evidence on patient experiences for under 16's and that post-treatment care for children and young people should be delivered more appropriately (Teenage Cancer Trust 2019).

Difficulties in the communication of information between the HCP and the parent, resulting in inadequate or incorrect information being given to the CAYA cancer survivor, was reported by Vetsch et al. (2017). This concept of 'miscommunication' or filtering of important health information had previously been alluded to by Clarke, Sheppard and Eiser (2008), who reported a trend of 'information shielding' by parents of retinoblastoma survivors. Clarke, Sheppard and Eiser (2008) reported that this reflected a protective mechanism by the parents, with the aim to reduce distress, anxiety and fear in the child or young person.

Greenzang, Dauti, and Mack (2018) similarly described this concept of information shielding by reporting that parents who perceived their child's risk of long-term problems to be low, were able to accurately process and remember future health information given to them by the HCP. However, for those parents that perceived their child to be at a high risk of future late effects, they reported unmet informational needs of survivors and parents, suggestive of not being able to remember key information they had been told at the time, or that the

parents found it too distressing to talk about with their child (Greenzang, Dauti, and Mack 2018). Greenzang et al. (2018) also warned that this practice of information filtering by the parent or of the HCP may result in an increased level of unmet informational need and lack of awareness of the CAYA cancer survivor, increasing their risk of long-term future health complications.

Wright et al. (2014) also reported 'filtering' of information by parents with one report from a young male stating that that, due to his age his parents withheld fertility information to avoid causing additional distress. He reported that he was satisfied with this, however, he felt uncomfortable at being excluded from the conversation and embarrassed that he later had to discuss fertility with his parent. These findings suggest that conversations surrounding sensitive topics should be undertaken on a case-by-case basis and that HCPs and parents should be considerate to individual needs at that time.

5.5.3.4 Awareness

Awareness of late effects and future health risks relates to the awareness of the CAYA cancer survivor/parent and the HCP. The included studies in the review, all reported a lack of knowledge and understanding about individual risk of late effects. In particular there was a lack of knowledge reported about future reproductive health outcomes, especially for female CAYA cancer survivors (Lee et al. 2019, Brand, Fasciano, and Mack 2017, Vetsch et al. 2017, Lie et al. 2015).

Lee et al. (2019) in a cohort study of 73 adolescent and young adult survivors

aged 14–21 years old from the USA, reported that survivors demonstrated poor awareness and knowledge of their unique risks for treatment-related late effects, with a mean accurate knowledge score of 54.29%. Survivors who were at elevated risk for a number of late effects were also found to possess less knowledge of late effects than those at minimal risk of complications. When applied to future fertility late effects, 28 out of 60 participants defined as at-risk were unaware of their elevated risk or believed that they were at minimal risk of complications (46.67%).

Gianinazzi et al. (2014) recommended that by improving the method of communication for late effects information, this might help to empower CAYA cancer survivors and provide them with a feeling of control over their long-term health outcomes. This improved feeling of control can be related to a better understanding what they are physically and psychologically capable of following treatment and how they can make adaptations to their lifestyle and behaviours to ensure that they remain healthy in the long-term (Gianinazzi et al. 2014). Improved awareness of late effects risk was also linked to a greater ability to self-manage future health outcomes by Lie et al. (2015). Lie et al. (2015) proposed that a re-information session for CAYA cancer survivors around the age of 25 years would help to increase awareness of future health risks and would help to promote healthy lifestyle behaviours of CAYA cancer survivors.

Parents were reported to want information on actionable late effects, so that they could encourage healthy lifestyle or behavioural modifications for their child (Lee et al. 2019). Greenzang, Dauti, and Mack (2018) and Sisk et al. (2018) agreed with this findings and reported that parents of CAYA cancer survivors wanted more knowledge of actions they could take to help reduce late effects risks for their child. This suggests that there is a desire to know about and take action to mitigate the risk of future health complications. Greenzang et al. (2018) stated that CAYA cancer survivors and their parents should be provided with an opportunity to plan for, and to make lifestyle adaptations based on accurate evidence, that might help to lower their risk of future health complications. This view was also shared by Wakefield et al. (2012).

Awareness of the CAYA cancer survivor about their individual risks of future health complications was discussed in a Delphi study by Zebrack et al. (2004). The recruited a multi-professional stakeholder group to explore how to improve CAYA cancer survivor care services. They recommended the use of self-advocacy training for survivors and advanced training for primary care physicians who may treat childhood cancer survivors as they transition into adulthood as a method to increase awareness and reduce adverse long-term health outcomes. A lack of awareness about the risk of late effects has been strongly linked to an increased level of psychological distress in CAYA cancer survivors (Cox et al. 2019). Vetsch et al. (2017), Lie et al. (2015), Gianinazzi et al. (2014) and Hess et al. (2011) all suggested that unmet informational needs hold a greater and more extensive impact upon the long-term psychological outcomes of CAYA cancer survivors and requires further investigation.

Vetsch et al. (2017) and Gianinazzi et al. (2014) causally linked increased anxiety and depression levels of CAYA cancer survivors with unmet informational needs. Crawshaw et al. (2009), the first of the included studies to examine this relationship, revealed that female CAYA cancer survivors with high levels of unmet informational need have higher psychological distress levels than their male counterparts. Male CAYA cancer survivors, in comparison were reported to be generally happy with their level of late effects information, (Crawshaw et al. 2009). Likewise, Lie et al. (2015) reported that male CAYA cancer survivors were more satisfied with the information they were given by HCP and less likely to have long-term distress related to unmet informational need than females (Lie et al. 2015).

However, Wright et al. (2014) highlighted that although male CAYA cancer survivors may be happy with their level of information, they remain unaware of the permanence of late effects such as infertility. Wright et al. (2014) reported that an assumption of infertility can lead to unwanted pregnancies and a higher rate of sexually transmitted infections. This suggests that awareness of future late effects and knowledge surrounding what may happen in the long-term future needs to be reinforced at a later time point, to ensure that survivors have the full clinical picture and avoid unnecessary surprises (Wright et al. 2014).

Wakefield et al. (2012) proposed a two-way, awareness model to improve the way that risk of late effects was communicated to families. They detailed that the model of awareness must be adaptive and responsive to individual patient need, reflective of the NICE (2005) guidelines (Wakefield et al. 2012). A caveat to this model, however, is the need to ensure delivery of information at the right

time for the CAYA cancer survivor and/or their parents. This point is also echoed by Sisk et al. (2018) who recommended that the timing of the communication is an important factor to successfully addressing unmet informational need of CAYA cancer survivors. More recently, Baenzinger et al. 2020 showed the use of a 'model of trust', used to empower CAYA cancer survivors and HCPs to collaborate and build trust in communication of information and would be recommended for any future service re-design for this patient group. Vetsch et al. (2017) and Gianinazzi et al. (2014) suggested that CAYA cancer survivorship services must be improved to include a strategy for improving awareness of HCPs, from both the paediatric oncology and primary health care settings to the individual and changing needs of CAYA cancer survivors, including the subtle differences between male and female priorities (Vetsch et al. 2017).

5.5.3.5 Timing, format, and delivery of information

The format, timing of, and method of delivery for late-effects information was a secondary outcome of the review but was rarely reported within the included studies. Timing of information was not reported by the majority of included studies. Lie et al. (2015) reported that CAYA cancer survivors and parents welcomed late effects risk information right from the time of the initial diagnosis. Crawshaw et al. (2009) highlighted that there is an assumption by HCPs in some circumstances, that a CAYA with cancer would not want to hear this type of information at diagnosis. Greenzang, Dauti, and Mack (2018) suggested that some HCPs perceived that the discussion of issues such as future fertility might

induce stress or affect the belief of hope for a cure from their cancer. However, this assumption was refuted by Lie et al. (2015). Greenzang, Dauti, and Mack (2018) also argued that parents of CAYA cancer survivors found late effects information to be very or extremely important during the first year following diagnosis.

Keats et al. (2019) reflected a preference of participants for a detailed follow-up care plan with a comprehensive timeline outlining what tests should be conducted and when. Parents/guardians also wanted an ongoing communication model that considered new research and could be provided to the survivor at regular intervals. Sisk et al. (2018), in their questionnaire-based report of study data from 382 parents of CAYA with cancer; reported that at diagnosis was the most preferable time point for the provision of late effects information (94%). They also reported that late effects information should be reinforced at specific time points such as four months post treatment (91%) and again at 12 months post treatment (96%). Parents in the study reported to prefer late effects information at diagnosis (85%).

Hess et al. (2011) previously reported a preference for communication of late effects information at sequential time points within the entire cancer journey and reported that in their cohort, the majority of CAYA with cancer had been told about fertility impairment caused by treatments at diagnosis. Wright et al. (2014) had also reported that the format for delivery of late effects risk information, including the extent/detail of this information varied widely among participant's experiences. They also highlighted the contrasting views of male and female survivors and the level of satisfaction with receiving late-effects information.

Males appeared to be more satisfied with the level of information, content, and approach to future fertility late effects information (Wright et al. 2014). However, one female participant reported that she felt the fertility information she received was insufficient and conveyed in an insensitive manner (Wright et al 2014). This finding suggests that more research needed to ascertain how information should be communicated, in what format, and when.

Furthermore, Lie et al. (2015) recommended that future research needs to consider the comprehension and retention level of the CAYA cancer survivor and/or their parent following communication of late effects information. This would include an analysis of how information can be processed, understood, and then recalled with accuracy, long-term (Lie et al. 2015).

Studies that reported data for format of communication reflected that CAYA cancer survivors in the majority received verbal information with some receiving a form of a survivorship care plan. CAYA cancer survivors reported that this standard approach (verbal information) with a back-up option (written advice sheet) is most preferable (Signorelli et al. 2019b, Gianinazzi et al. 2014). This method allowed them to refer back and re-consider the information at a later date, when they felt ready (Signorelli et al. 2019b, Gianinazzi et al. 2014). Online sources of future health information were perceived with a sense of fear and a source of anxiety for CAYA cancer survivors in the study by Wakefield et al. (2012). They reported that survivors felt they could not trust the accuracy of information online and preferred the traditional verbal/written format (Wakefield et al. 2012). An important note for HCPs was also illustrated by Vetsch et al. (2017) who revealed that in many cases, information resources about late

effects risk contained too much jargon and was not easily accessible for all. HCPs were encouraged to appraise information for understandability and comprehension.

The role of the HCP that communicates late effects information to CAYA cancer survivors and their parents was in the majority, the Paediatric Oncologist (Crawshaw et al. 2009, Wakefield et al. 2012). Wright et al. (2014) suggested that nurses, advanced HCPs, and other supporting professional roles hold a key influence in the effective delivery of late effects information and that further exploration surrounding the role of the HCP that communicates late effects information would be recommended (Wright et al. 2014). Sisk et al. (2018) suggested that in order to address unmet needs of CAYA cancer survivors, more research into the method of communication, an assessment of parental learning style and method of delivering information and when to revisit this with families is needed.

Lie et al. (2015) explored the method of delivering information and resulting unmet informational needs and emphasised that if information is communicated in a blunt and impersonal manner, it can be hurtful and cause unnecessary worry to both the survivor and parent. If the information is communicated too soft, or downplayed, the survivor might not remember it or appreciate the relevance/importance of it for their future health outcomes (Lie et al. 2015). Likewise, downplaying or trivialising the risk of late effects was found to result in a lack of trust in the information provider (HCP) (Lie et al. 2015).

5.5.3.6 Summary of themes

The themes from the 15 included studies in the review have provided an insight into the CAYA cancer survivor, parent, and HCP perspectives. The tabulated findings and the themes have highlighted areas in the research that would benefit from further exploration, such as defining future fertility status. A need for an open, active, and ongoing partnership between the CAYA cancer survivor, their parents and the HCP is needed to facilitate conversations around sensitive subjects. An improved education and awareness of HCPs about late effects risk of CAYA cancer survivors (particularly those related to future fertility and reproductive health) is also needed including further investigation into the appropriate timing, method, and detail of late effects information is also recommended with the consideration of psychological well-being alongside physical health surveillance.

A risk of bias assessment at the review level will now follow, with a critical discussion of the overall findings from the review and relevant application to clinical practice.

5.6 Risk of bias across studies

The following assessment for risk of bias at the review level (across studies) was performed using the CASP tool applicable to the study design. The following categories will now be considered and explored:

5.6.1 Selection bias

Many of the participants recruited into the included studies represented CAYA cancer survivors that would normally be actively engaged with follow-up services. Only one of the included studies used data from a comparator group that did not attend for follow-up care as standard (Gianinazzi et al. 2014). The purposeful selection of participants increases the risk of bias as conclusions cannot be drawn against a comparable control group. However, it is accepted that to recruit from a population that does not access services, and may not want to be contacted, would be extremely difficult and may cause unwanted distress to the survivor.

5.6.2 Reporting bias

The reporting of outcomes in the studies were not found within the main body of the text. This can be seen commonly in research publications featuring self-reported outcome data or when using data registry data. Where apparent, this was acknowledged by the authors in the limitations section of the study findings.

5.6.3 Methodological bias

The studies varied widely in their methodological approach and methods. The justification of methods by the authors of the included studies was not reported in 14/15 of the included studies. It is not possible to assess methodological bias between studies of this kind due to the heterogeneity between and within the design, data collection and synthesis methods used.

5.7 Additional analyses

There were no further additional sub-group or statistical analyses performed in the review.

5.8 Discussion

5.8.1 Summary of evidence

The primary outcome for the systematic review was to appraise and collate experience of communication of late effects information to CAYA cancer survivors. The review demonstrated that late effects, and in particular, future fertility outcomes had the most unmet informational needs (Greenzang et al. 2018, Greenzang, Dauti, and Mack 2018, Sisk et al. 2018, Vetsch et al. 2017, Lie et al. 2015, Wright et al. 2014, Wakefield et al. 2012, Crawshaw et al. 2009). Lack of knowledge about individual fertility status was correlated with a higher rate of long-term psychological distress for CAYA cancer survivors (Greenzang et al. 2018, Sisk et al. 2018, Vetsch et al. 2017) Greenzang et al. (2018) highlighted the need to assess the priority of unmet informational needs from the point of view of the HCPs, the parents and the CAYA cancer survivor as there may be differences or assumptions which can affect the level of unmet need and when information should be communicated.

5.8.2 Themes – implications for clinical practice

A discussion of the identified themes included studies, and wider literature in the context of possible implications of the findings for clinical care will now be presented. Theme sub-headings will be used to divide the categories.

5.8.3 Future fertility

The systematic review findings revealed that late effects information, and in particular future fertility status, carried the highest level of unmet informational need for female CAYA cancer survivors and their parents. Comparable data was limited in the included studies, due to the studies not using matched control groups for analysis and many studies not being specific to the UK population or health care system. A strong link between future fertility unmet informational needs and long-term psychological distress was found and warrants acknowledgement and further investigation. Likewise, the timing of discussions surrounding fertility preservation, including an adequate level of counselling for the CAYA with cancer and their parents is needed in CAYA cancer survivorship care. This will assist in the management of future childbearing expectations, using the use of the most up-to-date evidence and provides an opportunity for proactive self-management of long-term health.

There is a depth of evidence reporting sub-optimal future reproductive health outcomes of female CAYA cancer survivors (Polanco et al. 2021, van de Loo et al. 2019, Reulen et al. 2017, Anderson et al. 2015). However, strategies outlining the optimal communication of this information to CAYA cancer survivors and their parents, reflective of an individualised risk basis are rarely reported within the literature. To enable effective communication of the most up-to-date evidence, more research is needed to investigate safe toxicity levels of treatments (van der Loo et al. 2019). Direct irradiation of the ovaries during radiotherapy treatments is known to induce premature ovarian failure in up to 90 per cent of female CAYA cancer survivors (Kim et al. 2018). However, there is a

lack of data for safe toxicity levels of the uterus and associated long-term consequences of treatments for female CAYA cancer survivors (Reulen et al. 2017). Likewise, the causational relationship between permanent radiotherapy damage and the age of the child at the time of treatment is under-researched (Van der Loo et al. 2019).

The future reproductive health risks of female CAYA cancer survivors have been reported to include an increased risk of premature labour and birth, a higher risk of a small for gestational age baby, and a higher risk of miscarriage following pelvic-abdominal radiotherapy as a child or adolescent (Polanco et al. 2021, van der Kooi et al. 2019). This increased risk during pregnancy and birth also carries economic ramifications for health care services such as the NHS. The NHS identified premature birth and miscarriage as key priority areas for immediate improvement within UK health care services (Tommy's 2018). To achieve this target, adequate identification of and early risk-stratification of populations at risk of adverse outcomes is needed. Despite the evidence to support that female CAYA cancer survivors are an at-risk population; they are omitted from the at-risk criteria by health regulatory authorities (e.g., NICE) during risk assessment for pregnancy and childbirth (Polanco et al. 2021). Without acknowledgement of all at-risk patient groups, the long-term health of women and babies cannot be addressed effectively and have a maximum impact upon reducing adverse outcomes.

However, the CAYA cancer survivor population has been reported to be a complex, multi-factorial, and evolving population (Otth et al. 2021). This makes service redevelopment to suit all patients a difficult challenge (Signorelli et al.

2019a). However, by acknowledging the limited evidence, sharing of communication models for late effects and by increasing the awareness of the risks and challenges that CAYA cancer survivors face after treatment, it provides a starting point for improvement. This level of transparency for the communication of future health risks aligns with the professional responsibility of HCPs to communicate all known future health risks, referred to by the Nursing and Midwifery Council (NMC) as 'duty of candour' (NMC 2015). This is further defined as the need to explain fully to the patient…the short and long-term effects of what has happened to them (NMC 2015). This level of communication should form a set of minimum expectations for HCPs working in CAYA cancer survivorship care.

Despite future fertility status and associated reproductive health outcomes being reported as an unmet informational need by CAYA cancer survivors and parents over the last ten years (Cox et al. 2019, Vetsch et al. 2017, Cox et al. 2016, Lie et al. 2015, Wright et al. 2014, Reulen et al. 2009), the issue has still not been addressed adequately (Hendriks, Harju, and Michel 2021). This suggests that unmet needs for future fertility and reproductive health outcomes is still an area noteworthy of further investigation.

5.8.4 Partnership

Partnership, or a collective effort to optimise the long-term health outcomes of the CAYA with cancer, necessitates a joint approach by the CAYA with cancer or survivor, parent, and HCP (Hendriks, Harju, and Michel 2021). Brinkman et al. (2018) suggested that an open two-way communication system between

HCPs and CAYA cancer survivors/ their parents would help to optimise the standard of information given to families. Vetsch et al. (2017) suggested that by improving the method of communication for late effects, this could in turn result in the adoption of healthier lifestyle choices or behaviours due to an increased awareness of future health risks (e.g., a reduction in smoking/alcohol consumption due to being more aware of the considerable risk of future disease).

Supported self-management of long-term health features as part of the NHS Long Term Plan (NHS England 2019a). The NHS has committed to the adoption of personalised care for patients as standard across the health and care system. There is a focus on proactive awareness, knowledge, improved skills, and confidence of HCPs to provide patients with the tools to manage their own health (NHS England 2019a). HCPs are encouraged to tailor their approach to patient care and consider a person's individual needs and preferences, as well as acknowledging any inequalities and accessibility barriers. This way of working aims to provide a health care service that focuses on what matters to the individual (NHS England 2019a).

Collaborative and multi-disciplinary working between the CAYA cancer survivor, the parents and the HCPs to address unmet informational need was also described as the optimal model for survivorship care by Smith, Link, and Effinger (2020). There have been examples of projects that have attempted to improve collaborative working with limited success such as the National Cancer Survivorship Initiative (NCSI) by NHS England and Macmillan Cancer Support (NCSI 2013). The NCSI aimed to ensure that those living with and beyond

cancer, could receive the level of care and support they needed. The NCSI promoted the adoption of a healthy and active life, armed with the information survivors need to make healthy lifestyle choices and manage their own health needs (NCSI 2013). This initiative aligns with recommendations from the included studies in the review (Cox et al. 2019, Signorelli et al. 2019b, Greenzang, Dauti, and Mack 2018 and Brand, Fasciano, and Mack 2017). However, the included studies were published after the launch of the initiative, which suggests that it was not successful in addressing the need for an improved model for collaborative working in CAYA cancer survivorship care.

On a European level, PANCARE (a European collective organisation of HCPs and patient representatives producing evidence-based research and guidelines for the long-term care of CAYA cancer survivors) have several working groups tasked with collating published evidence and producing guidelines for the clinical care of CAYA cancer survivors (PANCARE 2021). Salchow et al. (2020) published their protocol for a 'CARE for CAYA-Program' designed to use a needs-based intervention to improve long-term outcomes of CAYA with cancer. However, the findings have yet to be published, which still leaves the current evidence base for CAYA cancer survivorship care improvement strategies sparse.

In conclusion, a better understanding of parent and patient-reported barriers to the communication of future health risks is needed (Signorelli et al. 2019a). Findings from Smith, Link, and Effinger (2020), Wright et al. (2014) and Crawshaw et al. (2009) all support the use of a collaborative, triadic shared-decision making model that promotes communication of information between

the parent, the CAYA cancer survivor and the HCP.

5.8.5 Awareness

Knowledge and awareness have been conceptualised as necessary building blocks in the promotion of self-management of health outcomes (Reed-Knight, Blount, and Gilleland 2014). The findings of the systematic review revealed that there is a lack of awareness by CAYA cancer survivors, parents, and HCPs about individual risk of late effects (Lee et al. 2019, Keats et al. 2019, Signorelli et al. 2019b). HCPs were also found to be lacking in awareness of potential adverse long-term fertility and reproductive outcomes (Signorelli et al. 2019b, Sisk et al. 2018, Vetsch et al. 2017, Wakefield et al. 2012). This finding demonstrates a gap in the knowledge and understanding of future health risks that could attributed to a number of factors including poor information retention skills or poor communication of risk during treatment and would benefit from further research.

Investigation surrounding what type of late effects information is most important to CAYA cancer survivors, their parents and HCPs is unclear in the findings of the review (Sisk et al. 2018, Signorelli et al. 2019b). Furthermore, Lee et al. (2019) demonstrated the assumption of several researchers and HCPs, that measurable late effects are only physical with the use of The Survivor Knowledge Questionnaire that measured 11 late effects, none of which were psychological (Lee et al. 2019). This is despite strong evidence to support adverse psychological outcomes of CAYA cancer survivors as a late effect of treatments (Michel et al. 2020).

Therefore, HCPs should be encouraged to gain a more in-depth awareness of both physical and psychological late effects, designing a CAYA cancer survivorship service based upon the needs and preferences of their patients (Haupt et al. 2018). Smith, Link, and Effinger (2020) also suggested that increased involvement and awareness of the wider multi-disciplinary team, such as primary health care professionals, should also feature as a key factor in the development of an optimal survivorship care model.

Lee et al. (2019) demonstrated how a lack of HCP awareness can impact upon the survivorship care and communication of late effects. An example of a HCP in primary care reported the quote “If he’s not complaining of anything I’m confident that there’s nothing wrong”. This supports previous findings from CAYA cancer survivors that late effects were sometimes only addressed once they had arisen. Also, when HCPs were asked if they believed a survivors’ risk of developing late effects increased or decreased with age, 14% of primary health care professionals believed it decreased with time. This contradicts the data showing an increase in morbidity and mortality with age for CAYA cancer survivors (CRUK 2021a).

5.8.6 Timing, format, and delivery of information

The review findings highlighted that research into the timing of communication for late effects information was rarely reported as a measurable outcome with 50% of the studies not reporting any detailed data. A recommendation for the ongoing needs assessment and possible re-information for families was suggested by Lie et al. (2015), however only Sisk et al. (2018) provided any

measurable data about the timing of information and survivor/parent preferences.

Wright et al. (2014) reported in their cohort study of teenage cancer survivors based in the UK, that late effects information should be delivered openly, honestly and HCPs should adopt an intuitive and responsive approach that reflects survivors needs. This transparent approach to the communication of future health information was also supported by Brand, Fasciano, and Mack (2017) and Greenzang et al. (2018) who recommended the use of a communication model that was understandable for families.

A barrier to the ongoing communication of late effects risks between CAYA cancer survivors and HCPs has been reported to be linked to a poor experience during the transition of care between paediatric and adult health care services (Smith, Link, and Effinger 2020). Otth et al. (2021) previously identified the transition of care between the paediatric and adult services to be complex and challenging for both HCPs and CAYA cancer survivors. Challenges in the successful transition of care have been reported to include inequality of access to services, poor service engagement and complex individualised care plans that do not fit within the constraints of the adult health care service infrastructure (Otth et al. 2021).

Keats et al. (2019) and Wright et al. (2014) suggested that a gradual and risk-based approach for the transition of care from paediatric oncology to adult services should be implemented. This approach has also been recommended in more recent literature by Smith, Link, and Effinger (2020) who recommended a flexible approach to the transition of care, with the ability to revisit and revise

plans as necessary to meet the changing needs of the CAYA cancer survivor.

In regard to the format for communication of late effects, the widely used format for verbal consultation followed by written summary was the most popular choice for CAYA cancer survivors, parents and HCPs (Greenzang et al. 2018, Sisk et al. 2018, Wright et al. 2014, Hess et al. 2011). However, the increased use of online platforms for communication highlights the need to explore alternative methods of communication. Also, how psychological late effects of treatment can be included into late effects discussions and written treatment summaries. As Sisk et al. (2021) stated in their systematic review, many studies addressed communication of prognosis, diagnosis, treatment, and toxicity, yet only a small number focused on communication needs or psychological needs related to survivorship and late effects.

Crawshaw et al. (2009) highlighted an important consideration with strong support for conversations to be directed at the patients and not through parents. Mulder (2021) also recommended further research into communication preferences of the survivor and whether it should be done with/without the parent. Newton et al. (2021) who investigated the barriers to CAYA cancer survivor communication from the nurse's point of view, also highlighted this as an area for further research as they reported that the parents' constant physical presence during conversations can sometimes act as an obstacle to open communication.

In conclusion, a survivorship care service that addresses the physiological, psychological and educational needs of CAYA cancer survivors has been recommended in the literature since 2010 (Henderson, Friedman, and

Meadows 2010). The need for an improved survivorship care service was later highlighted by Haupt et al. (2018) in their recommendations for the care of CAYA cancer survivors and again by Smith, Link, and Effinger (2020). This demonstrates that the issue has not been addressed adequately and that a responsive, patient-led survivorship care service for CAYA with cancer is still needed.

5.9 Limitations

Acknowledgement of limitations to the research study and findings are important for the transparency of the methodological process, contextualisation of the findings, and to provide a replicable format for other researchers.

This systematic review was conducted according to CRD guidance for systematic reviews (CRD 2009) and in accordance with PRISMA reporting checklist (Moher, Liberati and Tetzlaff 2009). The PRISMA reporting flow chart was used and a recognised risk of bias tool (CASP 2019) used for appraisal of included studies. The new PRISMA guidelines were published after the review had been completed and therefore were not used to report the findings or guide the design of the review (Page et al. 2021).

5.9.1 Reliability of the evidence

The included studies in the review were a mixture of quantitative, mixed-methods and exploratory qualitative studies. The applicability and quality of the evidence may be criticised by some researchers due to the heterogeneity of the

study methods. However, the researcher emphasises that this review asked, ‘what happens now and what is missing?’ rather than ‘what’s the best method of filling a gap?’. Therefore, a quantitative methodological design for included studies would not have been a suitable choice but they researcher acknowledges a limitation of high-level evidence and comparable evidence in this field. There is also an acknowledgement that the 15 included studies contain self-reported or in some cases missing data. Difficulties in the accurate documentation of treatments, dosage, and diagnosis history for CAYA cancer survivors treated up to 40 years ago has been acknowledged by authors of previous epidemiological studies using this cohort (Reulen et al. 2017).

The review has provided an extensive and rigorous appraisal of current evidence for the communication of late effects from the CAYA cancer survivor, parent, and HCP perspectives to answer the research question.

The qualitative data from the included studies, can be subject to bias at the study level and across studies, affecting the validity and translatability of the findings to the wider population (Chow et al. 2016). Chow et al. (2016) also highlighted that studies dependent on self-reported data might lack accuracy and translatability due to missing data and recall bias of participants.

Methodological choices for the review were reflected upon and discussed together with the research supervisory team and PPIE representative in this review. Consideration of alternative methods also featured in the design of the review and have been discussed by the researcher. Outcome measures selected in a review aim to collect a wide range of data that is filtered down to report on selected outcomes. The focus of physical late effects of cancer

treatments in many survivorship studies reflects an example of outcome selection and reporting bias. The researcher does acknowledge, however, a risk of bias in the design and selection of topic for the review due to the epistemological standpoint and professional/personal background of the main researcher (adoption of a critical realist standpoint and being a parent of a female child that had cancer).

5.9.2 Applicability to clinical practice

A notable limitation to the findings of this review is the rapidly changing medical and scientific advancements in CAYA cancer treatments and survival rates. For example, Intensity-modulated radiotherapy (IMRT) and Proton beam radiotherapy are now part of standard care and will impact upon the long-term outcomes and risk of late effects for CAYA cancer survivors in the future (The Christie NHS Trust 2021) Van de Loo et al. (2019) reported that there may also be unknown late effect risks for newer chemotherapy agents and immunotherapy treatments. Mulder et al. (2021) agreed that future research should consider the risk of late effects from newer chemotherapeutic agents and should also consider genetic risk factors.

Data included in this review is retrospective, and therefore not representative of current innovative treatments. Long-term outcomes of current CAYA cancer survivors treated in the last 10 years, will not be represented in the findings of this review and data will not be able to be measured for another 20-30 years. Although clinical application of the review findings is limited the need to conduct further research in this area is clear. The increasing CAYA cancer survivor

population within the UK (35,000 per year) and the link between unmet informational need and adverse physiological and psychological outcomes of CAYA cancer survivors requires more in-depth investigation.

5.10 Conclusion

The systematic review has appraised and presented the published evidence for the unmet communication and information needs of CAYA cancer survivors and parents. Unmet late effects informational need, in particular future fertility risks for female CAYA cancer survivors was revealed as a major area of unmet need with long-term psychological distress reported as a result. A lack of awareness of HCPs about long-term fertility and reproductive health risks from cancer treatments and the associated lack of evidence for this outcome, further illustrates a need for more research in this area.

The method of communication for future health risks, the timing of the communication, and the HCP responsible for communicating the late effects information, have been reported as important variables to addressing the unmet informational needs of survivors and families. CAYA cancer survivors and parents have requested an improved ‘collaborative’ approach to survivorship care with accurate data, consideration of non-physical late effects and more communication between HCPs from paediatric oncology, adult survivorship services and primary care. Likewise, CAYA cancer survivorship services and commissioners need to be aware of and acknowledge the high rate of morbidity and mortality of CAYA cancer survivors to ensure that services adequately meet life-long patient needs.

An improved level of awareness for late effects risk, including future fertility outcomes was recommended for both HCPs (including primary care) and CAYA cancer survivors, including their parents. This would encourage the development of a self-management approach to the survivorship care model of care. CAYA cancer survivors and parents would be given the opportunity to take an active lead and responsibility for their ongoing health needs and vocalise their unmet needs, such as late effect risks. This approach is advocated by health care commissioners (NICE) and the NHS Long Term Plan (NHS England 2019a).

In conclusion, communication of late effect risks, namely future fertility risks of female CAYA cancer survivors, were reported to be one of the largest unmet informational needs. There is a lack of evidence surrounding what information should be communicated, in what environment, by whom (which HCP), and when. These are key areas that require further research. Equally, an investigation into the perception of need from the point of view of the CAYA cancer survivor, the HCP and the parent, would benefit from further exploration to explore potential misconceptions of unmet informational needs.

5.10.1 Next steps

Following this review, the findings from the second part of PICCS1 (online questionnaires) will be presented, exploring the real-life experiences of CAYA cancer survivors, HCPs, and parents in the communication of late effects information in the UK. The online questionnaires and subsequent semi-structured interviews will utilise a multi-methods approach creating a

comprehensive and robust representation of what currently happens in the UK with regards to communication of late effects information for CAYA cancer survivors and their families. Published evidence from the systematic review and the findings from the online questionnaires and interviews will then be triangulated and presented prior to the findings from PICCS2 (modified Delphi technique).

Chapter Six – Findings

This chapter presents the findings from the remaining elements of PICCS1 (online questionnaires and semi-structured interviews) and will be followed by the presentation of the findings from PICCS2 (the modified Delphi technique). Subsequently, Chapter Seven – Discussion, will synthesise the overall findings of PICCS1 and PICCS2, providing a critical discussion, reflexive account of the researcher and a critical discussion surrounding implications for future practice including next steps.

6.1 PICCS1 - Online questionnaire findings

6.1.1 Introduction

The online questionnaires for PICCS1 were designed for female CAYA cancer survivors and parents of CAYA cancer survivors (Appendix 1). The HCP questionnaire was then adapted using more formal and medicalised terminology for the HCPs participants (Appendix 2). Both questionnaires were distributed using social media links via Twitter, Facebook, LinkedIn and private cancer survivor and parent support groups (the researcher was a member of these groups prior to the study). Questionnaire data captured within PICCS1 reflected the ‘Real’ domain of reality as discussed in in Chapter Three – Methodology.

6.2 CAYA cancer survivor/parent questionnaire

Responses were received from 105 participants, with 48 of those completing

>90% of the questionnaire. The response rate of the participants that completed >90% of the questionnaire was 45.7%. Participants were automatically sent a reminder by the software programme to complete their entries if incomplete, after 28 days, after which their responses were discounted if not >90% complete. The factors influencing the dropout rate of almost half of the participants are unknown as the software (*Qualtrics*) does not allow for this type of analysis. However, upon examination of data from a selection of the non-completed questionnaire entries, possible reasons for this could have been participation from outside the UK (using an internet protocol address linked to the USA, for example). Individual analysis of each question based on number of responses was not performed.

The first question asked participants about their background. Participants reported that 18 were parents of a child that had cancer, 19 described themselves as a female CAYA cancer survivor, and 11 identified as female CAYA cancer survivors that had been pregnant and/or had a child (Figure 14).

The time interval since cancer treatment had been completed was recorded as > 11 years ago by 29 participants, four had completed treatment 6-10 years ago, six recorded completing treatment five years ago, eight recorded treatment completion as 1-5 years ago and one participant did not complete this question (n=1) (Figure 15). Treatment modality was then explored, with participants being asked if they/their child had received chemotherapy, radiotherapy, or a combination of both. Of those that selected that they/their child had received radiotherapy (n=44), 21 reported that they knew how much radiation they/their child received. A further 19 participants indicated that they did not know the

dosage and four participants indicated that they were not sure on the level of radiotherapy given. In total 23 out of the 44 responses (52.3%) did not know or were unsure about the level of radiotherapy received as part of their/their child's cancer treatments (Figure 16).

A sub-question for those who received/their child had received radiotherapy, asked for their age at the time of treatment. A range of 0-24 years inclusive was offered. Out of the 44 participants that received radiotherapy, 22 selected 0-5 years of age, 14 chose 6-12 years old, 5 opted for 13-17 years old and three participants indicated that they/their child received radiotherapy between the age of 18-24 years old (Table 31).

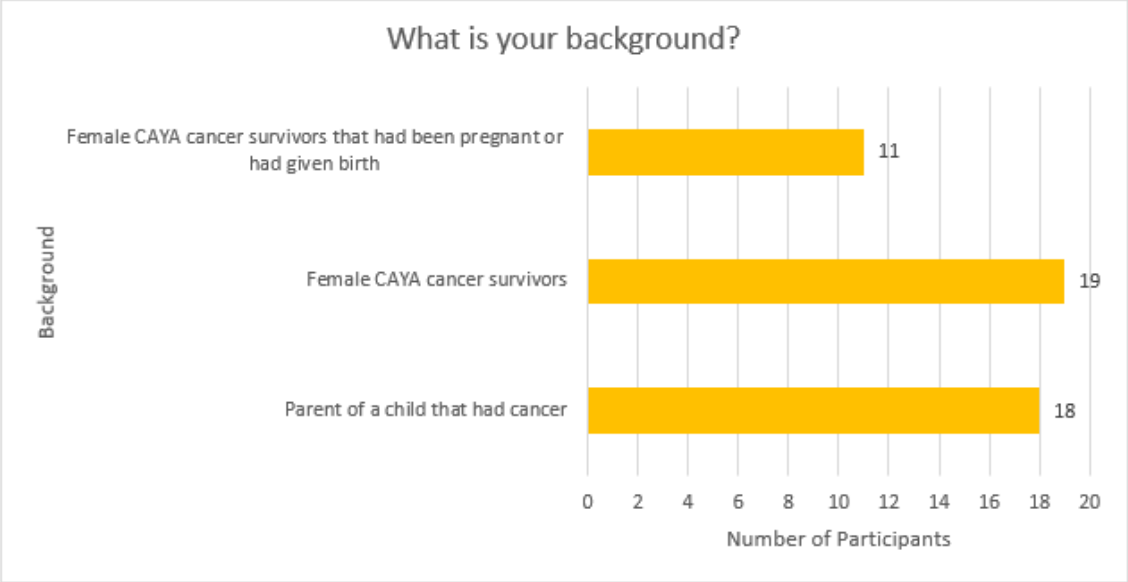

Figure 14 - CAYA cancer survivor/parent background (n=48)

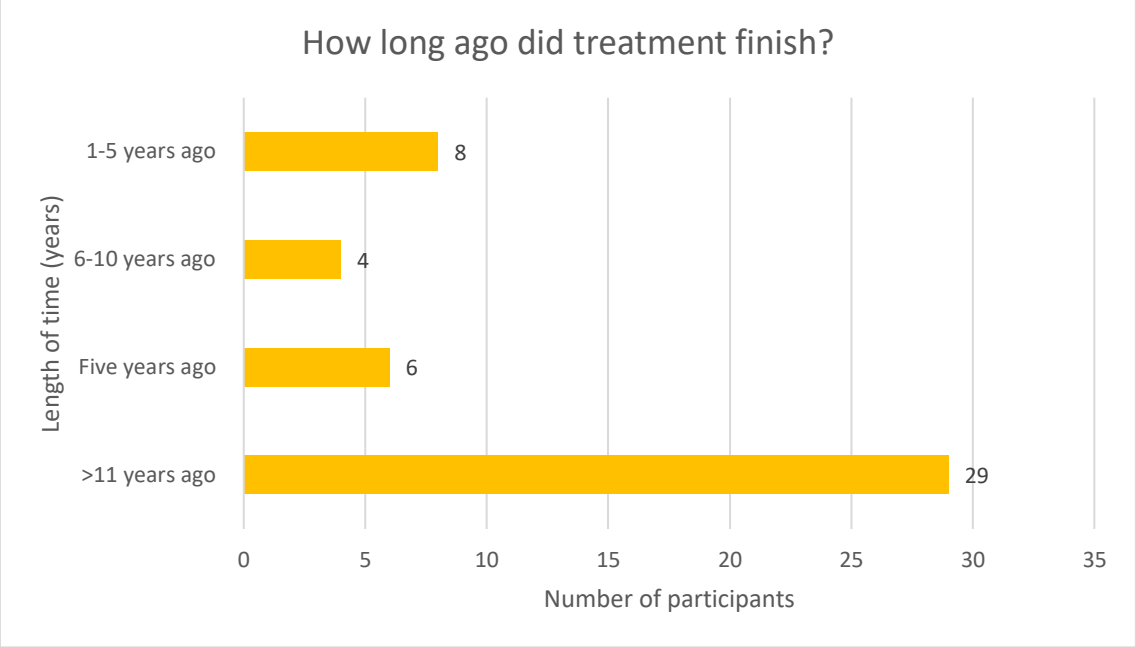

Figure 15 - Age at time of treatment completion (n=47, n=1 missing data)

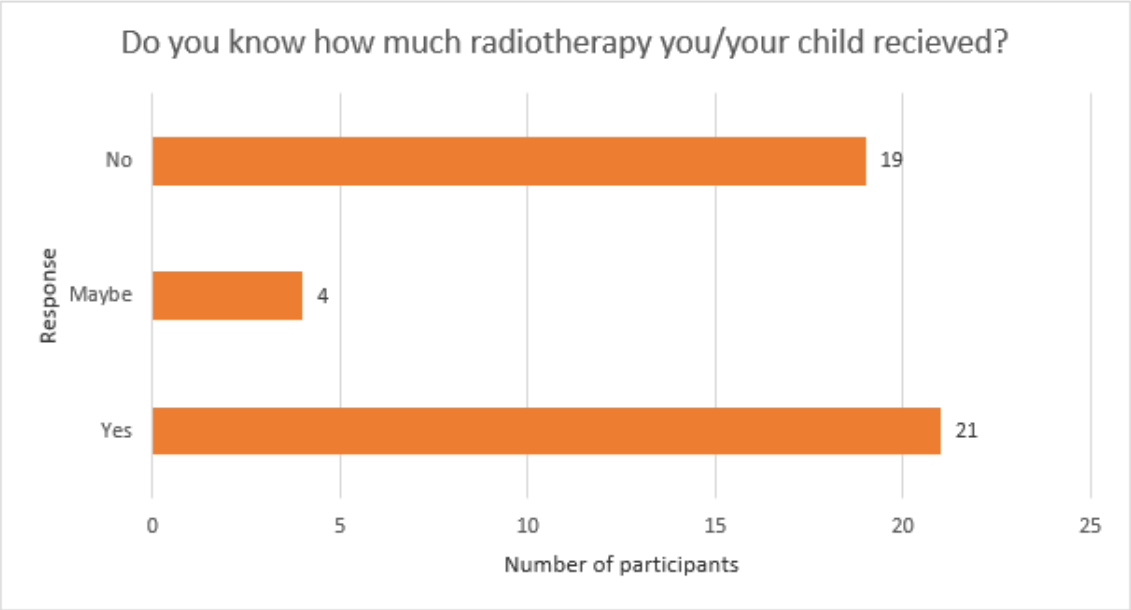

Figure 16 - CAYA cancer survivor/parent knowledge of radiotherapy received as part of treatment (n=44)

Table 31 - Age at Radiotherapy Treatment (n=44)

Age range	Number of respondents
0-5 years old	22
6-12 years old	14
13-17 years old	5
18-23 years old	2
24 years old and over	1

The next question then explored communication of information relating to future fertility and pregnancy. This issue had been identified as one of the biggest unmet informational needs in the PICCS1 - Systematic review. A total of 44 participants completed the question (n=4 missing data). Responses indicated that 70.4% (n=31) had been told of an impact upon their/their child's future fertility or ability to have a baby, caused by cancer treatments. This was followed by five participants selecting that they had not been told of any future impact, five participants selecting that they were not sure if they had been told (maybe), and three participants selecting that they did not know (Figure 17).

For those participants that indicated 'yes' or 'maybe' (n=36) when asked if they had been told about future fertility/pregnancy implications for them/their child, an additional question about the type of risk they were informed about was asked. The participants were able to select more than one response to this question, as they may have been told about more than one risk/complication. In total the 36 respondents selected a combination of 130 options. The option, 'difficulty becoming pregnant' was revealed as the top-ranked risk/complication with 29.2% of the selections and a risk of early menopause ranked as second

with 20.8%. Potential risk of abnormality in a future baby was ranked as the lowest communicated risk with 3.8% of the participants indicating that this had been discussed with them by a HCP (Figure 18). A free-text box was offered for those participants that had selected ‘something else’ from the options (3%). Data from this revealed that communication about probable infertility, the need for future IVF treatment and the need for additional care in future pregnancy had also been discussed (Table 32).

The format of future fertility and/or pregnancy risks information was then explored. This was designed as a sub-question that was only revealed to those that had selected ‘yes’ or ‘maybe’ to having received any information about future fertility and pregnancy risk (n=36). The participants could again select more than one option to this. The findings showed that 72.5% of participants had received verbal information, 15.7% had received written information, 2% had been directed to internet resources, and 9.8% selected ‘other’. Audio-based information did not receive any selections (0%) (Figure 19).

A free-text option was then provided for participants to elaborate on their selection of ‘other’. Free text data revealed that communication of future risks had taken place with a fertility specialist, or only when problems arose in their health and also through self-directed education (seeking out information online or in textbooks themselves) (Table 33).

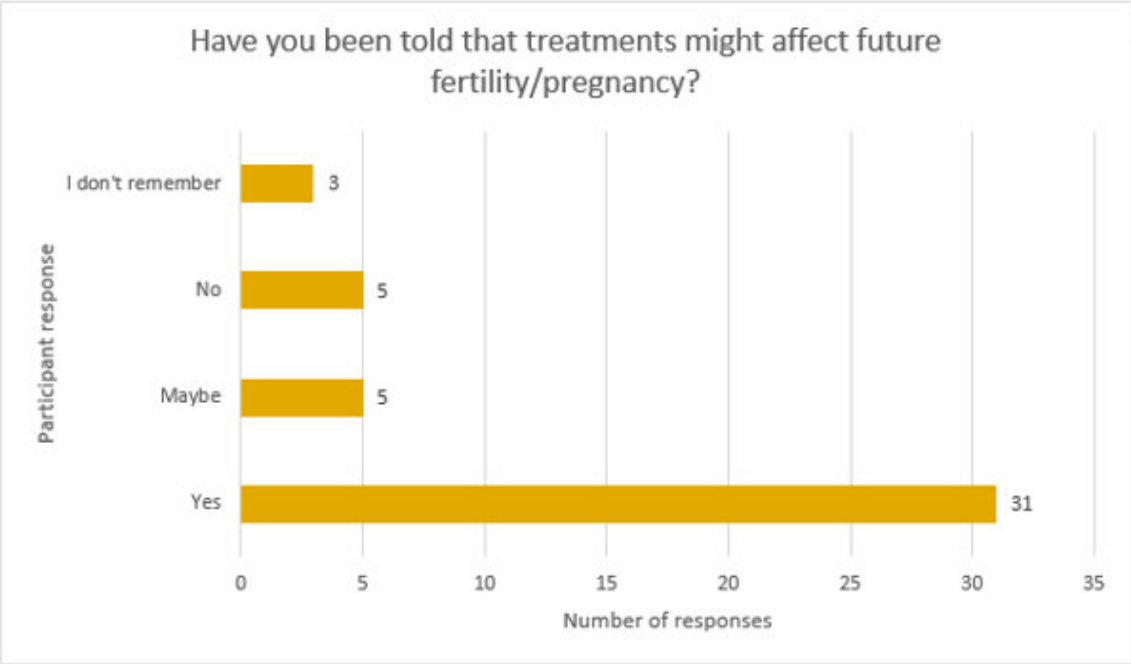

Figure 17 - CAYA cancer survivor/parent questionnaire – recall about communication of future fertility/pregnancy risk (n=44, n=4 missing data)

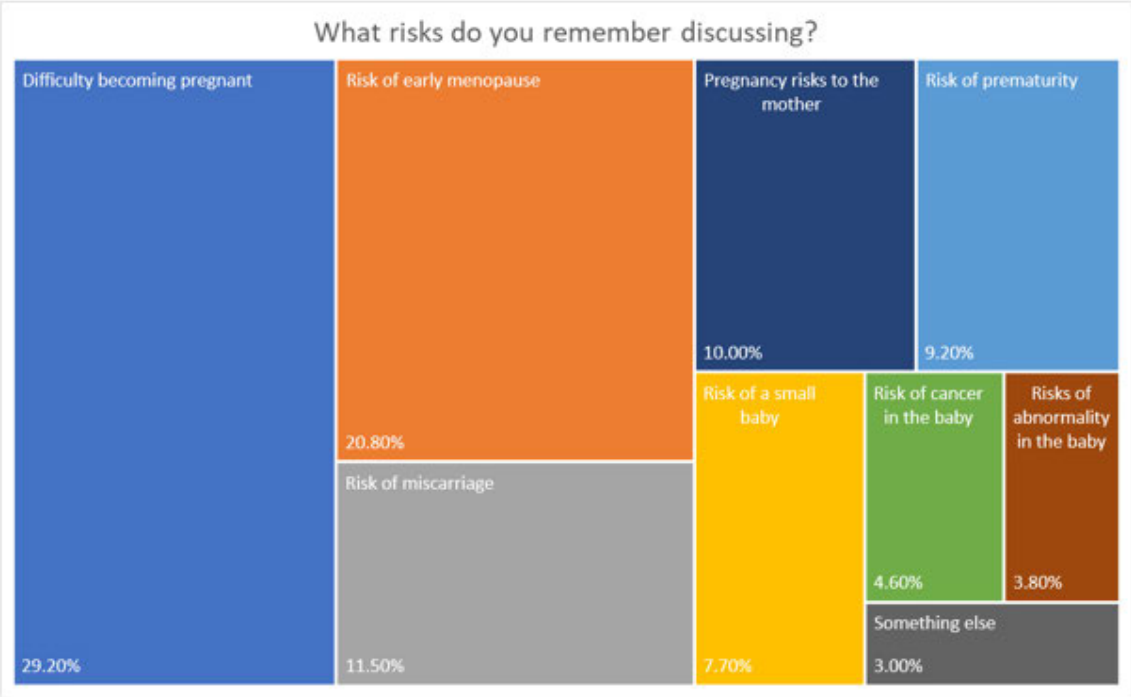

Figure 18 - CAYA cancer survivor/parent questionnaire - specific risks for future fertility/pregnancy that were discussed by HCP (n=36)

Table 32 - Free text responses to sub-question ('something else' option)

Free text responses to sub-question
Infertility will be likely
Will need IVF due to ovarian transposition
Unable to have children due to high-dose chemotherapy
Would need additional monitoring in pregnancy

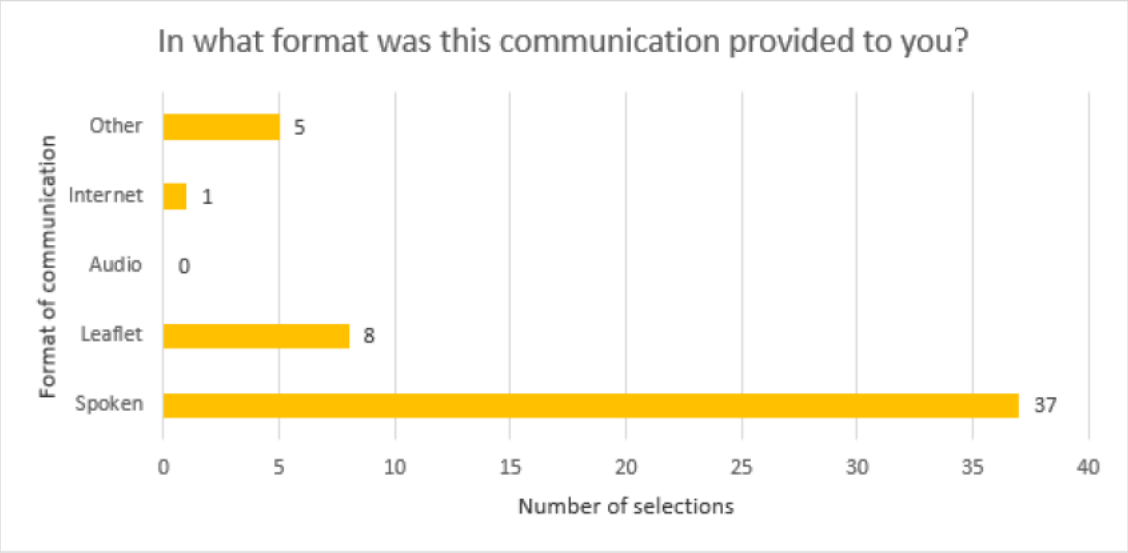

Figure 19 - Format of communication for fertility/pregnancy risks (n=36 participants, n=51 selections from multiple choices)

Table 33 - Free text responses to information source ('other' option)

Free text responses to information source
Consult with fertility specialist
Read about it when she was in early teens
None
My own research
Information wasn't given up front during before/after treatment, only after treatment when issues with my menstrual cycle became obvious

The time point at which information was communicated to CAYA with cancer or their parents during the cancer treatment timeline was designed to allow multiple responses. This reflected the high likelihood of information being delivered on multiple occasions during diagnosis, treatment, and aftercare. Out of the 48 participants, 41 answered the question with 55 combinations of the available options selected. The timepoint ‘during treatment’ and ‘upon treatment completion’ both received 18 selections (32.7%). At the point of planning a family received 12 of the selections (21.8%) selections, with ‘at diagnosis’ being selected five times (9.1%). At the time, the CAYA cancer survivor became pregnant was selected twice (3.6%) (Figure 20).

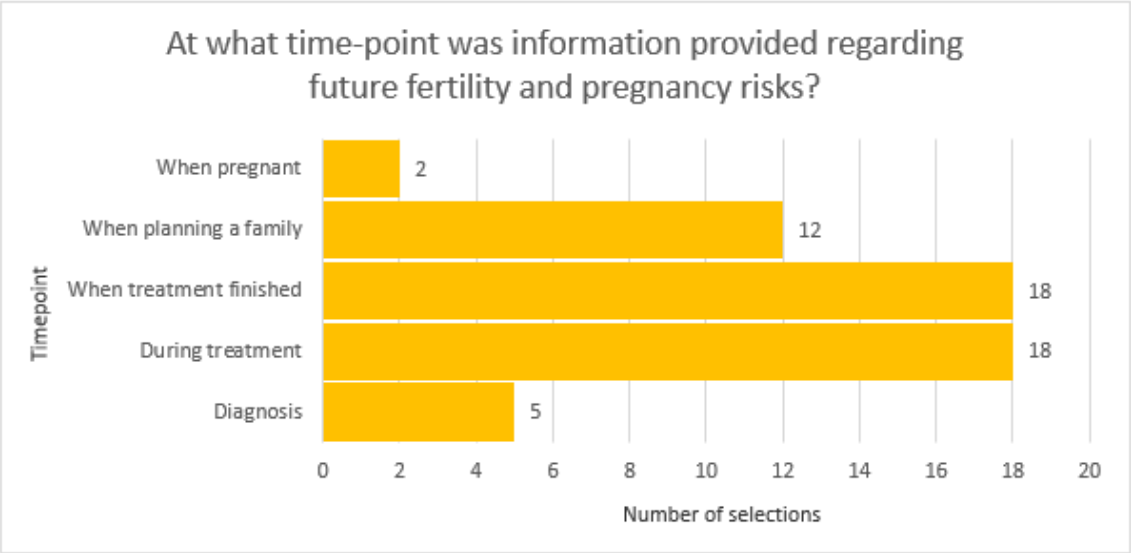

Figure 20 - CAYA cancer survivor/parent questionnaire - Timepoint for communication of future fertility/pregnancy risk information (n=41 respondents, n=55 selections)

Comparative analysis of data from the survey was not possible between the questions in the survey due to the inclusion of multiple responses and the choice by the researcher to use the ranking design for individual questions. Statistical advice from an academic institution was sought by the researcher,

which confirmed that the only comparison possible within this dataset was ‘Risks communicated vs. Timing of this information’. A comparison analysis using *SPSS* software was performed using these variables and demonstrates that out of 105 selections by respondents, future risks such as early menopause and infertility are reported to be discussed more often during the active treatment phase or when the active treatment for cancer has just finished. On the other hand, communication of information relating to future pregnancy or birth risks is less and is reported to be communicated when the CAYA cancer survivor is planning a family or when they become pregnant. The wide spread of selections for communication of risk of cancer in the future baby or miscarriage for example, suggests that the most appropriate time to discuss this type of information may be unknown or not investigated previously (Table 34).

Table 34 - CAYA cancer survivor/parent questionnaire – data comparison table (communicated future fertility/pregnancy risk vs. timing of communication of the information by the HCP (n=41, n=105 selections)

	Diagnosis	During treatment	When treatment finished	When thinking about starting a family	When pregnant	Total (multiple responses allowed)
Difficulty becoming pregnant	5	16	17	9	2	36
The risk of early menopause	5	12	13	8	1	26
Possible risk of miscarriage	3	7	7	6	1	14
Possible risk of a small baby	1	4	4	6	1	10
Possible risk of premature baby (born early)	3	5	6	5	1	12
Risk of cancer in the baby	1	3	2	3	1	6
Possible pregnancy risks to the mother	1	3	4	8	1	13
Possible risks of abnormalities in baby	1	2	3	3	0	5
Something else	0	3	2	0	0	4

6.3 Health Care Professionals questionnaire

The HCP version of the questionnaire was accessed by 33 health care professionals via the link provided, with 29 proceeding to complete >90%. The incomplete responses of <90% were automatically sent a reminder after 28 days by the software, *Qualtrics*. If their entry remained incomplete, then their data was removed from the analysis. The completion rate for this questionnaire was 87.9%.

The first question enquired to the background of the participants, with multiple selections permitted. This was allowed due to the increased likelihood of HCPs working within one or more CAYA cancer specialties and also to capture data from those that might not consider themselves to fit into one category or another. Out of the 29 respondents, 83 selections were recorded. Professionals who provide care to CAYA with cancer (0-24 years old inclusive) represented 31.3% (n=26) of the selections, n=18 selected that they provide long-term care to CAYA with cancer once treatment has been completed (21.7%). The category ‘you provide care to CAYA with cancer that need radiotherapy services’ was selected by n=15 (18.1%), and ‘you discuss long-term health risks related to treatment with CAYA cancer survivors and their families’ was selected by n=24 (28.9%). The distribution of HCP specialisms demonstrated a majority of Paediatric Oncologists (n=13), with Paediatric Haematologist selected by n=9. Paediatric Oncology Nurse represented n=5 and Paediatric Radiotherapy specialist was chosen by n=2 (Figure 21 and Figure 22).

The participants were then asked to consider the timepoint for the

communication of information relating to future fertility preservation options (Figure 23). This question differed from the CAYA cancer survivor/parent questionnaire as HCPs would possess a deeper understanding in the difference between fertility preservation and future fertility and pregnancy risks. Multiple options were allowed, as the researcher acknowledged that this information might be introduced and then revisited throughout the cancer treatment timeline. The question was completed by all 29 participants with the option ‘at diagnosis’ receiving the most selections with 28/117 responses (23.9%). This was followed by ‘before high-dose chemotherapy/radiotherapy with 26/117 selections (22.2%). The timepoint ‘at the end of treatment’ was selected 23 times (19.7%), ‘at relapse’ 22 times (18.8%) and ‘during treatment’ was selected 18 times (15.4%). The wide variation in distribution demonstrates a lack of agreement or knowledge surrounding the correct or most appropriate time to communicate this type of information and suggests a gap within the research to investigate this further (Figure 23).

When asked about personal awareness of late effects or risks relating to future pregnancy or fertility of CAYA cancer survivors, all participants answered ‘yes’ (100% n=29). This question was designed to investigate the level of awareness of previous published work in that has demonstrated a higher risk of premature birth, small for gestational age babies (<2500 grams at birth) and miscarriage for female CAYA cancer survivors (van der Kooi et al. 2019). Further enquiry surrounding what risks HCPs would you feel comfortable in discussing with CAYA cancer survivors and their families was then presented. One participant did not complete this question (therefore n=28 out of n=29 possible responses

were recorded). Multiple selections were again permitted to allow for a number of risks that might have been discussed rather than one individual risk.

The multiple option data illustrated that HCPs felt comfortable discussing a risk of premature menopause the most with 28/108 selections (25.9%). Difficulty in becoming pregnant in the future was ranked second with 27 selections (25.1%). This was followed by communicating the risk of not being able to carry a baby to full-term (i.e., 37 completed weeks of pregnancy) with 20 selections (18.5%), the risk of having a small baby in a future pregnancy (i.e., <2500 grams) was recorded in 11/108 selections (10.2%). Information pertaining to the future risk of cancer in the offspring of CAYA cancer survivors and the risk of abnormality in a future baby recorded 9/108 selections respectively (8.3%). The option 'something else' was selected four times (3.7%) and the final option 'none of these' received zero selections (0%) (Figure 24).

Noteworthy to this data is the increased confidence of paediatric oncology HCPs in discussing future fertility affects with families (premature menopause and difficulty in getting pregnant in the future), but the lower levels of confidence being shown in discussing future obstetric risks or complications. This finding correlates with data from the CAYA cancer survivor/parent questionnaires, where future pregnancy and birth risks were discussed less often and often not during treatment by paediatric oncology professionals (see section 6.2 CAYA cancer survivor/parent questionnaire).

To explore the definition of 'something else' to this question, a free text option was provided. Data recorded here demonstrated reinforced the finding above, illustrating that HCPs feel comfortable with communication of fertility-related

information in the majority, but in response to delivering specific future pregnancy advice or risk, this was considered 'out of scope' and the responsibility of other medical specialties (Table 35). The quotation below helps to illustrate this point of view:

> *"I am aware of all the complications and would discuss with patient/family but it would not normally be my role and so I would not describe myself as 'comfortable'"* ***(HCP)***

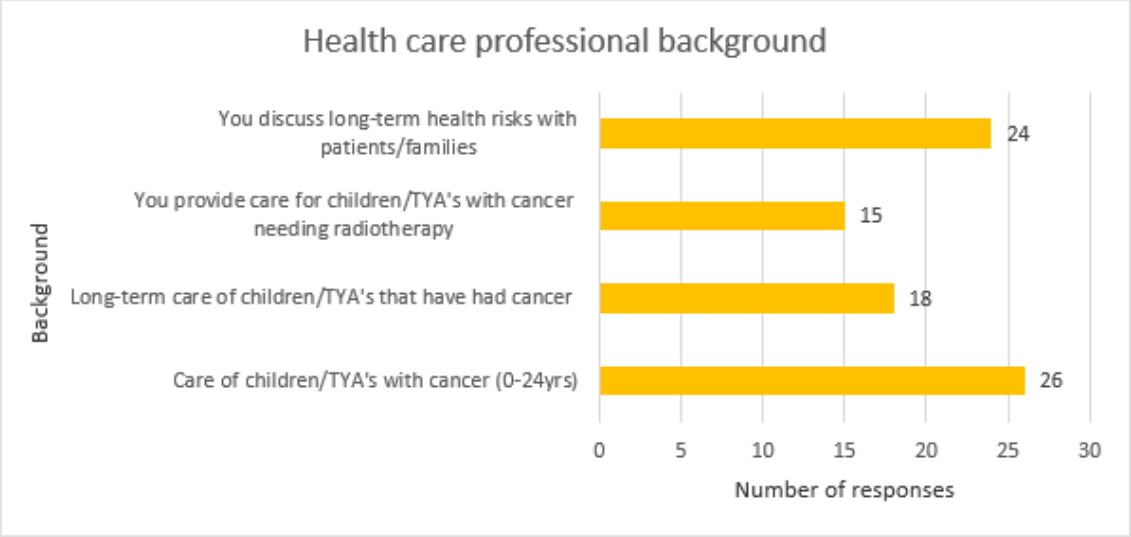

Figure 21 - HCP questionnaire - Professional background (n=29, n=83 selections)

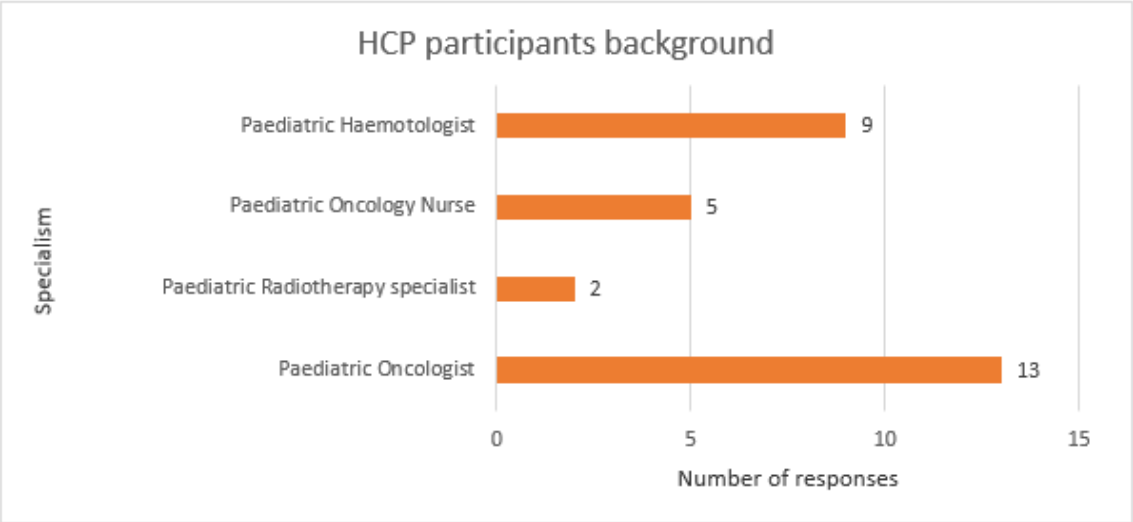

Figure 22 - HCP questionnaire - Background specialty (n=29)

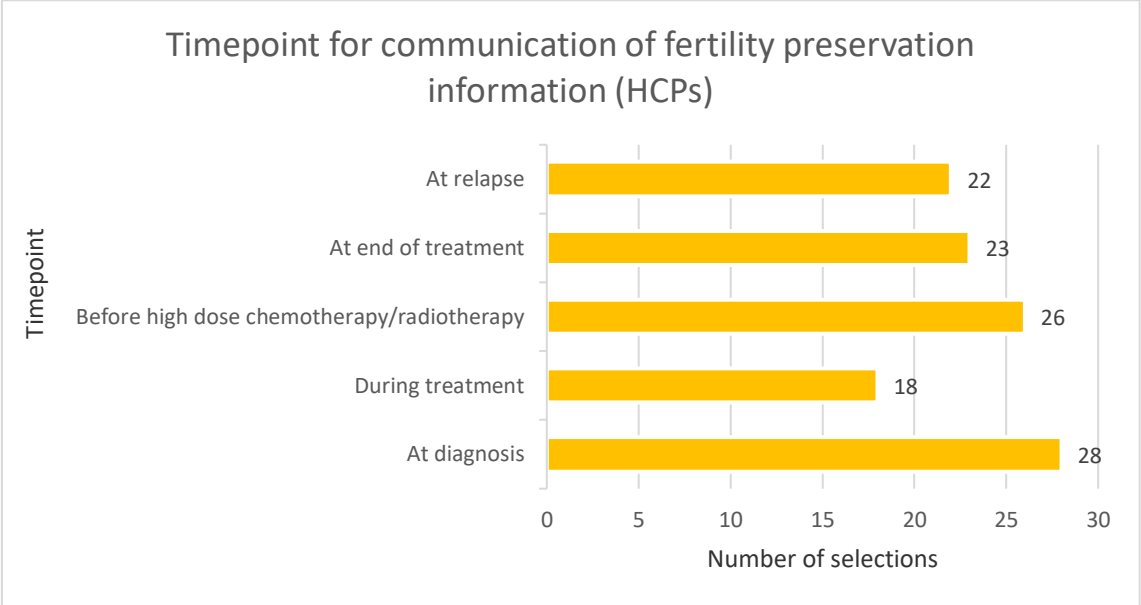

Figure 23 - HCP questionnaire - Timing of communication for fertility preservation information (n=29, n=117 selections)

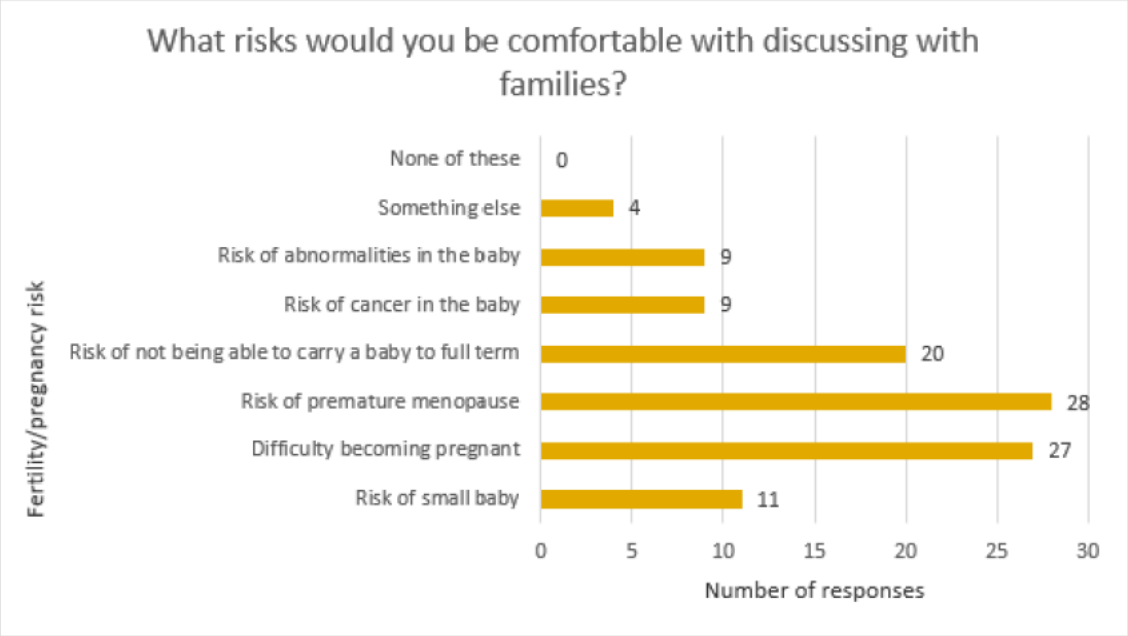

Figure 24 - HCP questionnaire - What future fertility/pregnancy risks would you feel comfortable communicating with families? (n=28, n=108 selections)

Table 35 - Free text responses – 'Other' option for HCP questionnaire (specific fertility and pregnancy risks) (n=4 selections)

Free text responses – HCP
Delayed puberty
I would explain that conceiving would be more difficult, I would explain about IVF support
I am aware of all the complications and would discuss with patient/family but it would not normally be my role and so I would not describe myself as 'comfortable'
Ovarian failure (hormonal) not just difficulty conceiving

The format of information commonly provided to CAYA with cancer and their families was the focus of the proceeding question. Multiple answers were again permitted, in acknowledgment of the empirical evidence that suggests in many cases, a combination of sources would be used to discuss with CAYA cancer survivors and their families (Wakefield et al. 2012). All 29 participants recorded a response with 54 selections recorded from the multiple choices. Verbal

communication was identified as the top preferred communication method with 29 selections (53.6%). This was followed by 15 selections of written information as a preference (27.8%), internet resources and 'other' (n=5 selections respectively, 9.3%). Audio-based communication methods recorded zero selections (0%) (Figure 25). The option 'other' was investigated further using a free text box, revealing that some HCPs preferred to refer patients to a fertility specialist or record a written entry into a 'survivorship plan'/patient medical notes (Table 36).

A second investigation, this time directly replicating the question asked to the CAYA cancer survivors/parents, explored the most common or 'appropriate' timepoint for discussion of wider future fertility or pregnancy risks caused by cancer treatments. All 29 participants recorded a response with 118 selections from the multiple-choice options. 'At diagnosis' was selected 26 times (22%), during long-term follow up or in the survivorship clinics was chosen 25 times (21.2%), 'at the end of treatment' reflected 23 selections (19.5%), at the point of radiotherapy or following radiotherapy received 19 selections (16.1%), 'during treatment' was recorded 13 times (11%), and finally when CAYA cancer survivors are considering a pregnancy was chosen 12 times by the respondents (10.2%) (Figure 26).

This data demonstrates, similar to the CAYA cancer survivor/parent questionnaire, a lack of consensus for the correct or most appropriate time to discuss future fertility or pregnancy late effects risk. The multiple-choice option of the question helps to illustrate that this information is likely to be repeated at different timepoints, however, further investigation using singular time point

variables would further assist in the provision of conclusive answer to this enquiry.

HCP views surrounding whose role it is to communicate future fertility and/or pregnancy late effects demonstrated was answered by n=29 respondents and reported on n=97 selections from the multiple options provided (Figure 27). The Paediatric Oncologist was reported as the most common professional with 25 responses (25.8%). The Paediatric Radiotherapy consultant ranked second with 19 selections (19.6%), followed by the Paediatric Haematologist (n=18 selections, 18.6%). The Paediatric Oncology Nurse received 15 selections, along with the Advanced Nurse Practitioner (n=15, 15.4%). A CLIC Sargent or other charity professional was chosen five times (5.2%). This final selection came with the caveat that this was not a registered HCP (Figure 27).

The findings of this question demonstrated a wide distribution of data, suggestive of a perceived lack of agreement about whose role it is to discuss this type of information with families. Further investigation using individual variable choices would be recommended to limit bias and explore this issue further.

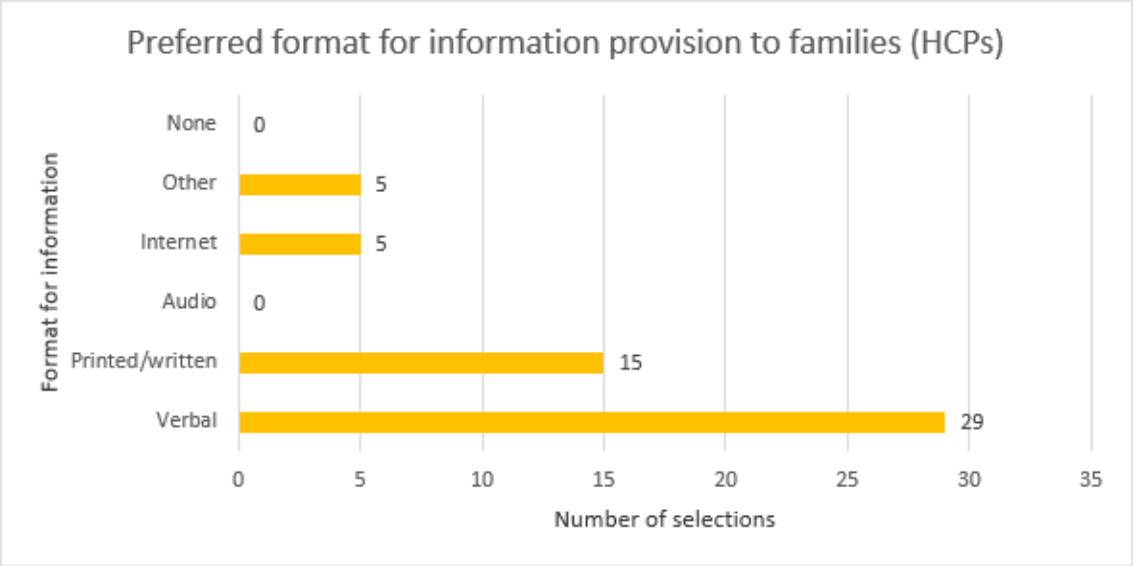

Figure 25 - HCP questionnaire – Preferred format for information given to CAYA cancer survivors and families (n=29, n=54 selections)

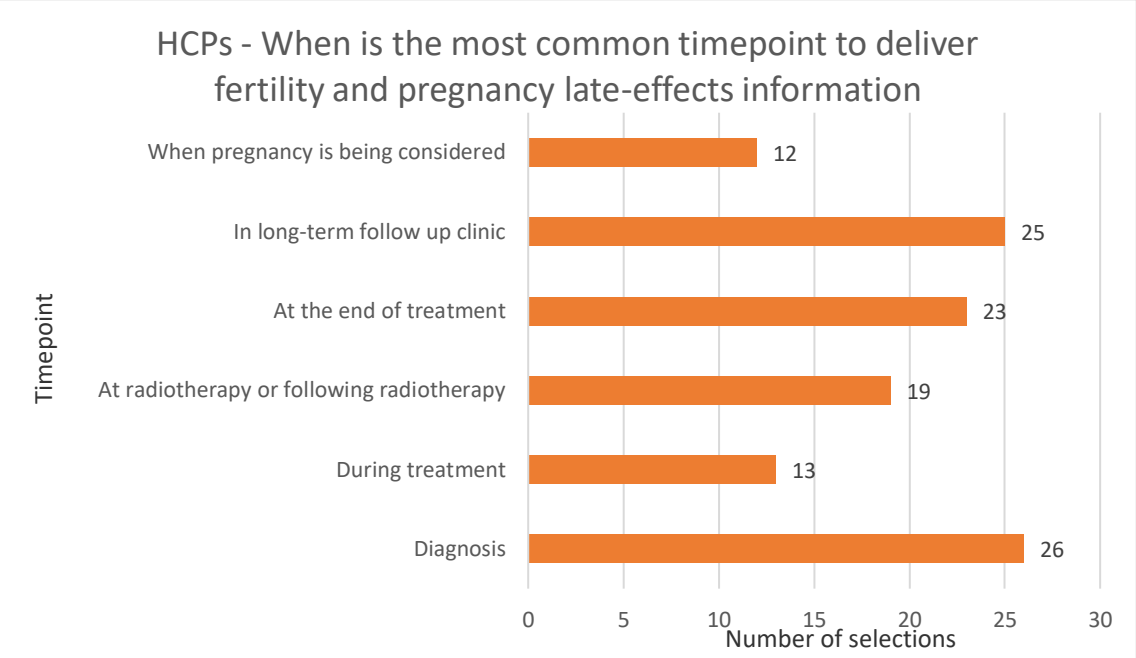

Figure 26 - HCP questionnaire – Most common timepoint for discussing future fertility and pregnancy risk (n=29, n=118 selections)

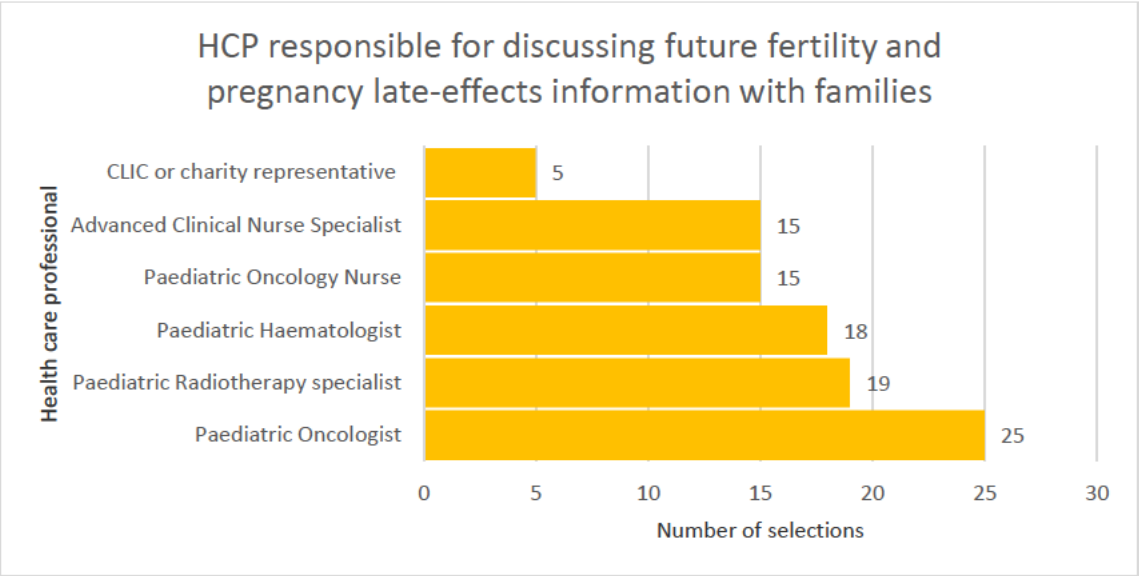

Figure 27 - HCP questionnaire – the role of the professional who discusses future fertility and pregnancy information with families (n=29, n=97 selections)

Table 36 - Free Text option (HCP) communication format

Free text option
Usually, verbal
Printed in context of long term follow up or if ovarian or sperm preservation planned"
Referral to fertility expert teams
Referral to specialist fertility service for check on ovarian function post treatment if patient wishes
Printed information is in the form of the written individual treatment summary and long term follow up care plan
Copy of consultation letter to parent/child

To conclude the HCP questionnaire, participants were asked to consider the information they currently provide to CAYA cancer survivors and their families. They were asked a series of sub-questions relating to future fertility and/or pregnancy risks and asked to rank their responses with 'agree' 'disagree' or 'neither agree nor disagree'. The first question asked them to consider if the

information they currently to families about future fertility and pregnancy risks is sufficient. This aim of this was to illustrate evidence of a possible gap in knowledge in this area, or to confirm that HCP knowledge surrounding future fertility and/or pregnancy late effects was comprehensive enough for them to feel confident in the communication of information to families.

Out of the 29 participants in the questionnaire, all 29 completed this question (n=29). The first sub-question asked if they thought the information, they currently provided to families about future fertility and pregnancy was ‘sufficient’, i.e., answered their questions, and was answered by all 29 HCPs. Out of the 29 participants, 44.8% (n=13) selected that they disagreed, therefore that the information they provide is not sufficient. Of the remaining responses, 37.9% (n=11) expressed an ambivalence to the statement, therefore indicating they are unsure. Finally, 17.3% (n=5) indicated that they agreed that the information they provide to CAYA with cancer and their families is sufficient in their opinion (Figure 28).

An exploration of HCPs perceptions surrounding appropriate timing of information delivery to families was then asked (Figure 28). Out of the 29 respondents to this sub-question, 58.6% (n=17) neither agreed nor disagreed that the information they provide is sufficient. The option ‘the timing is optimal’ was chosen by 34.5% (n=10) and 6.9% (n=2) participants disagreed with the perception that the timing of information delivery was ‘optimal’ for families (Figure 28). This data suggests that HCPs need further guidance to ensure that information is communicated to families at the optimal and most appropriate time.

Sub-question three, the awareness and knowledge of specific treatment-related fertility and pregnancy complications was answered by all participants (n=29). It revealed that HCPs in the majority did not agree or disagree with the assumption that they had enough knowledge on the subject with 41.4% (n=12) responses. In 37.9% (n=11) of responses, HCPs did not think they had enough knowledge to communicate all potential future fertility and pregnancy risks to CAYA with cancer and their families and 20.7% (n=6) perceived that they had had sufficient knowledge of future fertility and pregnancy risks caused by cancer treatments to be able to discuss these confidently with CAYA with cancer and their families (Figure 28).

Finally, HCPs were asked to consider if they thought the information, they provided to CAYA cancer survivors and families was retained and understood long-term. The definition of long-term was not provided to the participants, however it was intended to signify a period of a number of years following treatment. The topic for this sub-question arose from the findings of the PICCS1 systematic review, where it was reported in the literature that many CAYA cancer survivors and/or their parents do not recall key late effects information given to them at the time of treatment (see section 5.5.2.1 Summary of included studies). Data from this sub-question again demonstrated ambivalence (that they neither agreed nor disagreed with the statement) and was selected by 51.7% (n=15). HCPs that did not agree with the statement that patients and families retained their information long-term was chosen by 34.4% (n=10). The lowest scoring option, with only 13.7% (n=4) selections was that HCPs agreed with the statement that parents and CAYA cancer survivors retained the

information they gave them long-term. This finding supports the published evidence from PICCS1 and suggests that further investigation is needed to measure CAYA cancer survivor and parent recall and find better ways to improve this.

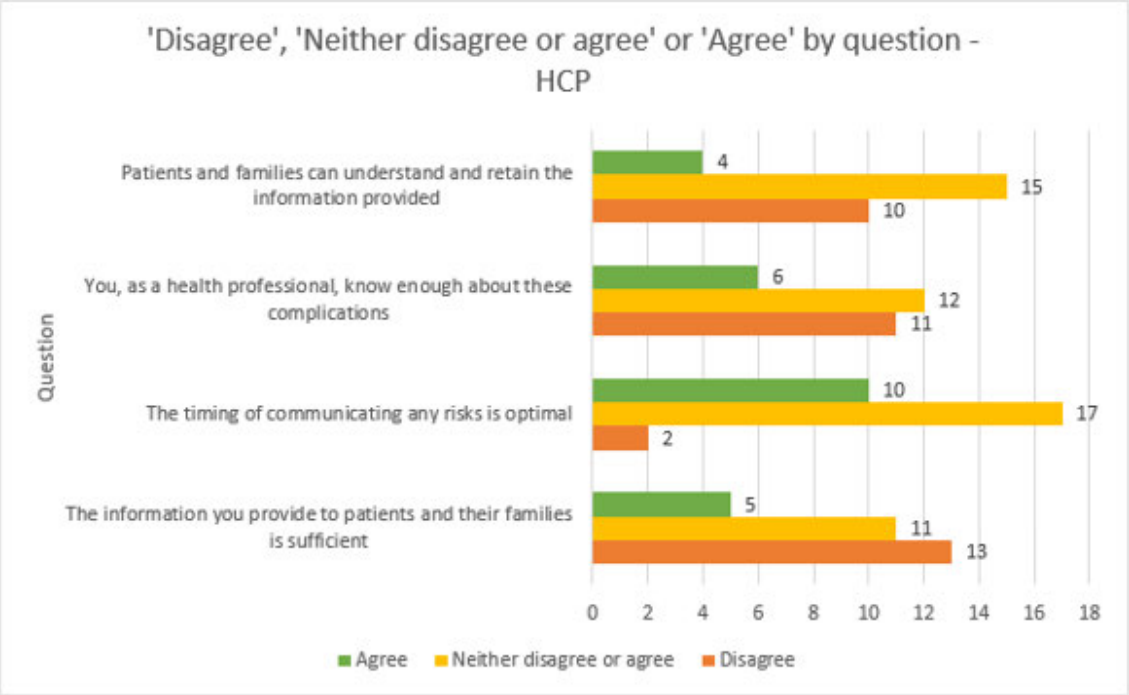

Figure 28 - HCP questionnaire (sub-questions ranking) – overall HCP views on information provision to families (n=29)

The end of the HCP questionnaire featured a free-text box, offering the participants a chance to feedback any additional thoughts or experiences relating to the topic. Data recorded here, provided an additional source of primary data that the researcher was able to take forward into the development of the semi-structured interview questions. Data reflected the HCP perspective, that most communication with families is dependent on the individual circumstances of the patient, the family and the level of treatment that has been received as to what level of information needs to be communicated. HCPs

acknowledged that there is a lack of evidence-based resources to help them with the communication of fertility preservation options and future fertility and pregnancy risks caused by treatments. Free text data also highlighted the view that the active phase of cancer treatment and survival of the CAYA is paramount and that sometimes there is not time, or it is not appropriate to discuss this information, for example at the time of relapse. Full data from the free-text feedback is presented in full in Table 37.

Table 37 - Free text responses from HCP questionnaire

Free text response
In patients with leukaemia, fertility preservation is rarely an option at diagnosis, but risks of infertility are discussed, even if the risk is low. The majority of discussions I have are in patients with relapsed disease and those who are going to have a bone marrow transplant, where we discuss this in detail at the time of relapse or once we know the child will need a transplant. We then offer fertility preservation at that point
So much of the information is given at diagnosis if the risk is generally low and there is an actual choice. Treatment & preservation of life paramount. It's probably much easier to discuss prior to bone marrow transplant, at which point there is usually even less choice and involves informing about a considerable risk of infertility. Non-malignant patients are easier as they may be able to undertake fertility preservation strategies
I think it is important that a potential sub study be considered. Different sized paediatric haematology/oncology units have differing levels of staffing. For example, we have no paediatric oncology nurse specialist to discuss these issues, nor do we have registrars that can. We rely on ourselves or specialist nurses who have other competing demands on time and cannot devote enough time to this important topic
At diagnosis there is an enormous amount of information shared and later fertility is often not a priority, especially for parents of young children. My own practice has evolved to try and discuss these issues pro-actively at end of treatment discussions and, at the point of relapse or referral for transplant. I am not aware of a good general printed resource to share with families or patients

Free text response
We have the luxury of ovarian strip harvesting in my area, so this makes conversations easier to have. There is little written evidence I am aware of in paediatric oncology units. Young people may well prefer a YouTube approach to information dissemination. There are different hurdles to overcome in referring on for "pre starting a family" advice depending on whether you work in a paediatric hospital or in an adult environment
Timing of conversations and amount of information provided needs to be adapted to each family/patient situation. Discussing fertility at relapse is not usually done as treatment of relapse to maximise chance of survival is paramount
Would be helpful to have a national resource - with up- to- date information
In my experience information giving is in stages and several different individuals may be involved. I don't see what happens in late effects clinic, but it is discussed again there
I was unable to agree or disagree to the previous questions because Information provided to patients and family's needs to be according to their wishes. In long term follow up I try to ensure patients are aware of their individual risks by providing written and verbal information. This happens over a period of years but often does not become relevant to the young person until early adulthood. The complexities of providing information and young people and family wanting, understanding, absorbing that information cannot easily be assessed in a questionnaire. Add to that the difficulty in ascertaining individual risk (evidence base is limited, medical records are not clear e.g., radiotherapy field, surgery) and conveying what that might mean for an individual
Difficult to decide when to have the conversation with the child vs. when to have the conversation with parents. As a specialist paediatric radiation professional, I am often finding that the referring paediatric oncology team have not had these conversations with families which makes my job considerably harder, never mind that many of the systemic therapy agents used before radiation can have an adverse impact on future fertility

6.4 Summary

To surmise, data from the two online-questionnaires were extracted from the *Qualtrics* software programme, collated, and analysed. Data were presented using narrative and pictorial commentary using graphs, tables and where appropriate comparative analysis using the *SPSS* software. Findings from the systematic review assisted the researcher with the design of the questionnaires and allowed for further exploration of areas where further research would be warranted. The themes from PICCS1 (systematic review) were replicated within the findings of the online questionnaires. There was also evidence to support that HCPs have a gap in their knowledge about future fertility and pregnancy risks, thus supporting the need for further research.

The identified themes from the PICCS1 systematic review and data from both questionnaires were used to shape and design the semi-structured telephone interview questions, guiding the most appropriate choice for method of enquiry. Data up to that point, had suggested several areas worthy of further investigation. This included recall of key late effects information, timing of fertility preservation, the provision of future fertility and reproductive health late effects risk information and the format chosen for this type of communication. The choice of HCP who is responsible for the delivery of key late effects information was also identified as an area where there was demonstrable lack of consensus.

As with the PICCS1 questionnaire design, the semi-structured interviews were designed with two formats to ensure that the content of the questions and the

terminology used was appropriate for both the HCPs and the CAYA cancer survivors/parents. Methods for the recruitment of participants can be found in the PICCS1 semi-structured interviews section of Chapter Four – Methods. Findings from the semi-structured interviews, themes within the dataset and a summary of PICCS1 as a whole will now be presented.

6.5 PICCS1 – Semi-structured interview findings

6.5.1 Introduction

The semi-structured interviews with CAYA cancer survivors, their parents and HCPs represents the 'real' domain of reality in the cog template used for this thesis (see section 3.2 Mixed methods in research). A more in-depth investigation of the lived experiences of both CAYA cancer survivors, parents and HCPs provides the researcher with an additional dimension to the published data and online reports, allowing for the consideration of personal values, attitudes and opinions into the findings and reflects the critical realism approach to the studies.

An excerpt from an anonymised transcript is presented in Appendix 12. Two versions were used: one with language and terminology suitable for CAYA cancer survivors/parents' and one using more medicalised terminology and critical discussion for HCPs. The adaptations were made to ensure that the language and the content of the interview questions reflected the participant perspective and knowledge base. This also assisted the researcher to adapt tone of voice and mannerisms to the participant, facilitating the ease of

discussion points of issues that were sensitive in nature. The positionality of the researcher when conducting the interviews aligned with the critical realist methodological approach to the study. The interviewer remained objective, but allowed for the exploration of feelings, experiences and data relating to extrinsic influencing factors that might have influenced their opinions. The interviewer also allowed responsive questioning, tailoring the questions and order of questions to the interviewee's needs and willingness to share personal information.

Transcription was performed by the interviewer verbatim using a software app *Otter* (Otter AI 2021) to assist with audio-to-word speed and accuracy. Transcriptions were checked for accuracy, anonymised, and validated with oversight from the director of studies before thematic analysis using *NVivo* (QSR International 2021) took place.

6.5.2 Participant recruitment

Volunteer responses for the interview stage of PICCS1 were received from ten participants of the online questionnaires. Eight of those volunteers then progressed to consenting and taking part in the telephone interviews. The two that did not take part were contacted by email seven days after the invitation was sent. If they did not respond within 14 days, they were excluded from the interview section of PICCS1. The two that did not want to take part did not return a consent form or reply to the email and did not disclose their reason for doing so. The professional/patient backgrounds of the remaining eight interviewees were:

- 3 female CAYA cancer survivors
- 1 parent of a CAYA that had cancer
- 3 Long-term survivorship nurse specialists
- 1 Paediatric oncology doctor

6.5.3 Thematic analysis – theme generation

After the interviews had taken place, data were analysed using thematic analysis, based upon the framework by Braun and Clarke (2006) (see Figure 8). Anonymised transcripts were uploaded to *NVivo* (QSR International 2021) and coded by key words that represented similar terms by colour (for example, time of information delivery, and period of time when information was given).

The key words highlighted in the transcripts and associated colour codes represented the ideas, opinions, and first-hand experiences of the participants. Key terms were analysed and placed into colour coded groups of similar content and tabulated. This provided the opportunity to view them as a whole and seek out similar concepts and words. Key terms were then merged together if they were similar in their description or re-grouped if felt that they did not represent or reflect the concept of the key term or idea they were allocated to. The key terms and colour codes were then merged into draft theme headings that represented data from the questionnaires as a whole. The draft theme generation process followed the thematic analysis assumptions method used by Braun and Clarke (2006) (Table 38).

Table 38 - Thematic analysis assumptions

Thematic analysis assumptions
A theme was defined as a level of patterned response or collective meaning within the dataset
The analysis of data aimed to provide a rich description of the dataset concerning the personal experience of late effects communication within the clinical setting
Abductive reasoning was used to 'cast a net' and then 'summarise and deduce' the themes from data. Data were developed into focused and categorised theme headings from draft theme categories
Themes were constructed with a combination of semantic and latent intent. This represented the dual-paradigm approach to the study. This is further explained as using a combination of surface and explicit meaning within data and the underlying ideas, assumptions, and values of the interviewees.
A critical realist approach was adopted during the thematic analysis
Comparison to the overarching research question for PICCS1 with the final themes was made

Draft theme terms were chosen to describe and summarise data in a way that could be understood by simply looking at the chosen word or term. The term chosen for the draft theme also needed to be reflective of the emotion, the personal values, hidden mannerisms, and experiences of the participants. The original key terms along with their associated colour codes are illustrated below (Table 39):

Table 39 - Theme ideas for PICCS1 Interviews

Theme ideas
1. HCP knowledge and awareness (RED)
2. What is done versus what patients would like (GREEN)
3. Long-term psychological impact (PURPLE)

Theme ideas
4. The role of maternity within cancer survivorship? (YELLOW)
5. Translation of knowledge (BLUE)

These key terms were then discussed within the supervisory team and further refocused to draft theme categories. The revised draft theme data were then explored further, in the context of existing evidence and knowledge gained from previous elements of PICCS1 (systematic review and questionnaire data). This evidence-based knowledge and real-life experience data then allowed for a further examination of the chosen themes, to ensure that the key findings and concepts had been represented and could be clearly seen. The draft theme generation process is illustrated below (Figure 29).

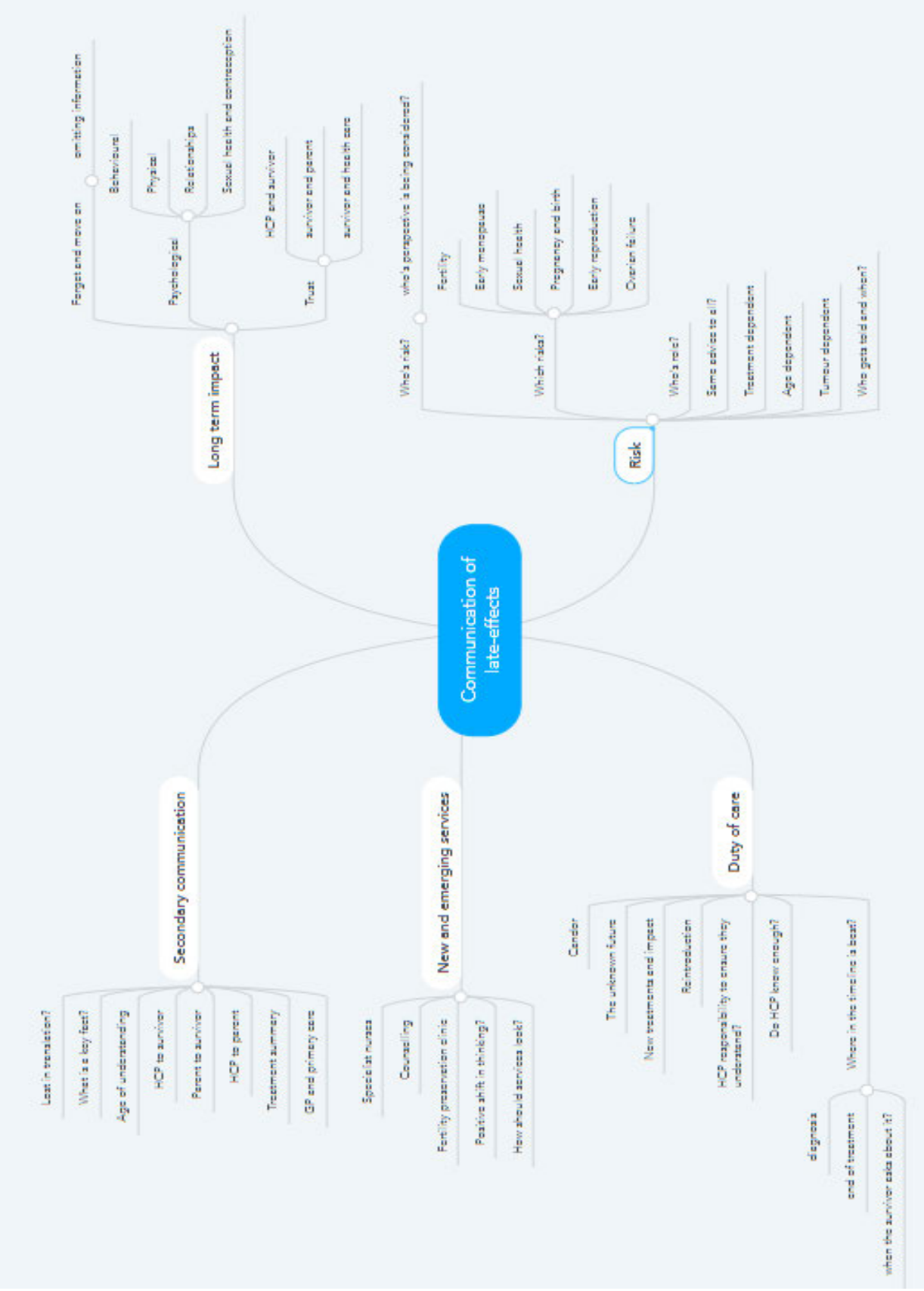

Figure 29 - Draft theme generation process (PICCS1 combined interview data)

The draft themes and the sub-elements in the mind map exploration were also compared to the original transcripts from the interviews, ensuring that data still reflected what the participants reported. This extra level of assessment was undertaken to reduce the risk of researcher bias. Following this process, the draft themes in their current form needed to be expanded to adequately represent the entirety of data as illustrated in the mind map (Figure 29). Therefore, new themes were constructed and reflected upon with the director of studies and the PPIE representative prior to final data synthesis and presentation of findings. The final theme generation process is presented in Table 40.

Table 40 - Theme generation process from PICCS1 semi-structured interviews

Original draft themes	Mind map categories	Final theme generation
The role of maternity within cancer survivorship? (YELLOW) →	New and emerging services →	Emerging practice
What is done versus what patients would like (GREEN) →	Duty of care →	Who, what, when?
HCP knowledge and awareness (RED) →	Risk →	Which late effects risk?
Translation of knowledge (BLUE) →	Secondary communication →	Honest and transparent communication
Long-term psychological impact (PURPLE) →	Long-term impact →	Long-term distress

The final theme choices, the pathway to selection and modification were shared

with the wider supervisory team to ensure transparency. The PPIE representative was asked to review the final themes and provided with anonymised extracts from transcriptions. He was also asked to confirm agreement on the themes and their representativeness within participant data. Each theme, including a presentation of evidence using direct quotations from the interview transcripts, will now be presented, and discussed.

6.5.3.1 Emerging practice

Participants revealed that discussions surrounding future fertility and wider reproductive health following treatment for CAYA cancer had improved in their content and frequency throughout the cancer journey, with many services now implementing new initiatives (i.e., discussion of fertility preservation at diagnosis) and were working to promote collaborative ways of working by using a wider multi-disciplinary team (MDT) for clinical discussions. Participants A, B and F described their service and how it had evolved in recent months to meet the needs of CAYA cancer survivors:

> ***Participant A*** *– "It's a new service …we are kind of still in our infancy…we have an MDT meeting which is dedicated to after-cure, where we discuss patients, and we've…started inviting one of the gynaecologists to come".* ***(HCP – Nurse)***
>
> ***Participant B*** *– "Now we do a 'ready, steady, go' transition programme with nurses".* ***(HCP – Nurse)***
>
> ***Participant F*** *– "Previously we haven't had a late effects clinic, we tended to look after our own patients… now we have developed a late effects clinic…at the point at which someone would be transitioning to it, you would re-introduce the concerns about fertility".* ***(HCP – Doctor)***

One CAYA cancer survivor described how this approach to collaborative MDT working using specialist roles, had impacted them and why they thought it was an important feature in their care:

> ***Participant C*** *– "The teenage cancer trust unit has just got a life after cancer nurse…she specialises in talking through things with the teenagers about long-term side effects…so that you don't feel like you've been dropped in the deep end right after treatment".* ***(CAYA cancer survivor)***

The structure of the MDT groups, whether professionals were included or invited and who was perceived as 'important' to be involved in the discussions, varied widely in the interviews of HCPs. Participant B described how their own multi-disciplinary team had expanded to include more diverse specialties:

> ***Participant B*** *– "We are lucky to have a paediatric endocrinologist now…we have access to adult endocrinologist that I work very closely with…we have a radiologist; oncologist and our adult long-term follow up team has a childhood cancer fertility specialist".* ***(HCP – Nurse)***

> ***Participant B*** *– "Obstetricians or gynaecologists are not included in our meetings, but we have good strong links with the fertility clinic".* ***(HCP – Nurse)***

The importance of acknowledging how a wider MDT team can positively impact the patient and the clinical team was discussed by Participant A:

> ***Participant A*** *– "Now as we've got someone that comes to our MDT we can say, this is what I will do, this is what you need to tell her and you know that is what the patient wanted…we are getting a lot more information and a lot more accurate information…rather than just sort of*

signposting, we…know what to tell the patients to expect". ***(HCP – Nurse)***

Participant B also agreed that the sharing of important late effects information should be extended to those professionals outside of paediatric oncology such as GPs. They described their feelings surrounding their responsibility as a HCP and what is required as part of their role:

Participant B *– "It's our job as long term follow up nurses, to ensure that young people are armed with the information they may need to pass onto services such as maternity care…we write it in their treatment summary in their care pack, which is given to the GPs".* ***(HCP – Nurse)***

However, Participant E and F reported that within their hospital MDTs, the 'collaborative model' approach was not yet happening. They described the stakeholder representation within their current MDT team and compared this to the perceived fertility and pregnancy needs of CAYA cancer survivors in their services:

Participant E *– "We don't have professionals in the MDT who provide the fertility advice, I don't know if the gynae MDT team do either".* ***(HCP – Nurse)***

Participant F *– "We are very involved with the endocrinology department, we haven't been so involved with obstetrics, but we have had several conversations…we tend to by-pass that stage".* ***(HCP – Doctor)***

Perhaps an explanation to the inconsistent MDT practices within the HCP interviews, can be explained by a lack of awareness of the most important late effects for CAYA cancer survivors? The findings from the systematic review and wider literature by Sandheinrich et al. (2018) and Nieman et al. (2007) reiterates the importance of effective communication for future fertility and reproductive health late effects risk for CAYA with cancer. However, as Participant A reported, in some cases they have not come across the need for this communication in some survivorship services to date:

> ***Participant A*** *– "I haven't come across anyone that needs that (pregnancy) information…I don't think it's a widely spoken thing at the hospital".* ***(HCP – Nurse)***

Fertility preservation is an innovative and rapidly developing element of CAYA with cancer care. Fertility preservation options and availability of specialist centres were of particular interest to the interviewees. Participant A recounted what was happening in their hospital at present:

> ***Participant A*** *– "Particularly for the girls there has been a lot of advancement in fertility preservation…a lot of the younger ones have gone for fertility preservation and they've had ovarian tissue taken for storage".* ***(HCP – Nurse)***

However, as Participant E described the referral pathway for fertility preservation is not yet standard practice within all treatment centres (if deemed medically appropriate at the time of diagnosis). Participant E described their current services and how things are beginning to change:

> ***Participant E*** *– "It depends on what treatment they're having as to whether they then are offered egg harvesting. Over the last 2 years we have sent more girls routinely now for egg harvesting at the beginning of treatment".* ***(HCP – Nurse)***

Conversations relating to fertility preservation, if they had taken place, were reported to have been within the first few weeks following diagnosis. Participant F discussed that such discussions are becoming more common place within CAYA cancer care:

> ***Participant F*** *– "With developments in ovarian reservation…discussions are now in the diagnostic conversations. There are arrangements to have ovarian strip preservation in the initial part of staging and treatment…so there is a change in practice".* ***(HCP – Doctor)***

Participant E described the situation where the CAYA with cancer may not want fertility preservation, reporting that even when this is the case, the conversation still needs to happen to provide the option:

> ***Participant E*** *– "Even if they don't want to harvest their eggs…they will discuss it with one of the specialists…it is offered to probably all our girls at the beginning".* ***(HCP – Nurse)***

In relation to future reproductive health information, interviewees reported that information tends to be delivered at the beginning of treatment:

> ***Participant A*** *– "We give information about how it (treatment) might affect their fertility…we say to them, we don't know what that will look like*

> *for your future, but if you want that looking into further then just get in touch with us…and we put them in touch with the gynaecologist".* ***(HCP – Nurse)***

Future pregnancy care advice for CAYA cancer survivors was discussed only by Participant B, who detailed what advice they would give during a consultation:

> ***Participant B*** *– "We make it clear that they should have an echocardiogram in their pregnancy period…it might be considered a high-risk pregnancy and that they should indicate to their maternity team that they've had abdominal radiotherapy".* ***(HCP – Nurse)***

> ***Participant B*** *– "We make sure that every patient has a treatment summary and also an individualised care plan". (HCP – Nurse)*

This finding was reflected in the discussions with CAYA cancer survivors and their parents with interviewees revealing little knowledge surrounding any extra measures needed during pregnancy or birth. This is despite the published evidence of increased pregnancy risks for female CAYA cancer survivors after receiving abdominal radiotherapy (van der Kooi et al. 2019). Participants G and H reported their experience of being pregnant as a CAYA cancer survivor and the care they received:

> ***Participant G*** *– "During pregnancy they didn't do any extra testing or scans or anything like that…no"* ***(CAYA cancer survivor)***

> ***Participant H*** *– "I saw an obstetrician and I told him about my history… I had all these concerns and he told me he had never heard of any complications from the treatments I've had, and he wasn't expecting anything to happen…he was expecting me to have normal pregnancy. So, at that point I was completely reassured".* ***(CAYA cancer survivor)***

> ***Participant H*** *- Any extra scans or any extra treatments during the pregnancy...no, no nothing, long-term follow up services?... no, they didn't mention anything about pregnancy risk".* ***(CAYA cancer survivor)***

The importance of future fertility to the CAYA with cancer was emphasised by Participant E as one of the most prominent issues facing young people affected by cancer. This reinforced data from the published evidence in the systematic review and the online questionnaires.

> ***Participant E*** *– "Fertility is one of the biggest issues for young people in survivorship…it's much easier these days for girls to go and harvest their eggs…it is far more routine practice for us to send them for fertility, egg harvesting".* ***(HCP – Nurse)***

However, data appeared to be unclear when discussing the importance of communicating future fertility risks at the time of diagnosis, when curative treatment is thought to be the sole focus. Participant F discussed the difficulty in getting the balance right for the family in clinical consultations:

> ***Participant F*** *– "At the beginning the emphasis is really on understanding the diagnosis, understanding the treatment, and getting on with the treatment for curative intent. We say late effects are very*

> *important, we do have to worry about those, but our first concern is to cure your child…then we will worry about the late effects later…they need to be alive for them to get a late effect. I think most families appreciate and understand that and are appreciative of the information".* ***(HCP – Doctor)***

Participant B reflected on the age of the individual and how if late effects information was communicated at a younger age and throughout the cancer continuum, then it was perceived to be easier to digest and would be more likely to be remembered long-term:

> ***Participant B*** *– "I would say the younger the child…the easier it is to share late effects information and to have…discussions over a period of years, building upon the information and responding to what the young person and their family need".* ***(HCP – Nurse)***

Ongoing support for CAYA cancer survivors following treatment completion and the re-introduction of key late effects information was reported to be variable between health care settings. Participant E discussed how support post-treatment tends to reduce unless patients contact the service:

> ***Participant E*** *– "Our role is to support patients throughout treatment and beyond…quite often the support tends to fade off when they've finished treatment. If need us they can always ring us, but we tend to be not as proactive at that point…most of the calls we get from people off treatment, I'd probably say a high proportion of that is how to access fertility treatment".* ***(HCP – Nurse)***

Signposting to other agencies was a theme within the discussions and as Participant A reported, survivorship services when faced with a question that they do not have the information to answer can often refer on to other departments and specialties. Interestingly, Participant A also reported that although HCPs refer on, they do not have much knowledge about what happens after the referral to be able to discuss with the patient and their family:

> ***Participant A*** *– "We can signpost for future pregnancy information…I don't know whether we know exactly, what that would entail when they got there…"* ***(HCP – Nurse)***

Good examples of supportive ongoing care for CAYA cancer survivors and their parents and the positive impact that this had upon long-term psychological well-being was discussed by Participant D:

> ***Participant D*** *– "They do a very good job…she obviously had a lot of questions…we had a meeting with long-term effects, and they scanned her again to be absolutely sure…they were very supportive of her, and they said, you know you had really awful treatment, it's just what they had to do at the time".* ***(Parent)***

Participant E discussed the role that the nurses play in this ongoing support for families, reporting that often the nurses are the ones that discuss the information in more detail following the consultation with the doctor:

> ***Participant E*** *– "We see 16-25-year-olds…the doctors get consent for the treatment and discuss future side-effects, but often they are followed up by the nurses for more in-depth discussions".* ***(HCP – Nurse)***

In conclusion, the theme 'emerging practice' encompassed the innovative, advancing techniques for CAYA with cancer and their future fertility. Reports from interviewees demonstrated that there was evidence of change to meet national standards and the needs of patients and their families, but services were not quite achieving this standard as yet. Pregnancy care for female CAYA cancer survivors was an area where little knowledge about individual risks or additional needs was demonstrated.

6.5.3.2 Who, what, when?

The theme who, what, when, relates to the views and experiences of the interviewees surrounding the HCP who delivered the late effects information, what that information consisted of and their opinion about when (i.e., time-point) the information should be communicated. The timing of future fertility late effects information, in particular 'at diagnosis' was a feature of the systematic review findings and also within the interview discussions as Participants A, D and E described in their own experiences:

> ***Participant A*** *– "Fertility preservation…that conversation happens at the beginning…The consultant discusses side effects as part of the work up…when they do their consent for chemotherapy, and they go through the side effects…fertility will be brought up then and they will go through it with them".* ***(HCP – Nurse)***
>
> ***Participant D*** *– "We had the fertility side-effects information right at the beginning because she started on chemotherapy without a diagnosis as*

she was so poorly…that's the best thing to do in the interests of the child because I think it's not good someone coming across that 10 years later and not have been told that's really not acceptable". ***(Parent)***

Participant E *- "They'll be given information on the risks to their fertility at the beginning".* ***(HCP – Nurse)***

However, consensus about giving information about future fertility late effects risk 'at diagnosis' was not evident in all the interviews. Participant C, G and H reported fertility information being discussed at various time-points throughout the cancer journey:

Participant C *– "The first thing I really heard about it (future fertility late effects) was when I was having my radiotherapy consultation…3 or 4 months after the initial diagnosis".* ***(CAYA cancer survivor)***

Participant G *– "It was around the time of being discharged…I don't really remember a lot; it was told to my parents and then was told to me".* ***(CAYA cancer survivor)***

Participant H *– "The information would have been given at the end of treatment".* ***(CAYA cancer survivor)***

The concept of 're-introduction' of information, as described in the literature of the systematic review, was also featured in interview discussions. Participant F, a HCP described how the re-introduction of late effects information took place in their treatment centre:

> ***Participant F*** *– "Later on we would re-introduce that conversation (fertility late effects) usually at the point where they are five years at the end of their treatment or moving into a late effects clinic".* ***(HCP – Doctor)***

Participant C elaborated on the concept of 'readiness' to receive late effects information, a theme also reported in the PICCS1 systematic review findings (Wright et al. 2014). CAYA with cancer have been reported as feeling blinkered and only able to visualise a future at the point of remission (Michel et al. 2020). This suggests that in individual cases, late effects information may not be appropriate at diagnosis, but would be welcomed upon the completion of treatment. This growth of curiosity about late effects, in particular future fertility risks, as remission approached was described by Participant C:

> ***Participant C*** *– "We didn't really touch on the subject (fertility) for a while, until I got close to remission, because that's when I was a bit more curious about it and could see the future at that point". (****CAYA cancer survivor)***

'Readiness' to receive the fertility or reproductive health information and the communication exchange between the parent (who had originally been given the information) and the CAYA with cancer was reflected upon in the interviews. The time point for when the exchange of key late effects information should take place between the parent and the CAYA with cancer, including the consideration of age and maturity suggested that parents of CAYA with cancer would welcome assistance and guidance as to how best to approach the issue. Participant G, H and C (CAYA cancer survivors) each discussed their thoughts

on age and understanding of key late effects information:

> ***Participant G*** *– "It's got to be at an age where the child can comprehend and understand what the information means…if they're so young say 7,8, 9 is not really going to be something that's in their thinking. I think it needs to be something that, targets the teenagers, as they know that fertility and pregnancy may be an issue".* ***(CAYA cancer survivor)***
>
> ***Participant H*** *– Around 11 or 12…my mum was on the lookout for signs of menstruation, because she was hoping that everything would be normal…she told me about it then, to kind of prepare me in case I didn't get my periods".* ***(CAYA cancer survivor)***
>
> ***Participant C*** *– My mum didn't really discuss it with me at the time…there's a lot of gory details that came out in that initial conversation. I wasn't part of that…it was my parents and my consultant. She wanted to make it as easy as it could be…so she withheld the information from me that point, but if I asked about it…she would have told me the information…it wasn't until a couple months after that I started asking questions…"* ***(CAYA cancer survivor)***

Participant B broached the issue of when it might be appropriate to talk directly to the CAYA with cancer about their risk of late effects. They alluded to the fact that this approach would be dependent on the age of the child. However, this raises the issue of who should be present during consultations of sensitive information such as future fertility. Wright et al. (2014) discussed this in PICCS1 systematic review findings, suggesting that the CAYA with cancer should be

provided with the opportunity to have this conversation without the parent (as long as deemed appropriate by the HCP). Participant B reported what happens within their service:

> ***Participant B*** *– "Communication of fertility late effects is usually a one to one with that young person, sometimes with their parent's present".* ***(HCP – Nurse)***

The HCP, and whose role it is to communicate fertility and pregnancy late effects information to CAYA with cancer and their parents, was described by two interviewees (HCPs):

> ***Participant B*** *– "My role is when they first come into clinic…we find out what they already know. I start with the parents, if the person is younger than 16, I find out what they know and then what they think their child knows, and we work from there".* ***(HCP – Nurse)***

> ***Participant C*** *– "I think the consultant would be the best because then you have that person…to go through the treatment with you and talk through the long-term side effects. Then after treatment, you can go back to that person and talk to them. I think the consultants are specialised enough and have the expertise but…maybe you need to have a specialist person such as a life after cancer nurse, that would be really important for people".* ***(CAYA cancer survivor)***

The content of the information – i.e. What future fertility late effects are discussed and if this is in enough detail for CAYA cancer survivors and their parents to make informed decisions about their care – revealed a lack of

agreement or knowledge surrounding the issue. Participant E described the challenge of trying to get the balance right:

> ***Participant E*** *– "I think it's really hard to know how much information to give them, how much they need at that point…I think probably at the end of treatment we could give more information".* ***(HCP – Nurse)***

> ***Participant E*** *– "I think because we're not fertility specialists, it's quite easy for me to say, 'you need to speak to the specialist team'…it's not our area of expertise…they might have questions, but we know the team that can help them".* ***(HCP – Nurse)***

6.5.3.3 Which late effects risk?

Specific fertility and pregnancy late effects risk were discussed by Participants A, E and F, who described their experiences from a HCP point of view. They detailed the specific late effects risks they would usually tell female CAYA cancer survivors and/or their parents during consultations:

> ***Participant A*** *– "I would start with…the problem you might face is that you'll be fertile for a shorter period of time, you know you're going to go into early menopause…don't wait to be having children".* ***(HCP – Nurse)***

> ***Participant E*** *– "We don't discuss the risk of carrying the baby or being able to carry a baby in utero…we focus more on whether they can get pregnant. Sometimes we mention there might be complications during pregnancy…if somebody had ovarian or gynae cancers, our surgeons*

quite often preserve as much function as they can, so they can hold a pregnancy…but I'm not always there for that type of consultation". ***(HCP – Nurse)***

Participant F *– "Families are warned more specifically if they are at a very high risk of infertility, whereas you just mention it to those have moderate or low risk".* ***(HCP – Doctor)***

From the CAYA cancer survivor and parent perspectives, interviewees recalled the information they were told in their consultations regarding possible late effects and their fertility. The comments below highlighted that there may be a discordance between the information the HCP gives to families and what they can understand and remember long-term. Participants C, D, G and H recalled their experience and what they remembered from their own consultations:

Participant C *– "I knew that it would cause late effects and I think somewhere in the back of my mind I knew that it would probably do something with my fertility…In the radiotherapy consultation I just remember this doctor just listing off all these side effects…infertility was one of them".* ***(CAYA cancer survivor)***

Participant D *– "They told me it could lead to ovarian failure…but at the time that didn't really mean much, to be honest…future pregnancy...no. I don't remember anything about that".* ***(Parent)***

Participant G *– "Pregnancy wise they had said I probably wouldn't be able to conceive…if I did conceive, I would have to be flat on my back for the whole of my pregnancy. I remember asking my surgeon 'what about*

having children?' and that's when he said, 'Well, we don't know whether you're fertile or not…but if you do become pregnant, he said you'll most likely be on bed rest for most of the pregnancy because your back will not be able to cope with the weight of the baby". ***(CAYA cancer survivor)***

Participant H *– "I was told that I might have fertility problems and if I could conceive that there may be problems carrying the baby".* ***(CAYA cancer survivor)***

The dilemma surrounding what specific late effects information (particularly for future fertility or reproductive health) should be provided, when and to whom to ensure long-term recall of key risks was discussed by Participant E:

Participant E *– "When is the right time to give them all of the information...because often they don't remember a lot of the consultation anyway, so I think even when they are given information, their recollection is that they've not had that information…so, I think knowing how much to give and when to give it is really difficult".* ***(HCP – Nurse)***

Late-effect risk classification, based on prior levels of treatment, the site of treatment, and age of the CAYA cancer survivor at the time of treatment were reported as important variables when discussing which late effects risks should be highlighted to CAYA with cancer and their parents. Participants B and F reported what they would consider when communicating future pregnancy risk:

Participant B *– "It depends on the treatment they've had …where they had the radiotherapy, what the dose was and chemotherapy, what the*

drugs were, what the doses were… we will discuss within our MDT what we think the risk might be for future pregnancy". ***(HCP – Nurse)***

Participant F *– "The range of infertility depends on how well an individual copes with treatment and the toxicity that an individual gets…it's very hard to give definite risk factors…we can put them in different risk categories of green, amber and red…but that is the most we can do right now".* ***(HCP – Doctor)***

Participant F *– "We would mention that there is a risk to fertility…the conversation would be different with a boy versus girl…future pregnancy risk in particular for female survivors depends on the diagnosis and the treatment…there are risks related to where it was given and what the risks are, so there is no one answer to that".* ***(HCP – Doctor)***

As an example of the discordance between what is communicated to families by the HCP and what is later remembered by families, sometimes years later was discussed by Participant D. They recalled their memory of being told about future fertility late effects:

Participant D *– "I remember being told…I've got lots of leaflets which do mention the radiotherapy and two lots of chemotherapy that she had…that can lead to infertility".* ***(Parent)***

Participant B highlighted an important caveat to being able to communicate all future risks, as some late effects from treatment are not yet known and may emerge unexpectedly into adulthood:

> ***Participant B*** *– "Even though two individuals might have had the same treatment it might be very different outcome for each…We've had girls where one side of their breasts have failed to develop, due to the radiotherapy field, which was not expected because it was flank, but that does make me think about what we really know?"* ***(HCP – Nurse)***
>
> ***Participant B*** *- Often it's felt that the uterus is tucked away, out of the way…I just feel that we haven't got enough information as professionals…if unexpected side-effects can happen to a breast which is so visible, then what's happened to a uterus that we can't see?* ***(HCP – Nurse)***

The communication exchange between the CAYA with cancer and the parent also featured in this theme and related to what specific future fertility and pregnancy risks should be communicated to families. Recall of conversations between parents and CAYA cancer survivors varied in detail between interviewees. The reliance on parents to effectively communicate key late effects information to their children by HCPs is therefore an area worthy of further exploration. Participants C and D described how key information was filtered by the parent or personally due to not wanting to accept the truth of their condition or future risks.

> ***Participant C*** *– "My doctor told my mum … that the radiotherapy and the chemotherapy would make me infertile…but my mom chose to keep that from me at that time because obviously there was a lot going on".* ***(CAYA cancer survivor)***

> ***Participant D*** *– "I know some of my friends, they just haven't remembered any information…and there's also that hope that it might not be true".* ***(Parent)***

Participants G and H recalled asking their parent for information about fertility and future pregnancy, but not obtaining any conclusive information to help them consider their risks:

> ***Participant G*** *– "I remember saying to my mum…will I be able to have children? and she sort of reiterated …'we just don't know'. She'd been made quite aware of the fact that my back would need to be quite well monitored because of the extra strain on it".* ***(CAYA cancer survivor)***

> ***Participant H*** *– "My mum told me to tell the obstetrician when I was first pregnant, that I'd had chemotherapy, radiotherapy because the doctors had told her to let them know, because there could be some complications with my pregnancy, if I did the conceive".* ***(CAYA cancer survivor)***

However, as Participant D reported, this does not happen in every case and there are instances of effective and clear communication between the parent and the CAYA cancer survivor:

> ***Participant D*** *– "We (parents) said to her that her ovaries were probably damaged…we explained that with girls who are able to and want to get pregnant, the fertility of their eggs or sperm after so much harsh treatment…there could be problems, and with the pregnancy…the ability to hold a pregnancy of a future child".* ***(Parent)***

Late-realisation of damage to reproductive organs caused by treatment for cancer was described by Participants B and H, as a shock. This led to concerns about the standard of health care they received and subsequent long-term psychological effects in adulthood. Participant H recalled their experience of finding out about late effects that could have occurred, following a pregnancy:

> ***Participant H*** *– "I found out years after that the drug I'd had can actually damage your heart, and that I actually should have had some sort of monitoring and an echo, which I've subsequently had and luckily my heart is completely normal, there is no cardiomyopathy. Having read up a bit more about it, I do think there were risks, potentially, and I read that if the radiation is near the uterus, then it can cause the uterus not to stretch properly and that sort of thing".* ***(CAYA cancer survivor)***

The theme, 'Which late effects risk' reflected that CAYA cancer survivors, parents and HCPs all agreed that a 'one-size fits all' approach is not appropriate when discussing late effect risks such as future fertility. Individual risk of late effects is variable and dependent on a multitude of factors (such as treatment received) and personal/emotional circumstances (maturity, age at time of treatment). Key late effects information was reported to be at risk of being filtered or held back by the HCP or parent, based upon assumptions that CAYA cancer survivor's might not be ready to receive the information or in a protective capacity as a parent, shielding possibly upsetting information at an already distressful time.

6.5.3.4 Honest and transparent communication

The manner and delivery of future fertility late effects information from the perspective of the CAYA cancer survivor, parent and HCPs interviewees were collated and presented within the theme 'Honest and transparent communication'. Recommendations for how health care services can adapt in their approach to communication of late effects to be more open and transparent were considered by participants, with an overall feeling that partnership between the CAYA with cancer, parent and the HCP was the key to addressing unmet informational needs.

Knowledge of future fertility status and reproductive health risks from cancer treatments were found to be the biggest unmet informational needs of CAYA cancer survivors in the PICCS1 systematic review (see Chapter Five – Systematic review of the literature). CAYA cancer survivors in the interviews reported a feeling of 'not being given the whole picture' when future fertility risks were discussed with HCPs or their parents. Participant A reflected on the information they provide to patients and how complete they considered this to be:

> ***Participant A*** *– "Future fertility and pregnancy advice…I think it's definitely an area that we are lacking…we need a bit more information to give out to families. I think that we could be a little bit clearer, and a little bit more direct with what we tell them…so rather than say if you've got a problem then we'll find out in the future…we could spend more time*

> *saying, 'I think you definitely need'…we need to be a bit more open with them".* ***(HCP – Nurse)***

Participant A also described an assumption of knowledge that CAYA cancer survivors would feel comfortable disclosing their medical history and future reproductive health risks to other HCPs outside of paediatric oncology. Participant A described their view that CAYA cancer survivors should be aware of their risks and be happy to discuss them with other HCPs:

> ***Participant A*** *– "I don't know whether I've got enough knowledge to answer…I think as far as carrying a child, I think if there was to be any issues, I'd hope that they'd have been told that…I would hope that anyone who was going to have the baby, would be able to inform midwives at the time and say there is a risk…and not be completely unaware…"* ***(HCP – Nurse)***

The issue of discussing late effects risk with wider HCP disciplines was also raised by Participant H who described the need for not only CAYA cancer survivors and parents to be aware of late effects risk, but also the wider HCP disciplines:

> ***Participant H*** *– "I think women need to be informed, but I think also the general medical population need some more information as well…they didn't seem to know stuff that I think they should have known…I could have had cardiomyopathy, for example and I didn't know, and I had 3 vaginal deliveries, births and labour and could have had a heart attack or*

> *whatever, you know…I think it is important for everyone to know the risks".* ***(CAYA cancer survivor)***

The difficulties that HCPs face when providing future fertility risk information to CAYA with cancer and/or their parents and if they considered their knowledge to be at a sufficient or competent level was debated by Participants A and F:

> ***Participant A*** *– "We still have a child with cancer, we will do whatever we need to do, so I think at that stage (at diagnosis) then definitely yes…they get told what they need to get told and basically we won't know how the future looks until the future happens".* ***(HCP – Nurse)***

> ***Participant F*** *– "I think in the beginning the information is usually enough and families have got enough to deal with…trying to deal with the immediacy of a diagnosis and the problem, and at that moment in time, concerns about the child's life are paramount. Trying to make sure that their treatment is directed expeditiously…I think at that point they are given sufficient information".* ***(HCP – Doctor)***

HCP participants in the interviews discussed the challenge of keeping focus at diagnosis on active treatment and cure and how late effects information is usually perceived as being the focus once active treatment is complete:

> ***Participant B*** *– "Prior to the patients coming into long-term follow up, the late effects information is sketchy at best. I think that until they come into long-term follow up, the focus still remains on treatment. Follow up focuses on looking for disease returning rather than preparing for the future…I think that sometimes that gap between treatment finishing and*

> *coming into long-term follow up is a missed opportunity…sometimes we are giving information too late".* ***(HCP – Nurse)***

Participant C reiterates that communication of late effects risk is very much dependent on when the individual is ready to receive it. However, by giving the information earlier, then it gives the CAYA with cancer and their family time to digest the implications and feel like they haven't been withheld key risks:

> ***Participant C*** *– "I think late effects information should be given fairly early on, maybe not right with the diagnosis…depending on who you are, if you can take all that information, right there and then, then maybe. Maybe within the first few months of diagnosis…I think it's simple enough to have a chat about the long-term side effects and things".* ***(CAYA cancer survivor)***

> ***Participant C*** *– "I think introducing information early on would help people feel like they're not being deceived or being withheld information…they can kind of focus on their futures a bit more, what they are going to do about the infertility".* ***(CAYA cancer survivor)***

Time to reflect upon the information, to be able to process key facts, and understand what that means for the future was a key factor highlighted by Participants B and C. They described that by communicating information in a complete, open, and honest way, then the CAYA with cancer can process the information properly and at their own pace:

> ***Participant B*** *– "If they've had radiotherapy and if there is any possibility of any scatter then, we should be letting young people know because,*

that at least then gives them something that they can work with, when or if they do come into fertility problems". ***(HCP – Nurse)***

Participant C *– "It's really important to tell the person early so that they can take action early, so that if they want to go down the route of freezing their eggs or their ovaries or their sperm, they can do, because that option was never given to me…maybe at the time, I would have wanted that".* ***(CAYA cancer survivor)***

Participants C and D reported how open and honest communication positively affected their psychological well-being:

Participant C *– "It helped me, that I kind of had my treatment time to just digest the information…begin accepting it and working it through in my head".* ***(CAYA cancer survivor)***

Participant D *– "I think we were very fortunate we were given all the information…I think just be totally open and honest, I can't fault that at all".* ***(Parent)***

However, Participant G reflected on their experience and how things have changed over time and their experience of being told about risk of fertility late effects second-hand from their parents:

Participant G *– "Things have changed a lot…I think children do need to know how the effects will affect them for the future…it isn't just something, like a cold, you just get over it and then you're fine…it does*

actually come into play when you think about fertility and pregnancy". ***(CAYA cancer survivor)***

Participant G *– "I think you need to be completely fully aware. It was quite hard for me, because I was only 14 when it happened…my parents were more informed than I was…it was very much a case of 'we tell the parents things that the children don't need to know".* ***(CAYA cancer survivor)***

Information recall of parents, sometimes many years after treatments and the transfer of communication between parents and the CAYA with cancer was a prominent feature within the theme of honest and transparent communication. Participant H described what they thought their ideal method for parental-child communication of late effects risk was:

Participant H *– "I think the information needs to be put on the child's medical file…so the GP can print off some information when they get pregnant…and you need it in a record in your own notes as well as the parents being told the information I think, because what if your parent dies or what if you just don't get the information?"* ***(CAYA cancer survivor)***

However, as Participant H described, sometimes information was communicated effectively by the parent to the child. This suggests that there might not always be a problem in the communication exchange or recall of parents:

> ***Participant H*** *– "As a child you're relying on your parents to take on board the information and then pass it to the child at the right time, or as the adult…my mum she got a big pack of all the stuff from years ago, but she can hardly remember now what she was told and when she was told, but she retained the important bits to tell me about fertility and pregnancy".* ***(CAYA cancer survivor)***

Working together across HCP disciplines to share key information about the CAYA cancer survivor and their future reproductive risks, e.g., treatment-related pregnancy risks, was highlighted by participants as an important area to address. The transcripts revealed that paediatric oncology HCPs perceive issues such as future pregnancy to be out of their scope of practice. Participant E revealed in their experience, a lack of awareness about possible health risks in pregnancy and recommends that wider HCP disciplines need to have a knowledge of this area to be able to communicate risks to patients effectively:

> ***Participant E*** *– "The cancer arises in our setting doesn't it…I wouldn't know what problems there might be beyond our setting, so I don't know how it might affect the maternity services and whether there are common issues…we don't have any feedback, so I guess you have to ask the gynaecology teams or obstetric teams".* ***(HCP – Nurse)***

> ***Participant E*** *– "I think at the point for them carrying a baby we tend to not have too much involvement, so I wouldn't know what the risks are…I don't know if we need to work more closely with those who do know how to look after them".* ***(HCP – Nurse)***

Participant H discussed the assumption that HCPs in maternity services know about the possible health risks for female CAYA cancer survivors and that they would be expected to have the knowledge and skills to appropriately risk-assess and support women with this medical history:

> ***Participant H*** *– "In the midwifery sphere, they need to know about late effects, and they should be informed and have some information, so that they're prepared to give the best care…I think in the community, not one of the community midwives knew what the risks were, of having had the treatment I'd had, so I think it would be useful for health care professionals to have some basic information".* ***(CAYA cancer survivor)***

However, as Participant B highlights, trying to raise awareness of a HCP discipline as a whole, such as maternity services would be difficult to achieve:

> ***Participant B*** *– "It would be very difficult to ensure that everybody in maternity services is aware…I think it's a good idea to have an understanding…but informing specific individuals would be very difficult".* ***(HCP – Nurse)***

The issue of future reproductive health risk and providing accurate information to CAYA cancer survivors was also discussed in the context of sexual health and sex education. Participant B highlighted that future fertility and reproductive health extended beyond being fertile or becoming pregnant:

> ***Participant B*** *– "Also things like discussing sex with young people, you know I think it's all very well thinking about pregnancy but actually how do you get pregnant in the first place?"* ***(HCP – Nurse)***

6.5.3.5 Long-term distress

The interviewees in PICCS1 reported a link between not having the late effects information they needed for adulthood, and an increased level of emotional distress and unrest. This mirrors the evidence from the PICCS1 systematic review (see section 5.5.3.4 Awareness). Participants shared their personal thoughts and feelings reflective of their experiences and the long-term psychological impact of unmet informational needs. Participant D, a parent of a CAYA that had cancer, described in detail their experience and how this has affected her child:

> ***Participant D*** *– "I do remember at the time of being told (about infertility) …and just looking at her thinking 'oh' that's awful, but we have to do what we've got to do now…We've been through quite a lot of testing, since she was about 12, and she is totally infertile…It's really difficult for her to cope with obviously because she was told when she was 12. We had a good inkling it might be a possibility…but for her to hear that was very very hard and it wasn't done in the best way either, quite blunt…we weren't expecting the kind of brutality of being told like that…she was only a child".* ***(Parent)***

Participant G described that in their experience, the manner in which late effects information was communicated to them was very different to what happens today and is now much improved:

> ***Participant G*** *– "I was never told anything about any long-term effects…so hence when the long-term effects did hit me, it was a big*

> *shock…the mindset…your better now, leave the hospital, forget about it and don't mention it again is damaging…thankfully, that doesn't happen anymore because it's damaging psychologically. They are so much better now at treating children and young adults in the whole scheme of things".* ***(CAYA cancer survivor)***

Delivery of future fertility late effects information and the compassion and sensitivity of HCPs were discussed by CAYA cancer survivors and parents. The transcripts highlighted that if this information is not communicated sensitively then this is damaging for families. Participant D recalled their experience and the effect it had upon them:

> ***Participant D*** *– "The doctor was very blasé thinking that it wouldn't be menopause…that nothing would show up at this point, but as soon as she did the bloods, she just said, 'oh you're totally infertile, you'll never have a child, you'll have to have a surrogate'. My daughter was just like 'oh, ok'…there was no preparation…we went to get to get results and there was no, like, 'oh I'm really sorry' or anything, it was just very very brutal".* ***(Parent)***

Long-term psychological effects caused by the diagnosis of infertility were described by Participant D. The concept of 'one's own child' or 'being able to have a normal family' in adulthood was felt to be very important to both the CAYA cancer survivor and the parent:

> ***Participant D*** *– "It does affect her quite a lot… she does have therapy… but obviously she's very upset as that's what she wanted in life, to have*

children and have a little family. There's been times when she's been angry with us…I can certainly appreciate how she feels". ***(Parent)***

Interestingly, not all the CAYA cancer survivors reported an adverse psychological impact of being told they would be infertile. Participant C described their point of view and how early communication of potential late effects helped them process their thoughts around childbearing in the future after cancer treatment:

Participant C *– "At that time I wasn't really bothered about future fertility, I kind of just kept it to myself. I talked to my mum about it every so often, but I never got upset or anything because, you know, I knew that there were bigger hurdles…it was kind of a small problem in a heap of larger ones…I would have felt a lot more upset if I kind of found out after the treatment or say, you know, however many years' time and then I was trying for a baby and then realise I couldn't".* ***(CAYA cancer survivor)***

Participant C *– "It (infertility) definitely doesn't impact my everyday life. I'm quite lucky…I've accepted it and I can see a way forwards, I don't see it as a thing that will hold me back as such, there's other methods out there like adoption. I don't see it ever affecting my lifestyle in a way, or my mental health or anything like that. So, I'm quite lucky that I have that perspective on it".* ***(CAYA cancer survivor)***

The perception that the CAYA with cancer might not survive long enough to consider future fertility issues or pregnancy and the impact of this on their psychological well-being was discussed by Participant G:

> ***Participant G*** *– "I kind of just thought, oh I'm not going to live long enough to have children anyway, so I just put it to the back of my mind and that was that. I wasn't too upset because I didn't think I would live long enough to have a family".* ***(CAYA cancer survivor)***

The individual experiences and insights of CAYA cancer survivors, parents and HCPs provided a unique reflection of how communication of information impacts upon families long-term. Participant G reflected upon another aspect to the communication of late effects risk, highlighting that sometimes survivors might not want to acknowledge their cancer diagnosis as a child once they reach adulthood. HCPs need to be aware of this medical history omission risk and not rely on the survivor to communicate their cancer history, but to utilise medical record data as standard. Participant G discussed how they approached their cancer history as a child when they became pregnant:

> ***Participant G*** *– "I became very much in denial about the fact I had ever been poorly, I wouldn't mention cancer, I think I told the midwife once and then never mentioned it again. So, I was sort of like, if they don't talk about it, I'm not going to talk about it. When I got pregnant the second time, I just didn't mention it from the start…I just didn't tell anybody and didn't remind anybody, I didn't want any extra care, I didn't want anybody to be giving me anything that reminded me that I'd been ill".* ***(CAYA cancer survivor)***

> ***Participant G*** *– "The pregnancies were the healthiest I've ever been! I did tell the midwife when I was pregnant with my first child, I did tell them about my back, but kept it very sort of light-hearted and didn't really give*

> *them much of an idea of the severity of it. I was under consultant care for the first pregnancy, but I was so well, that I didn't have to have a consultant for the rest of them".* ***(CAYA cancer survivor)***

Retrospective thoughts surrounding what complications could have happened during pregnancy was raised by Participant H. This unique insight, although reflective of one person's view, suggests that a lack of information about risks can affect CAYA cancer survivors psychologically, even many years after treatment, a healthy pregnancy and optimal birth outcome for mother and child:

> ***Participant H*** *– "Nobody told me about the pregnancy risk…I knew about the fertility thing, which I think is important for every female to know, and I knew there was a risk to the pregnancy…but the obstetrician told me there wasn't. I could have had cardiomyopathy, for example, and I didn't know, and I had 3 vaginal deliveries, births and labour and could have had a heart attack or whatever, you know…I think it is important for everyone to know the risks".* ***(CAYA cancer survivor)***

Another long-term psychological impact of an infertility diagnosis or high-risk of future pregnancy complications caused by cancer treatments is whether this information affects future childbearing choices of CAYA cancer survivors. Participant D recalled their daughter's feelings surrounding her diagnosis of infertility:

> ***Participant D*** *– "She's kind of resigned to it now…she says, 'well my body probably wouldn't have coped with it anyway'…she's got quite a small womb and it's got a section down the middle of it as well".* ***(Parent)***

Participant G described the advice they were given by a HCP regarding risks in a future pregnancy:

> ***Participant G*** *– "If you do become pregnant, he said you'll most likely be on bed rest for most of the pregnancy because your back will not be able to cope with the weight of the baby".* ***(CAYA cancer survivor)***

Long-term distress or adverse psychological impact caused by unmet informational needs was a strong theme throughout the CAYA cancer survivor and parent transcripts. HCPs thoughts surrounding the psychological impact of cancer treatment as a CAYA and the link to communication of late effects risk was not seen on a comparable level within collected data.

6.5.4 PICCS1 interviews – theme summary

Interviews were conducted with eight participants, representative of four patient/parent and four professional categories. The analysis from data provides evidence of a CAYA cancer survivorship care pathway that is beginning to change and adapt to meet the constantly individualised unmet needs of CAYA with cancer. However, the timing of information, the content and detail of risk communication, the person who communicates the information and the way it is communicated still requires further investigation and resolution. When communication of risk is applied to the communication of future fertility and reproductive health late effects risk (including pregnancy and birth), it is particularly pertinent to raise awareness of the link between long-term psychological distress and levels of unmet informational need, even years after

treatment has been completed.

The interviews illustrated a CAYA cancer survivorship service that is reactive, not proactive, reflecting a ‘learn as we go’ approach. This method, although assisting HCPs to pilot new interventions, explore what works in their service and consider feedback from families, takes time to filter through into a measurable and effective long-term impact for patients. HCP awareness surrounding a number of future fertility and pregnancy late effects risks is evident, however there is notable ambiguity surrounding whose job it is to discuss this with patients, what to discuss, and when. The CAYA cancer survivor and parent perspectives call for an honest, understandable, and compassionate method of communication, recognising that future fertility is a significant priority for them as an individual and as a family and that it may affect them long-term many years past treatment completion.

There are a wide range of clinical variables that affect the risk of late effects, such as type of cancer, treatment modality, age at the time of treatment/diagnosis and their likelihood of survival. HCPs in the interviews reported difficulty in trying to balance accurate evidence-based information about late effects risk and retaining a focus on survivorship and treatment of the cancer.

Long-term psychological impact of unmet informational need was a key finding within the interview transcripts. The experiences of the interviewees reflect multiple factors that contribute to the level of distress experienced by CAYA cancer survivors and that a solution to this cannot be a ‘one size fits all’ approach. Likewise, parents need support and guidance to help them

communicate important future health information and in a format that they can keep and give to the CAYA cancer survivor, to reduce recall bias and the omittance of important health risk information.

The themes generated from the thematic analysis of the transcripts; Emerging practice, Who, what, when?, Which late effects risk?, Honest and transparent communication, and Long-term distress, reflects the experiences, opinions and values of the interviewees and provide the basis for the next study PICCS2, identifying the key areas for further investigation by the expert panel.

6.6 PICCS2 – Modified Delphi consensus

6.6.1 Introduction

Following the completion of PICCS1, the PICCS2 study (using a modified Delphi consensus technique) was designed by the researcher. The use of the modified Delphi technique represented the ‘actual’ domain of reality, in the context of the philosophical framework. An expert panel of 19 stakeholders took part in three rounds of email (round one), email (round two) and web-based face-to-face (round three) meetings with an overall participation rate of 91.2%. The design of the PICCS2 statements were guided by the cross-cutting themes from the individual elements of PICCS1.

6.6.2 Design and recruitment

A set of draft suggestions for statements/questions were emailed to consented

panel members for their consideration and agreement, prior to the commencement of round one of the modified Delphi technique (see Appendix 5). A copy of the draft statements was also sent to the PPIE representative for approval.

6.6.3 Expert panel

Invitations to prospective expert panel members were sent to 30 individuals from a wide range of stakeholder backgrounds. Out of the 30 invitations sent, 20 participants consented to take part in PICCS2. The composition of the expert panel (see Table 14) represented five parents/survivors, five wider HCPs, four fertility/pregnancy specialists, and five paediatric oncologists.

6.6.4 Round one

Feedback received from the panel members and the PPIE representative from the draft statements were considered by the researcher and then incorporated into the design of the round one template. Recommendations were received requesting edits or amendments to the terminology, numbering of statements and some panel members expressed their thoughts about statements being mutually exclusive or too similar. This feedback was considered, and edits made.

There was a pause in the PICCS2 study (due to a three-month clinical redeployment of the researcher caused by the COVID-19 pandemic). Therefore, panel members that had originally consented to the study prior to the pause in

recruitment were asked to re-confirm their consent at the point where round one re-commenced. Panel members were asked by email to re-confirm that they were happy and able to take part in the study once more. One panel member confirmed that they would have to withdraw due to clinical work commitments caused by COVID-19. This left 19-panel members who consented to take part in round one.

Round one commenced on 29th June 2020, the panel were asked to read statement (or question) and rank each possible option for each ranging from 1-9, using the Likert scale. The panel were asked to respond within 14 days. A reminder email was sent after seven days of the deadline. All 19-panel members returned their responses. Two of the panel members failed to rank all the question options, resulting in missing data. Where this occurred, the number of missing responses has been indicated in the results table.

The findings were then analysed by the researcher to produce the mean, the total number of votes in the 7-9 category and calculated for 70% consensus achievement. The result was then marked on the results table as a pass or fail. The justification for the 70% cut-off can be found in section 4.3.2.3 Statistical analysis. A full report of all the outcomes can be found in Appendix 9.

Data were adjusted for missing data if present in the question options. The mean and the calculations for the 70% pass rate were performed by the researcher. The 70% consensus rate was calculated by multiplying the number of selections under numbers 7-9 of the Likert scale. If the responses in the 7-9 category reached 70% of the total responses for that option, then they passed (e.g., 19 responses for the question, 2 participants selected 9 from the Likert

scale = 18. No other selections for the 7-9 of the scale. Therefore 70% of 19 = 13.3. Total from responses was 18, so option passed the 70% rate).

Table 41 - PICCS1 Round one top ranked statements

What are the most important themes for future fertility and pregnancy?														
Theme	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**Missing**	**Total**	**Mean**	**Total 7-9**	**70% Rate**
Identifying the best time to communicate information							6	5	7	n=1	18	8.05	18	Pass

Q1 Which of the following late effects risk for future pregnancy do you think are HIGH PRIORITY for communication to the female child/teen/adolescent (CAYA) with cancer and/or their parents?														
Late effects risk	**Not important**			**Unsure**			**Agree**			**Missing**	**Total**	**Mean**	**Total**	**70% Rate**
Difficulty becoming pregnant						1	4	4	10		19	8.21	18	Pass

Q2 What STAGE in the cancer journey do you think is the most appropriate TIME to FIRST communicate any future PREGNANCY or FUTURE FERTILITY risks related to treatments?								
Appropriate Time	**Not important**	**Unsure**	**Agree**	**Missing**	**Total**	**Mean**	**Total**	**70% Rate**
ALL OPTIONS FAILED TO REACH CONSENSUS								

Q3 What STAGE in the cancer journey do you think is the most appropriate TIME to REINTRODUCE information about any future PREGNANCY or FUTURE FERTILITY risks related to treatments?													
Appropriate Time	**Not important**			**Unsure**			**Agree**			**Missing**	**Total**	**Mean**	**Total**	**70% Rate**
Upon wanting to start a family	4						2	3	10		19	6.94	15	Pass

Q4 What STAGE in the cancer journey do you think is the most appropriate TIME to speak DIRECTLY to the female CAYA cancer survivor and REINTRODUCE information about any future PREGNANCY or FUTURE FERTILITY risks related to treatments?													
Appropriate Time	**Not important**			**Unsure**			**Agree**			**Missing**	**Total**	**Mean**	**Total**	**70% Rate**
Upon wanting to start a family	1	1			1		1	8	6	n=1	18	7.38	15	Pass

Q5 WHO do you think is the most appropriate professional to FIRST DISCUSS information with the CAYA with cancer and/or their parents?													
Professional	**Not important**			**Unsure**			**Agree**			**Missing**	**Total**	**Mean**	**Total**	**70% Rate**
Paediatric oncology consultant				1	1	1	5	2	9		19	7.73	16	Pass

Q6 WHAT is meant by being FERTILE following cancer treatment?													
Meaning	**Not important**			**Unsure**			**Agree**			**Missing**	**Total**	**Mean**	**Total**	**70% Rate**
Being able to conceive a pregnancy naturally					2		1	3	13		19	8.31	17	Pass

Q7 A summary of treatments received, and late effects related to future fertility and pregnancy should be COMMUNICATED to the following professionals outside of paediatric oncology upon treatment completion:													
Professional	**Not important**			**Unsure**			**Agree**			**Missing**	**Total**	**Mean**	**Total**	**70% Rate**
GP							1	4	14		19	8.68	19	Pass

Q8 The FORMAT of a treatment summary with late-effect risk information for FUTURE FERTILITY and PREGNANCY should be available for CAYA cancer survivors and health care professionals as an:														
Format	**Not important**			**Unsure**			**Agree**			**Missing**	**Total**	**Mean**	**Total**	**70% Rate**
A combination of written information and online resource						1	2	2	14		19	8.52	18	Pass

Q9 PARENTS should be offered a session with a health professional at treatment completion about HOW to communicate late effects to female CAYA cancer survivors regarding FERTILITY and PREGNANCY with:														
Type	**Not important**			**Unsure**			**Agree**			**Missing**	**Total**	**Mean**	**Total**	**70% Rate**
Face-to-face session with the nurse or other health care practitioner					4		3	3	8	n=1	18	7.61	14	Pass

Q10 A glossary of terms or lay summary which helps to EXPLAIN information used in relation to late effects of treatment and FUTURE FERTILITY and PREGNANCY should be included in the treatment summary plan														
Method	**Not important**			**Unsure**			**Agree**			**Missing**	**Total**	**Mean**	**Total**	**70% Rate**
Verbal explanation to female CAYA cancer survivor when reaches age of maturity					1	1	2	2	13		19	8.31	17	Pass

Q11 UNMET NEEDS for late effects regarding FUTURE FERTILITY and PREGNANCY of female CAYA cancer survivors and/or parents should be re-evaluated at the following TIME points:														
Time point	**Not important**			**Unsure**			**Agree**			**Missing**	**Total**	**Mean**	**Total**	**70% Rate**
When accessing fertility services		1			1		2	3	12		19	8.05	17	Pass

Q12 The UNMET NEEDS of female CAYA cancer survivors for late effects related to FUTURE FERTILITY and PREGNANCY should be evaluated BY:														
Professional	**Not important**			**Unsure**			**Agree**			**Missing**	**Total**	**Mean**	**Total**	**70% Rate**
Long-term follow up doctor (not oncology)	1				1		1	5	11		19	8	17	Pass

Q13 The UNMET NEEDS of female CAYA cancer survivors for late effects related to FUTURE FERTILITY and PREGNANCY should be evaluated WITH the following resources/tools:														
Unmet needs	**Not important**			**Unsure**			**Agree**			**Missing**	**Total**	**Mean**	**Total**	**70% Rate**
Face-to-face consultation with professional					1	1	3	2	12		19	8.21	17	Pass

6.6.4.1 Round one - Free text analysis

Round one offered the panel the option of providing feedback with free-text comments added to each of the statements (questions). Free text entries were collated using a *Microsoft Word* document and then uploaded to the *NVivo* (QSR International 2021) software programme. The text was then coded by colour and grouped by similarity in the meaning, concept, or terminology of the text. The researcher then filtered the colour-coded groups into draft themes or contextual groups. A summary of data within each contextual group was then fed back to the panel (see Table 42). This replicated the thematic analysis and theme generation process used in PICCS1 based on the framework by Braun and Clarke (2006). The process in this instance was simplified as the quantity of data was small and in-depth analysis was not required to provide informative feedback to the panel before round two. This simplified analysis method allowed for rapid consideration of the summarised themes from free-text data alongside the findings from round one that had passed or failed consensus. The summary themes from the free text entries provided to panellists from round one is illustrated in Table 42.

Table 42 - Themes from the free-text (PICCS2 round one)

Themes from the free text (PICCS2 round one)
Face-to-face conversation with someone that knows about future fertility
Is difficulty becoming pregnant the most important risk?
The right age, at the right time, what does this mean?
Reiteration of information, evaluation of needs, openness, and honesty
What is the correct definition of fertility or being fertile?
Combination of format for information delivery advised

The panel were emailed the findings of round one and the free-text feedback using the Bcc function to uphold anonymity of the panel. The panel were asked to email the researcher with any comments, queries, or questions within seven days of sending the findings. All panel members were satisfied with the summary and feedback and no rebuttal or questions were raised for round one.

6.6.5 Round two

The revised statements for round two were emailed to the panel on 9th September 2020. Any feedback received from the findings of round or the free text summaries were considered and reflected upon by the researcher, prior to the design of the second round. Feedback from round one was minimal and related to the terminology of the statements rather than content or number of options provided. There were no comments relating to the free text summaries, the process for calculating consensus, nor the options that were identified to be borderline. Therefore, the borderline statements were left in by the researcher for round two to enable panellists to consider this option once more before

removal from the list.

The proposed statements for round two were assessed for comprehension and readability by the PPIE representative prior to being sent to the panellists. The format of the statements was altered in this round to be more reflective of statement of advice, rather than being framed as a question. This choice was made to ensure that the statements aligned with the Delphi consensus technique model of agreement (see Chapter Three – Methodology).

The ranking of the first statement, (Q1 - What is the most important theme for future fertility and pregnancy late effects?) was removed for round two as consensus had been achieved for all options in round one (>70%). This signified that all options had been validated and were of importance to the CAYA cancer survivor/parent/HCP populations.

Panel members were asked to rank the statement options from 1-9 using the Likert scale, with no free text permitted. Responses were received by all 19 panellists. No queries or uncertainties were voiced during the round. Responses were analysed by the researcher to calculate the mean, the total number of responses marked 7-9, and responses calculated for the 70% consensus rate and marked pass or fail. This was calculated by using the total number of responses in the 7-9 category divided by the total number of responses for that statement option. There were no borderline outcomes in this round. The top ranked statements for round two are presented below (Table 43).

Table 43 - PICCS2 Round two findings

Q1 Health Care Professionals should communicate the following future fertility and pregnancy risks to female CAYA cancer survivors and/or parents (risks vary depending on treatment received):														
Time-point	**Not important**			**Unsure**			**Agree**			**Total**	**Mean**	**Total 7-9**	**70% Rate**	**Missing**
Difficulty becoming pregnant					1		3	2	13	19	8.36	18	Pass	

Q2 Health Care Professionals should FIRST communicate (either to the CAYA cancer survivor and/or parent) potential future fertility and pregnancy late effects:														
Time-point	**Not important**			**Unsure**			**Agree**			**Total**	**Mean**	**Total 7-9**	**70% Rate**	**Missing**
At diagnosis	1	1		1	1	1	3	2	9	19	7.15	14	Pass	

Q3 Health Care Professionals should RE-INTRODUCE potential future fertility and pregnancy late effects:														
Questions	**Not important**			**Unsure**			**Agree**			**Total**	**Mean**	**Total 7-9**	**70% Rate**	**Missing**
Upon completion of treatment				1	2		3	2	11	19	7.89	16	Pass	

Q4 The most appropriate age to discuss future fertility and pregnancy late effects with the female CAYA cancer survivor is:													
Age	**Not important**			**Unsure**			**Agree**			**Total**	**Mean**	**Total 7-9**	**70% Rate**	**Missing**
When the female CAYA cancer survivor reaches age 16 years	2		1		1		1	4	10	**19**	**7.31**	**15**	**Pass**	

Q5 Health Care Professionals should talk directly to the female CAYA cancer survivor about future fertility late effects:													
Time-point	**Not important**			**Unsure**			**Agree**			**Total**	**Mean**	**Total 7-9**	**70% Rate**	**Missing**
Upon the female CAYA cancer survivor wanting to start a family							3	4	12	19	8.47	19	Pass	

Q6 The most appropriate Health Care Professional to discuss future fertility and pregnancy late effects is:													
Professional	**Not important**			**Unsure**			**Agree**			**Total**	**Mean**	**Total 7-9**	**70% Rate**	**Missing**
Paediatric oncology consultant	1			1			4	7	6	19	7.52	17	Pass	

Q7 Being fertile following cancer treatment can be defined as:													
Definition	**Not important**			**Unsure**			**Agree**			**Total**	**Mean**	**Total 7-9**	**70% Rate**	**Missing**
Being able to conceive a pregnancy naturally	1		2				2	3	11	19	7.57	16	Pass	

Q8 A summary of treatments received and late effects risk for future fertility and pregnancy following treatment should be sent to:													
Person/ people	**Not important**			**Unsure**			**Agree**			**Total**	**Mean**	**Total 7-9**	**70% Rate**	**Missing**
The female CAYA cancer survivor and/or parents						1		3	15	19	8.68	18	Pass	

Q9 The most appropriate format for a treatment summary with future fertility and pregnancy late-effect risk information is:													
Format	**Not important**			**Unsure**			**Agree**			**Total**	**Mean**	**Total 7-9**	**70% Rate**	**Missing**
A combination of written, verbal, and signposting to trusted online resources	1							5	13	19	8.31	18	Pass	

Q10 The most appropriate format to assist parents with the communication of potential future fertility and pregnancy late effects is:													
Format	**Not important**			**Unsure**			**Agree**			**Total**	**Mean**	**Total 7-9**	**70% Rate**	**Missing**
Face-to-face session with a Health Care Professional						1	2	8	8	19	8.21	18	Pass	

Q11 The most appropriate way to explain medical terms and provide a lay summary of treatment received including future fertility and pregnancy late effects risk is:													
Method	**Not important**			**Unsure**			**Agree**			**Total**	**Mean**	**Total 7-9**	**70% Rate**	**Missing**
Given to parents in written format	1					3	3	6	6	19	7.47	15	Pass	

Q12 Unmet informational late effects needs of female CAYA cancer survivors should be re-evaluated at:													
Time-point	**Not important**			**Unsure**			**Agree**			**Total**	**Mean**	**Total 7-9**	**70% Rate**	**Missing**
Treatment completion				1			4	4	10	19	8.1	18	Pass	

Q13 The most appropriate Health Care Professional to assess unmet informational needs of female CAYA cancer survivors relating to future fertility and pregnancy is:													
Professional	**Not important**			**Unsure**			**Agree**			**Total**	**Mean**	**Total 7-9**	**70% Rate**	**Missing**
Paediatric oncology nurse		1		1	1	1	8	4	3	19	6.94	15	Pass	

Q14 The best format to assess unmet informational needs for female CAYA cancer survivors regarding future fertility and pregnancy late effects is:													
Format	Not important			Unsure			Agree			Total	Mean	Total 7-9	70% Rate	Missing
Face-to-face consultation with fertility counselling specialist				3	1	1	4	2	8	19	7.31	14	Pass	

6.6.6 Round three

Round three of PICCS2 took place on 10th December 2020. The final template for statements that had passed the 70% consensus rate from round two were emailed to the panel seven days before the web-based meeting. This was accompanied by a brief agenda for the meeting and the findings from round two for reference. Participants confirmed by email, before the meeting, that they were happy to disclose their name, profession and webcam image during the meeting and confirmed that they were happy for the session to be recorded. NR (PPIE representative) and EB (Director of studies) acted as independent facilitators during the session, which lasted one hour and was hosted on *Microsoft Teams*. Out of the 19 panel members, 14 participated in the final round. This calculated to a 91.2% participation rate overall for the three rounds of PICCS2.

After a short presentation by the researcher, the panel were asked to join a pre-defined break-out group to discuss a selection of the remaining statements. The

remaining five members of the panel that could not attend the meeting were asked to consider the final statements as a whole and decide to either agree/disagree for inclusion in the final guidance document. It was requested that any feedback and decisions be sent to the researcher within seven days of round three (web-meeting).

The group were pre-defined by the researcher into three groups. This choice was made to ensure that a range of specialties was represented within each of the groups. It also allowed for the discussion of all statements within the allocated time frame of the meeting. The composition of the groups was as follows:

- At least 1 patient/parent representative
- At least 1 obstetric professional
- At least 1 paediatric oncologist
- 1 facilitator per group

Group A discussed and evaluated statements 1-5, group B discussed and evaluated statements 6-10 and group C discussed and evaluated the remaining statements 11-14. The allocated facilitator encouraged discussions and ensured that the groups kept to time. The statements were discussed in numerical order and the options for each statement agreed/rejected for inclusion. Notes were taken by each facilitator to feedback to the main group. Suggestions for alternative terminology or other forms of feedback were recorded by the facilitators and fed back to the main group. The break-out discussions concluded after 30 minutes, after which the participants were brought back to

the main web-meeting by the researcher.

The facilitators then presented each groups discussion and final decisions about the statement and options agreed for the final guidance. They also presented any additional feedback within the discussions for wider consideration by the panel.

A draft final guidance document based upon the final choices and email feedback from those panel members not able to take part in the web-meeting, was emailed by the researcher to all panel members on January 11th, 2021. Panel members were asked to review the final draft guidance document and submit any amendments or queries within 14 days. The final guidance document was then disseminated to panel members on January 28th, 2021. Panel members were asked to keep the document confidential but feedback on any queries/amendments within seven days.

The final guidance document as an example of a published guidance document can be found in Appendix 13. The final consensus statements are summarised below (Table 44):

Table 44 - PICCS2 Final consensus statements

Statement	Final agreed guidance
1. Health Care Professionals should communicate the following future fertility and reproductive health risks to female CAYA cancer survivors and/or parents (N.B. risks vary dependent upon level of treatment received):	• You may have difficulty becoming pregnant • You will need high-risk pregnancy care and pre-pregnancy counselling • There is a low risk of abnormality in baby • There is a low risk of cancer in the baby

Statement	Final agreed guidance
2. Health Care Professionals should FIRST communicate (either to the female CAYA cancer survivor and/or parent) future fertility and reproductive health risks:	• At diagnosis
3. Health Care Professionals should RE-INTRODUCE future fertility and reproductive health risks to female CAYA cancer survivors/parents at the following time points:	• When treatment is complete (Paediatric or LTFU team) • Upon wanting to start a family (Fertility services or GP) • Upon becoming pregnant (Obstetrics/fertility teams)
4. The most APPROPRIATE AGE to discuss future fertility and reproductive health risks directly with the female CAYA cancer survivor is:	• At an appropriate age as defined by the female CAYA with cancer/parent or health care professional (N.B. This should be no later than 16 years of age)
5. The most APPROPRIATE Health Care Professional to discuss future fertility and reproductive health risks with female CAYA cancer survivors/parents is:	• The health care professional with the most knowledge in this area and with the best relationship with the female CAYA cancer survivor and/or parents (N.B. This may not be within the paediatric or LTFU teams)
6. Being 'Fertile' following treatment for cancer is best defined as:	• Being able to conceive a pregnancy naturally (not requiring fertility services)
7. A treatment SUMMARY including information about future fertility and reproductive health risks should be sent to: (N.B. This should also be in a 'lay' format to ensure adequate comprehension)	• The General Practitioner • The female CAYA cancer survivor and/or parents • The long-term follow up team (if still involved in the care of the patient)

Statement	Final agreed guidance
8. The most appropriate FORMAT to provide a treatment summary that includes future fertility and reproductive health risk is:	• Via input onto the electronic patient medical record • Through a combination of written and verbal information, with signposting to trusted online resources
9. The best method to support parents of female CAYA with cancer to communicate future fertility and reproductive health risks is a combination of:	• An information session (face-to-face) with a Health Care Professional (without the patient) • AND/OR A joint face-to-face session with the female CAYA cancer survivor and their parent (N.B. dependent on age and understanding/willingness of the patient to have their parent present)
10. Unmet future fertility and reproductive health informational needs of female CAYA cancer survivors should be EVALUATED at the following times (N.B. dependant on the age and maturity of the patient):	• At treatment completion • At 5 years following treatment completion • When thinking about becoming pregnant
11. The most appropriate Health Care Professional to EVALUATE unmet future fertility and reproductive health informational needs of female CAYA cancer survivors is:	• The health care professional with the best relationship with the patient • The health care professional with the most knowledge of future fertility and reproductive health risks (N.B. This may not necessarily be the paediatric or LTFU team)
12. The best FORMAT to evaluate unmet future fertility and reproductive health informational needs of female CAYA cancer is:	• By using a needs-based analysis questionnaire • THEN If deemed necessary or there are concerns voiced, a face-to-face consultation with a fertility specialist is recommended

An overview of the combined findings from PICCS1 and PICCS2 will now be presented, including triangulation of the combined findings. This will be followed by Chapter Seven – Discussion.

6.7 Triangulation of data (PICCS1)

Data from the three components of PICCS1 were triangulated and compared for similarities and cross-cutting themes using methodological triangulation as described by Flick (2018:10). This took place before the design and delivery of PICCS2 and used an in-between methods triangulation of data. This allowed for the combination of qualitative and quantitative data, but maintained the individual methods, philosophical underpinning, and logic of the study parts. The individual methods could not be combined to present an overall conclusion or finding, as this would compromise integrity of the individual study data. The findings of the studies if combined, would not be translatable or replicable for future research and therefore of limited use. Instead, data were compared, similarities and contradictions explored, and important findings highlighted (see Table). Summarised data and identified themes present a unique insight into the most prominent issues to CAYA cancer survivors, parents, and HCPs within the context of late effects communication of information.

Further triangulation of the findings from PICCS2 was not possible, due to data being representative of a set of individual recommendations. Therefore, they cannot be compared/contrasted or combined. Other methods of triangulation for PICCS2 would also not be suitable as the output cannot be conceptualised or represent any methodological theory.

Table 45 - Triangulation of data (PICCS1)

Systematic Review	Questionnaire CAYA/parents	Questionnaire HCP	Interviews
Lack of awareness of late effects	Spoken conversation was the most usual form of communication for late effects risk	Spoken conversation with written follow-up was most preferred form of communication for late effects	Who should communicate, what should be communicated, when should communication happen?
HCPs need education to help with communication	Most participants had some knowledge about fertility risk	Paediatric oncologist identified as most common HCP who discusses late effects information	Lack of knowledge about wider reproductive health outcomes (HCPs)
Treatment summary data held by HCP or hospital records	Participants were unsure about treatment dosages	N/A	Role of specialist nurses as 'gatekeepers' in addressing these unmet needs?
What is the extent of late effects upon future fertility?	Difficulty becoming pregnant and the risk of early menopause the most common late effect communicated (within future fertility)	Difficulty in becoming pregnant and a higher risk of early menopause were ranked as top known late effect (for future fertility)	What are the most important late effects risks that need to be discussed with families and when? (HCPs) Families report significant distress at not knowing outcomes

Systematic Review	Questionnaire CAYA/parents	Questionnaire HCP	Interviews
HCPs in primary care report not feeling confident to care for CAYA cancer survivors	Survivors and parents want to know early and want to know lower risks too (low risk of cancer in offspring)	Less knowledge of reproductive health risks (i.e., pregnancy)	Reproductive health or pregnancy risks out of scope (HCPs) Survivors report conflicting advice vs real life outcomes
HCPs want improved partnership with parents, survivors, and multi-disciplinary team	N/A	HCPs agree that the level of late effects information about future fertility is not sufficient to meet patient needs	Honest and transparent communication with families is needed Good examples of MDT working
Need for improved survivorship care model (holistic)	N/A	N/A	Poor communication and collaboration linked to long-term distress linked to unmet informational need in CAYA cancer survivors

Systematic Review	Questionnaire CAYA/parents	Questionnaire HCP	Interviews
Timing, format, and delivery of information needs further investigation	During treatment and end of treatment were the most popular times for communication of late effects	At diagnosis and within long-term follow-up clinic were the most popular times for discussing late effects	Evidence that fertility preservation discussions taking place at diagnosis Wider reproductive health advice more sparse Uncertainty as to who handles reproductive health surveillance Survivors and parents want clear information, early on and delivered sensitively

Chapter Seven – Discussion

This chapter provides a critical discussion of the findings from PICCS1 and PICCS2. This will include an outline for the contribution of new knowledge to methodological theory and clinical practice-based knowledge. How the findings can be translated into clinical practice and patient-level impact will also be considered. Recommendations for future research will be discussed, with Chapter Eight providing an overall conclusion to the thesis.

7.1 Communication

The PICCS1 interview transcripts emphasised that the manner, timing of, and use of language in the communication of late effects, is extremely important. There is a lack of research about the optimal timing for late effects communication with CAYA cancer survivors. However, PICCS2 and the final expert recommendation tool (Appendix 13) aimed to provide the first steps toward an expert evidence based for this area. PICCS2 provided a mechanism to address the areas of research that are lacking, with an evidence-based, multi-stakeholder approach.

7.1.1 Patient-parent-professional relationship

Participants reported that CAYA with cancer need to feel comfortable enough to talk about their worries and share concerns with trusted professionals (see section 6.5.3.4 Honest and transparent communication). Lin et al. (2020) supported this findings in their systematic review; 101 articles from 25 countries,

involving a total of 1870 childhood cancer survivors; and described that participants lost their trust in clinicians if they think they had been misinformed or lied to. This mistrust led to a higher rate of health care service disengagement in adulthood and should be considered as a priority for CAYA cancer survivorship service re-design.

The professional relationship between the HCP, the CAYA cancer survivor, and the parent was also identified as an important factor in the communication of sensitive and personal issues such as future fertility and reproductive health (PICCS1 interviews). The underlying relationship between the CAYA cancer survivor and the parent is an important variable in effective communication exchange as there is a need for trust, openness and honestly between the parent and the CAYA with cancer. Subsequently, HCPs should be encouraged to consider the parent-patient relationship, providing opportunities for consultations without the parent if the young person requests this (if deemed suitable and appropriate) (see section 6.5.3.3 Which late effects risk?).

This approach to offer consultations without the parent if deemed appropriate and acceptable, has been advocated by the Teenage Cancer Trust (2019) who called for adolescents and young adults with cancer to be an active part of clinical conversations. They recommended that HCPs should consider whether the young person would like their parent present or not (with the caveat that the young person is deemed old enough and mature enough to make that decision) (Teenage Cancer Trust 2019). They recommended this approach when issues such as reproductive health and fertility are raised, as CAYA with cancer may not feel comfortable with discussing this openly in front of parents (Teenage

Cancer Trust 2019).

Compassionate and responsive communication of late effects risk, tailored to needs at that time for the individual was recommended as the ideal approach by CAYA cancer survivors and parents in the PICCS1 (interviews). Participants recalled occasions when late effects information about future fertility, was delivered “insensitively’ and “cruelly” (see section 6.5.3.5 Long-term distress). Participants reported that in their experience, the level and depth of future fertility risk information given to them by HCPs, did not align with the level of informational need that they needed. This finding suggests that further exploratory research is needed to evaluate the impact of alternative methods of late effects communication upon levels of unmet informational need.

A tool by Epstein and Street (2007) focused on the assessment of communication through evaluation of; response to emotion, exchange of information, decision making, fostering of healing relationships, and enabling self-management, and is an example of a tool that could be applied to communication interventions for CAYA cancer survivorship care in the UK. While the communication methods proposed in this tool offer a holistic and compassionate method for assessment of need, this tool has not been appraised by research or applied to the UK CAYA cancer survivor population. Therefore, caution should be used when applying this tool to evaluate impact upon unmet informational needs and reduction of associated psychological distress of CAYA cancer survivors.

PICCS1 and PICCS2 identified new data to support the hypothesis that adequate communication of late effects risk, in particular future fertility and

reproductive health risks, was lacking for CAYA cancer survivors (Lee et al. 2019, Vetsch et al. 2017, Lie et al. 2015). Furthermore, HCPs in PICCS1 acknowledged that the information they currently provide is not considered to be extensive enough and may not be remembered long-term by the patient and their family.

To illustrate this finding, PICCS1 (questionnaires) demonstrated that 52.3% of CAYA cancer survivors/ parents did not know, or were unsure of, the dosage of radiotherapy they/their child had received, and therefore did not know their risk of late effects associated to radiotherapy damage. In the UK, treatment and dosage information is held solely in medical health records or treatment summaries that are not easily accessible to families. This suggests that an initiative such as the 'SurPass' (see 2.2.5 The Survivorship Passport) introduced by Haupt et al. (2018) might provide a solution to this lack of knowledge and recall about treatments received as CAYA for cancer. However, the 'SurPass' has encountered a number of barriers to Europe-wide adoption, currently only being used in Italy and not as standard practice for all treatment centres (Haupt et al. 2018). Therefore, the same barriers might also be present when attempting to introduce a similar 'survivorship passport' tool in the UK due to wide variance in service availability and care pathways for CAYA with cancer.

A recommendation would therefore be made for further exploration or testing of an interventional tool to discover the most feasible tool for clinical care use, but which also meets the unique needs of CAYA cancer survivors. This could include the testing of an digital survivorship passport linked to health care records or sharing of medical notes, similar to the introduction of online

pregnancy and maternity care notes that can be accessed by the patient at all times (NHS Digital 2021).

7.1.2 Psychological unmet needs

The PICCS1 findings (systematic review and interviews) from HCPs acknowledged that there was a need to recognise future fertility, reproductive health risks, and psychological well-being, alongside and equal to, the risk of physical late effects and signs of relapse.

An assumption that physical late effects are of more importance than psychological or non-immediate late effects (such as future fertility) by HCPs and academic researchers, may be reflective of the lack of evidence in this area. It could have also contributed to the underreporting of late effect risks for issues such as reproductive health and psychological outcomes as a primary outcome in late effects studies, a view supported by Lie et al. (2020). Newton et al. (2021) alluded to a possible 'discordance' in the prioritisation of late effects information between HCPs and CAYA with cancer in their study of 25 American childhood cancer survivors. They reported that HCPs dismissal of future fertility concerns was linked to a worsening of unmet informational needs and increased the risk of adverse psychological outcomes for childhood cancer survivors (Newton et al. 2021).

CAYA cancer survivors have reported high levels of psychological distress (including anxiety and depression) due to unmet informational needs, in particular late effects. (Brinkman et al. 2018, Devine et al. 2018). PICCS1

(systematic review) findings provided evidence to support this link (Lee et al. 2019, Cox et al. 2019, Sisk et al. 2018, Gianinazzi et al. 2014). Similarly, the SurPass survivorship passport initiative by PANCARE (Haupt et al. 2018) identified the need to address the psychological burden that comes with a personal history of cancer, followed by the PANCARE international clinical guidelines for the communication and ethical considerations of fertility preservation for CAYA cancer survivors (Mulder et al. 2021). The guideline further reiterated the need for long-term psychological assessment of CAYA cancer survivors to reduce adverse psychological outcomes (Mulder et al. 2021). Therefore, there is a clear need for a strategy to assess and address the psychological well-being of CAYA cancer survivors alongside unmet informational needs and physical risk of late effects (Hendriks, Harju, and Michel 2021, Szalda et al. 2017).

Mulder et al. (2021) highlighted the need to address both future risk of physical late effects and psychological well-being of CAYA cancer survivors. CAYA cancer survivors and parents in PICCS1 (systematic review and interviews) reported increased levels of distress, including higher rates of depression and anxiety, linked to unmet late effects informational needs (Sisk et al. 2018, Vetsch et al. 2017, Gianinazzi et al. 2014). CAYA cancer survivors, particularly females, reported a need to know their future fertility status and highlighted this as an extremely important unmet need (PICCS1 interviews). Zebrack et al. in 2004 previously reported the link between future reproductive health worries and the long-term impact on life after cancer and psychological well-being. They reported CAYA cancer survivors experiencing difficulties in forming and

maintaining personal relationships and in their attitudes towards contraceptive use due to the lack of knowledge surrounding their fertility status (Zebrack et al. 2004). Perez et al. (2020) also highlighted the negative consequences of not addressing unmet informational needs about fertility risks, linking unmet needs to negative attitudes towards childbearing. This evidence suggests that the psychological impact of not addressing unmet future fertility informational needs may carry negative effects long-term for the CAYA cancer survivor, outside of the scope of their cancer diagnosis and requires further research.

Further research into the prioritisation of late effects risk communications from the point of view of the CAYA with cancer, the HCP, and the parent, would provide more robust evidence for HCPs to help understand what information is most important to CAYA cancer survivors and when/how they would like to receive different categories of future risk information during their treatment journey (i.e. format and style).

Accurate information is also critical, and in order to further facilitate a positive and adequate communication exchange between CAYA cancer survivors, HCPs and parents about future health risks, a larger scale, prospective, data set is also needed to provide reliable, ongoing evidence (Vassal et al. 2015). Analysis of very long-term health outcomes of CAYA cancer survivors (50-60 years post treatment) and data reflective of current and novel cancer treatments is needed to ensure that the most up-to-date risk information can be communicated to families (Vassal et al. 2015). Pritchard-Jones et al. (2013) also recommended that data linkage between primary health care records, hospital episode statistics, and cancer registries will be needed to capture long-

term health outcome data outside of clinical trials (such as psychological outcomes) for CAYA cancer survivors and provide more in-depth detail about individual future health risks.

7.1.3 When, who and in what format?

Identifying the most appropriate time, age and format for the communication of late effects risk was identified as a key theme in both the PICCS1 and PICCS2 studies. The PICCS1 (systematic review) reported that traditionally, communication about late effects risk was conducted verbally in clinical consultations, with written information as a back-up being provided to families. Notably, for a rapidly advancing digital era, online methods of communication, or the use of online resources/platforms for obtaining late effects information was not a preferred option by CAYA cancer survivors/parents and HCPs (PICCS1 online questionnaires). Reasons for this included being worried about being given false information and concerns about not being able to locate the level of detail they wanted. The participants from the PICCS1 online questionnaires (CAYA cancer survivors and parents) reported fears about accessing information online or via un-official sources, linking this to increased levels of anxiety. This finding suggests that although in the majority families and HCPs prefer verbal and written information, this cannot be assumed for all. Likewise the findings about online information merit further research, in particular due to the rapid digitalisation of information and consultations brought about by the COVID-19 pandemic. It may be that online methods of information and communication are now widely preferred and used, therefore the findings

from PICCS1 need to be considered in the context of pre-COVID inquiry.

PICCS1 identified a lack of consensus for the optimal time-point for delivery of key future health information (including late effects). Greenzang, Dauti, and Mack (2018), Lie et al. (2015) and Wakefield et al. (2012) all reported a lack of agreement about the most appropriate time to provide late effects risk information to CAYA with cancer and their families (PICCS1 systematic review). The online questionnaire also revealed that only 13.7% of HCPs thought that parents and CAYA cancer survivors retained key late effects information they provided to them long-term. The HCPs interviewed in PICCS1 (interviews) reported a lack of consensus about the optimal timing for future fertility and reproductive health information. Similarly, when asked about the most appropriate age to communicate fertility information, no consensus could be reached (see PICCS1 interviews).

This finding suggests that there may not be an optimal time point for communication and that more research is needed to explore the effect of delivering small but frequent communication versus delivery at a specific time period. Consistency of information and continuity of HCP to discuss fertility and reproductive health with families are also important variables to consider in future research around timing. Equally, an in-depth investigation surrounding the ability of CAYA cancer survivors and parents to recall key late effects information would also be recommended to help understand how information can be delivered in a way that will still be memorable many years later.

PICCS1 identified that parents of CAYA cancer survivors wanted help to communicate late effects risk information to their children. This included advice

on the optimal time to broach discussions about future health risks and recommendations for appropriate language, tone and sensitivity. A mechanism also needs to be in place to accommodate circumstances where the CAYA with cancer does not feel comfortable discussing late effects risk with a parent or vice versa to ensure that this communication is still able to take place and the CAYA with cancer has the key health information they need for adulthood.

PICCS2 aimed to provide the first steps to addressing the gaps in research identified in PICCS1. Panellists agreed on the most appropriate time point for future fertility and reproductive health risk communication, the minimum age requirement of the CAYA with cancer to receive such information, and the HCP considered to be the most appropriate person to deliver this information (see Appendix 13). However, despite the statements meeting the 70% consensus level for approval, there is a caveat to the recommendations that highlights the need to consider the age, maturity, survival outlook, and the relationship of the HCP with the patient and family. Therefore, it is appropriate to recommended further research into the optimal timing of late effects information such as future fertility and reproductive health risks for female CAYA cancer survivors.

7.1.4 The digital era and health care

Digital health information seeking relates to the increased levels of people seeking health information online rather than face-to-face with a HCP (Devine et al. 2018). Digital health care and online consultations have become much more common due to the COVID-19 pandemic, that resulted in a rapid paradigm shift to e-healthcare, significantly changing the way patients and HCPs interact in the

UK and worldwide (Nekhlyudov et al. 2020). All non-urgent clinical consultations moved online and health care advice for chronic conditions, including services such as CAYA cancer survivorship were affected (Nekhlyudov et al. 2020). This sudden change in culture by the public and HCPs inevitably impacts the results of PICCS1, conducted prior to COVID-19.

PICCS1 reported that online methods for future health risk information were secondary to face-to-face consultations with a clinician (see PICCS1 results – Chapter 6). Benedict et al. (2021) (post COVID-19) explored informational preferences of female CAYA cancer survivors and reported that most now preferred a combined approach to future fertility and childbearing risk information using online resources and face-to-face communication. Digital platforms were reported as an acceptable means for accessing initial information, but with a face-to-face follow-up with a clinician preferred to discuss information in more detail (Benedict et al. 2021). Face-to-face interactions were still preferred for in-depth, individualised risk communication and counselling, due to the highly emotional topic of fertility. In-person communication also facilitated immediate feedback for concerns and provided an alternative method for female CAYA cancer survivors that had concerns about internet security.

The study by Benedict et al. (2021) supports the findings from PICCS1 that recommended a combined approach to late effects risk information provision (written/verbal communication). However, Benedict et al. (2021) more accurately reflects the rapid move to online healthcare interactions seen over the past year. Likewise, the PICCS2 expert consensus guidance document reported that online resources were not preferred as a means of future health

risk communication. However, it is probable that this opinion may have changed alongside the attitudes and behaviours of CAYA cancer survivors, parents, and HCPs to using online health information resources. This resource would therefore require further investigation and updates as needed.

It is also important to note, however, that the concerns reported by participants in PICCS1 regarding accuracy of information and evidence-based data are still valid despite the rapid adoption of e-healthcare across the UK during the COVID-19 pandemic. The risks associated with an increased reliance upon the internet, typically a conduit for rapid and extensive information provision, was highlighted by Fareed et al. (2021) in a population-based study of 4756 cancer survivors in the USA (aged 18-65+ years). This included a risk for cancer survivors in accessing inaccurate information, digital exclusion of certain demographic populations of CAYA survivors who cannot access the information and the risk of receiving anecdotal advice, not reflective of individual risk (Fareed et al. 2021).

Despite this, digital health and online health information provision is particularly attractive to the adolescent and young adult age group, who have been described as ‘pervasive users of technology’ (Devine et al. 2018). A study by Devine et al. (2018) representative of a sample of adolescents from the USA reported that 93% of adolescents aged 13 to 17 years and 99% of young adults aged 18 to 29 years were reported to be regular users of the internet. This study suggests that a large proportion of the CAYA population are now ‘online’ as part of their daily lives.

Digital health interventions have been briefly explored to address the barriers to

engagement in CAYA cancer survivorship health care as online technologies align with everyday behaviours of this age group (Davies et al. 2018). Signorelli et al. (2020) developed and tested a nurse-led, online survivorship information platform for childhood cancer survivors in Australia (*Re-engage*). Despite a small sample of 30, the programme demonstrated a high level of acceptability, feasibility, and efficacy by CAYA cancer survivors, providing them with useful and helpful information about their future health risks. *Re-engage* provides an example of how online-based CAYA cancer survivorship platforms can help to address unmet informational needs of CAYA cancer survivors and may be applicable following the increase in online-based healthcare following COVID-19 (Signorelli et al. 2020).

However, although the internet offers great promise in delivering high-quality and tailored information and support for CAYA cancer survivors, there is a reliance on the user to initiate use (Davies et al. 2018). A randomised pilot study of a web-based portal to provide adolescent and young adult cancer survivors with tailored treatment summaries and guidance regarding risk for late effects had low usage, with only 46% accessing the website and, of those, only one third logging in more than once (Emmons et al. 2013). This reiterates that with this patient population (0-24 years) a homogenous approach is unlikely to be effective and that staged and inclusive interventions that are flexible to the individual are needed (Fern et al. 2013).

Although PICCS1 (questionnaires) suggested a preference for face-to-face communication of late effects information, COVID-19 may have changed this view. Teenagers and young adults in particular might be a more accessible

group than previously thought, due to exponential increase in internet and digital platform use. HCP competence and skills within the digital space may also have been accelerated due to the impact of COVID-19 and digitized health care, but there remains a need for greater investment in training and engagement of the HCP workforce, as highlighted by The Topol Review (Health Education England 2019) who emphasised the need to continue investment in staff skills and training to promote digital literacy.

Social media platforms and existing charity/trusted information resources offer innovative ways of engaging CAYA cancer survivors, by using videos, blogs and applications to communicate important health information and to provide links for support e.g. *Cancer, Fertility, and Me* (University of Edinburgh 2020). This method of engagement provides a mechanism for reaching diverse audiences and can cover large geographical areas. However, an assessment of how such platforms impact the level of unmet informational need and late effects knowledge for CAYA cancer survivors has yet to be conducted (Devine et al. 2018). Likewise, it is also important to consider how online interventions and platforms for health care information may exclude those considered to be 'digitally excluded' or CAYA cancer survivors that may struggle with technology due to cognitive deficits caused by cancer treatments (Haupt et al. 2018). Furthermore, online resources, although enabling peer-support of CAYA with cancer, carry a level of mistrust (as reported by CAYA cancer survivors in PICCS1 questionnaires). This may affect the acceptability of online information and emphasises that one format alone is not sufficient to meet the needs of the entire CAYA with cancer population.

7.2 Partnership

Evidence from the PICCS1 (systematic review) emphasised the need for a wider, multi-disciplinary approach to survivorship care that cuts across paediatric and adult care services. This method of collaboration may help to address some of the challenges associated with transition of care from paediatric to adult health care services reported by CAYA cancer survivors (Cox et al. 2019, Signorelli et al. 2019b, Lee et al. 2019, Lie et al. 2015, Wright et al. 2014). A CAYA cancer survivorship service that meets the unique psychological, physiological, and changing needs of the CAYA cancer survivor population, with open and honest communication with the young person was recommended by Mulder et al. (2021), Smith, Link, and Effinger (2020), Lin et al. (2020) and in the PICCS1 (questionnaires).

Real-life examples of HCPs expanding their MDT meeting membership to include disciplines such as gynaecology, paediatric endocrinology etc. to meet the ongoing needs of CAYA cancer survivors were sparse, often reflecting a reactive approach to clinical concerns rather than a preventative, supportive care model. The PICCS1 (interviews) with HCPs reported that in most circumstances, MDT teams had been set-up due to professional links and previous collaborative working on other matters, rather than HCPs being approached due to skill and expertise for CAYA cancer survivors.

However, appropriateness of HCPs included into the MDT team and the current age of the CAYA with cancer is important as individual needs will change over time from childhood to young adulthood. Equally, MDT teams and relevant

expertise for CAYA cancer survivorship care services are not currently mandated in the UK, only recommended (NICE 2014). Therefore, at present it is unlikely that standardisation of an MDT care model for CAYA cancer survivorship will be adopted across UK CAYA with cancer settings.

Variance in the membership of MDT teams for CAYA cancer survivorship care in the UK (reported in the PICCS1 interviews) may be related to the finding that HCPs from wider disciplines (such as obstetrics) perceive CAYA cancer survivorship to be 'out of scope' for them. Likewise, psychological distress caused by unmet informational needs may be viewed as something that is 'out of scope' for the clinical team, requiring referral to a psychological support service outside of the MDT team. As the evidence from PICCS1 demonstrates however, psychological well-being is a key part of CAYA cancer survivorship care and future health outcomes. A view supported by Harju et al. (2020).

7.2.1 A 'gold standard' for CAYA cancer survivorship care

> *"Some problems are so complex that you have to be highly intelligent and well informed just to be undecided about them" (L. Peter - cited in Periyakoil 2007)*

The term 'a wicked problem' is often reported in the literature for issues which are complex to solve, or which result in a lack of consensus despite attempts to address the problem (Periyakoil 2007). This term adequately represents the challenges associated with re-designing a CAYA cancer survivorship care service to adequately address unmet needs.

Wicked problems are complex due to the fact that the perception of and definition of the problem are viewed differently by multiple stakeholders (Eoyang and Mennin 2019). A solution-based approach using small, incremental changes over time is therefore recommended (Eoyang and Mennin 2019). The iterative approach was also recommended by Smith, Link, and Effinger (2020) who recommended a CAYA cancer survivorship care service that can continuously adapt to meet the unique and varied needs of the CAYA population.

The vision of a CAYA cancer survivorship service that effectively communicates risk of late effects, tailored to individual needs, delivered slowly and sensitively, and responsive to the changing needs of the CAYA population, has been hypothesised as the 'gold-standard of CAYA cancer survivorship care'. Mulder et al. (2021), Otth et al. (2021), and Sisk et al. (2018), health care regulatory bodies (NHS England 2019a, NICE 2014), and international expert groups (PANCARE, Haupt et al. 2018) have all attempted to capture what they think a 'gold-standard' of CAYA cancer survivorship care looks like. However, PICCS1 (systematic review and interviews) revealed that this vision for a 'gold-standard' of CAYA cancer survivorship care is yet to be achieved. However, a caveat to the findings of PICCS1 is that the real-life experiences from CAYA cancer survivors and parents are reflective of a survivorship service from over ten years ago. Therefore, a more recent account and reflection of current CAYA cancer survivorship services and patient/parent satisfaction levels is needed to validate these findings and compare with targets set out in national recommendations.

The PICCS1 (systematic review and interviews) revealed that CAYA cancer survivors “just want to feel normal again” following their cancer treatment. This results in some cases, the avoidance of situations that remind them of being ill, being a patient, or that requires them to disclose a history of cancer. This suggests that CAYA cancer survivors may actively avoid survivorship care due to this, posing a challenge for HCPs trying to engage survivors in follow-up care and for health care commissioners when trying to plan future service needs of a population at a high risk of treatment-related mortality and morbidity (Suh et al. 2020).

The need for a patient-centred, adaptive, individualised, and holistic CAYA cancer survivorship care service is evident (NICE 2014, NHS England 2019, Suh et al. 2020). However addressing the unmet needs of a population that covers childhood, adolescents, and young adults will require a broad, innovative and collaborative approach with a range of multi-disciplinary groups, CAYA with cancer and parents. Walker et al. (2019) described the achievement of a ‘gold standard’ of CAYA cancer survivorship care as a huge and complex undertaking, fraught with challenges specific to the CAYA cancer survivor population. The solution, if achievable will require not one standardised approach, but a multi-layered, multi-staged approach, co-designed and focused on the unmet needs of the CAYA with cancer and their families.

7.2.2 Age-appropriate care and advice

The phrase ‘age-appropriate care’ is often referred to when describing optimal health care provision for CAYA with cancer, but rarely defined. The need to

provide individualised cancer care and 'tailored to the individual' communication of information is clear, both in the findings of the PICCS1 online questionnaires (CAYA cancer survivors and parents and HCP views), the PICCS1 interviews and in the PICCS2 recommendations. NICE (2014) and leading CAYA cancer charities have also vocalised the need to provide care and information to meet the unique and age-appropriate needs of the young person (CCLG 2021b). The UK has developed services specifically targeted at teenage and young adults with cancer, thanks to the Teenage Cancer Trust. However, a study by Lea et al. (2018) who interviewed 46 young cancer patients and health care professionals highlighted the challenges that still exist with the CAYA age group.

"It is like with any age group, just because you fall into that age group, it doesn't mean you all have the same needs[...] Just having the same age in common may not be enough…it should be about the individual patient and their individual needs." (Direct quotation from Lea et al. 2018).

Lea et al. (2018) further explained that communication of information, including future health risk communication is reliant on HCPs not only having an expertise in the condition, but also in the maturity assessment and psychology of young people, adapting their communication style to the young person in front of them. This helps to develop an understanding of young people's holistic needs, their life stage and commitments, so that cancer treatment has the least impact on important areas of a young person's life and priorities. This recommendation reflects findings from Fern et al. (2013) who undertook a participatory study with 11 teenage and young adult survivors (aged 13 to 25 years) in the UK and

reported that age-appropriate information and support services to help young people cope with the impact of cancer on daily life and life after cancer must be a priority for cancer care service redesign.

PICCS2 recommendations clearly emphasised the need to deliver information with a caveat of age-appropriate evaluation. The expert panel all felt strongly that each recommendation had a caveat of age-appropriate evaluation and that the HCP, the parent and the CAYA with cancer all have a role to play in this assessment.

7.2.3 Defining fertility

The term fertility and wider reproductive health outcomes was discussed in the PICCS1 (interviews). One HCP felt that the standard definition of fertility as either fertile or infertile was not enough. They emphasised that the meaning behind fertility is not simply whether a female CAYA cancer survivor can reproduce, or is fertile, but what that means within the entire spectrum of their reproductive health (i.e., sex education, sexual health, contraception, pregnancy and birth).

The World Health Organisation also defines fertility as a wider concept than just being fertile or infertile:

> *"Reproductive health implies that people are able to have a satisfying and safe sex life and that they have the capability to reproduce, and the freedom to decide if, when, and how often to do so" (WHO 2021b)*

The definition of fertility was also a feature of the PICCS2 expert panel

discussions (see section 6.6.4.1 Round one - Free text analysis). Panellists explored the meaning of being fertile, reflecting that the term was difficult to define. However the panel were able to come to an agreement for the definition as

"being able to conceive a pregnancy naturally (not requiring fertility services)".

This definition, although agreed by the panel needs a deeper understanding to explore what the term means to a wider population of female CAYA with cancer. Further insights into the meaning of fertility might also help to uncover a deeper understanding of the impact of infertility on the long-term psychological well-being of female CAYA cancer survivors.

In a phenomenological study by Nilsson et al. (2020) the concept of fertility and the way in which young adult survivors of childhood cancer understood their risk of being infertile was explored. Interviews with 19 childhood cancer survivors (aged 17–27 years old) revealed that survivors want HCPs to firstly assess the survivors' knowledge and understanding of their ability to have children before communicating information about future fertility issues. The authors highlighted that this background knowledge can enable HCPs to consider how survivors want to be treated, the importance of fertility to them as an individual, and reveal the type of information they may need or want (Nilsson et al. 2020).

Communication of potentially sensitive and upsetting late effects, such as future fertility risk is a complex ethical and moral issue for HCPs. Difficulties in discussing available fertility preservation procedures, adequate communication of future health risks, and the likely success rates for such procedures was

discussed by Anderson et al. (2015). They considered the risk of primary cancer recurrence during the re-implantation of harvested reproductive tissue (e.g. ovary or testicular tissue) and emphasised the need for HCPs to be aware of all the potential risks and benefits of fertility preservation procedures, some of which are still classed as experimental (Anderson et al. 2015). A clinical guidance document created by the European consortium of late effects specialists, PANCARE also aimed to assist HCPs in the communication of ethically challenging issues such as fertility preservation for CAYA with cancer (Mulder et al. 2021). However, although the recommendations use the available evidence and professional opinion, the evidence is classed as limited and low-quality. The European guidance is also limited in its applicability to the NHS and CAYA cancer services in the UK, due to the differences in health care organisation and funding across Europe. Therefore, more research is needed to expand the evidence base and explore optimal communication methods for fertility preservation in the CAYA with cancer group. Equally, the patient voice (PPIE) is missing from the current published evidence in this area, which would be a recommendation for future research to ensure data is representative and translatable to CAYA with cancer and their families.

Communication of future fertility status and the need to discuss this in an honest and open manner was a key finding in PICCS1 (interviews). The PICCS1 (interviews) with CAYA cancer survivors and parents highlighted the need for further research to explore the optimal method of delivery for sensitive and potentially upsetting information. HCPs in the PICCS1 (interviews) also reported that they would like to see more of a patient-led communication model that

allowed for prompt referral to specialist services for those at the greatest risk of long-term damage. This finding was also reflected in the PICCS1 (systematic review) studies that advocated for a model of CAYA cancer survivorship late effects communication that was open, honest, and demonstrative of an active two-way partnership between the HCP and the family (Greenzang, Dauti, and Mack 2018, Brand, Fasciano, and Mack 2017, Vetsch et al. 2017, Lie et al. 2015 and Wright et al. 2014). This affirms the need for further exploration of this issue. However, future research in this area would need to include data from more recent diagnoses, to reflect the current clinical landscape and not solely information recall from 20-30 years ago. A caveat to the PICCS1 findings is the representation of current HCPs and CAYA cancer survivors/parents treated between 5-30 years ago. Therefore the recommendations might not reflect the current methods of communication used by HCPs and is a limitation to the findings.

7.2.4 Beyond reproductive health

The need to include communication of future reproductive health risks for female CAYA cancer survivors was highlighted in PICCS1 (systematic review). Wright et al. (2014) reported that some adolescent cancer survivors only realised that they were fertile when they became pregnant or when they had fathered a child unexpectedly. Lehman et al. (2019) also described the lack of knowledge surrounding fertility and if this can change into adulthood when they reported that despite communication of high-risk for infertility based on cancer treatments, sometimes laboratory-evaluated fertility tests revealed that

pregnancy was still a possibility. Therefore, repeated fertility-related communication throughout survivorship was recommended as essential.

When female CAYA cancer survivors become pregnant, there is strong evidence to support an increased risk of adverse maternal and fetal outcomes (in particular when they have been treated with radiotherapy to the pelvic-abdominal region) (Polanco et al. 2021, van der Kooi et al. 2019). Despite this evidence, maternal and fetal outcomes of female CAYA cancer survivors have received little attention in paediatric oncology or obstetric research (Polanco et al. 2021). Likewise, national health care policies and guidance documents for the care of high-risk women in pregnancy, fail to identify women with a history of cancer as a high-risk group for pregnancy and birth (Polanco et al. 2021).

PICCS1 (interviews) with HCPs revealed that when asked if CAYA cancer survivorship would be an emerging issue within maternity services (due to the increasing survival rates and fertility of females following treatment), the participants were not sure or declared a lack of knowledge in this area. PICCS2 therefore aimed to address this ambiguity by demonstrating consensus for the need to communicate future reproductive health risks, including pregnancy outcomes with female CAYA cancer survivors and their families. Interestingly, the panel recommended that the communication of low risks, such as cancer in the offspring of the survivor and a low risk of fetal abnormality following CAYA cancer were equally important to communicate as reassurance. The expert panel reflected opinions from HCPs from obstetric and midwifery backgrounds, suggesting that future reproductive health risks for female CAYA cancer survivors is an important issue to discuss. However, wider opinions would be

needed, due to only four obstetric professionals being included in the PICCS2 expert panel.

Reproductive health, as defined by WHO (2021), encompasses more than just pregnancy and birth. The wider context that includes sex education, contraception advice, relationship guidance and in the specific context of female CAYA cancer survivors, how to cope with high possibility of early menopause and infertility. This area of CAYA cancer survivorship has been significantly under researched and overlooked within CAYA cancer survivorship research (Cherven et al. 2020). An important caveat to the gap in knowledge surrounding sex education and reproductive health of CAYA with cancer is the high likelihood of young people missing important education sessions usually held within school, due to hospitalisation or treatments.

How the communication of wider reproductive health information (e.g., sexual health and contraceptive advice) fits into a late effects risk communication model is an additional challenge for HCPs, and makes the likelihood of addressing unmet informational needs even more complex. Kirchhoff et al. (2017) acknowledged this difficulty and emphasised that clinicians need to recognise that sexual health advice is also an important unmet informational need of young people with cancer. However, issues surrounding the defined legal of age of consent and professional assessment of maturity and competence (Gillick or Fraser competence[6]) can influence the HCPs ability to

[6] **Gillick competence** is a term originating in England and Wales and is used in medical law to decide whether a child (under 16 years of age) is able to consent to their own medical treatment.

communicate this information directly with a CAYA. Gillick competence refers to the assessment of mental capacity of a child to consent to medical treatment under the age of 16 years without the need for parental permission or knowledge. Fraser guidelines (BAILII - The Law Reports 1986) specifically refer to the communication of sexual health and contraceptive advice, which is of direct relevance for female CAYA with cancer. HCPs are advised that when young people <16 years of age wish to discuss sexual health and/or contraceptive advice without a parent present then they should satisfy the following criteria (Table 46):

Table 46 - Fraser guidelines for providing sexual health advice for patients <16 years of age (adapted from NSPCC 2020)

Fraser guidelines for providing sexual health advice
The young person cannot be persuaded to inform their parents or carers that they are seeking this advice or treatment (or to allow the practitioner to inform their parents or carers).
The young person understands the advice being given.
The young person's physical or mental health or both are likely to suffer unless they receive the advice or treatment.
It is in the young person's best interests to receive the advice, treatment or both without their parents' or carers' consent.
The young person is very likely to continue having sex with or without contraceptive treatment.

7.2.5 Childbearing preferences

A better understanding of female CAYA cancer survivors reproductive intentions would allow HCPs to tailor conversations to the individual (Newton et al. 2021). A report by Perez et al. (2020) investigated the lack of sexual health

communication with female CAYA cancer survivors in the USA and found that often, such conversations were overlooked due to the content being classed as ‘uncomfortable’ to discuss (Perez et al. 2020). The authors reported a lack of knowledge by HCPs about how to appropriately communicate sensitive information with young people. A recommendation was made for HCPs to be more open in addressing issues such as sexual preferences, gender identity, childbearing preferences and cultural values of CAYA cancer survivors. Perez et al. (2020) reported that more open conversations about reproductive health correlated in a positive uptake of contraception, a better knowledge of future reproductive health risks, and facilitated better professional relationships between CAYA with cancer and their HCP.

Further exploration of childbearing preferences of female CAYA cancer survivors might also reveal more evidence to explain the lower rates of pregnancy in female CAYA cancer survivors when compared to unaffected siblings and the wider population (reported by Reulen et al. 2017). Newton et al. (2021) revealed that lower rates of childbearing, are not just due to biological causes or cancer treatment damage to organs but are affected by psychological worries about fertility status and a high risk of pregnancy complications. Female CAYA cancer survivors reported that future fertility worries negatively impacted their romantic relationships, caused by a fear of disappointing their partner with their infertility (Newton et al. 2021). This finding also reflects the PICCS1 (interviews) that suggested the psychological implications of unmet informational needs extended much further than expected and into every-day lives of CAYA cancer survivors.

A cross-sectional analysis study by Lam et al. (2020) reported that 22% of female cancer survivors in the USA were ‘voluntarily childless’ (defined as an active choice to not have children due to social, medical or personal preference). Interestingly, they suggested that the lower rates of pregnancy for female CAYA cancer survivors was not due to damage caused by cancer treatments, but intrinsically linked to sexual orientation and the age of the survivor at the time of being questioned (Lam et al. 2020). In contrast, however, Benedict et al. (2021) reported that in their cohort of 25 female cancer survivors, not knowing about their fertility status, led to indecision about starting a family and postponement/avoidance of pregnancy for fear of medical risk. Therefore, this highlights that assumptions by HCPs and parents about the future childbearing choices of CAYA with cancer should be avoided with fertility options and preferences openly discussed at regular time points together with the CAYA with cancer.

Similarly, it is also prudent to consider what information has already been given to the CAYA cancer survivor and consider the accuracy of this information at the present time (Lam et al. 2020). This will help to avoid confusion, misinformation and further distress to the CAYA cancer survivor, particularly when medical advancements may have changed the risks for the survivor. This recommendation was supported by a HCP in the PICCS1 (interviews) who advised that in their practice, they would first aim to discover what CAYA cancer survivors and/or parents had been told about their future fertility and reproductive health risks and then make a plan of care from that point.

7.3 Limitations and strengths

7.3.1 Personal reflection

Critical reflection of learning, development, and process, and looking back at what has been done and why; is an essential element in all stages of training, education, and revalidation requirements (NMC 2019). A critical reflection of the underlying motivations for the research topic and a description of the successes, barriers, and difficulties faced during the research study helps to analyse the positionality of researcher and assists personal growth and development as well as reducing bias within the study. CAYA cancer survivorship and the long-term effect of cancer treatments on fertility and reproductive outcomes of female survivors continues the researcher's inquiry and follows the HEE/NIHR funded master's project entitled 'Female Childhood Cancer Survivors and the impact of flank, abdominal and pelvic radiotherapy on live birth' (Polanco et al. 2021).

The primary interest in this area of research arose from the first-hand experiences of the researcher of having a child with cancer and the emotional journey the family takes. Parents of CAYA with cancer need to rapidly understand, comprehend and make life-changing decisions about the future of their child. The decisions made about cancer treatments also extend to potential risks of infertility for their child. Communication of future risk and having enough information to make an informed decision about the future outcomes of your child can be overwhelming, especially in cases where there is lack of evidence-based information.

The researcher has a 10-year background as a parent advocate and undertaking patient and public involvement and engagement activities in the field of CAYA cancer research. Combined with 13 years of clinical experience as a midwife, and five working within maternity clinical research trials, the researcher has been able to develop a unique insight into both the patient/parent voice in research as well as the HCP perspective that includes setting up, recruiting, and leading research trials. The researcher holds a passion for developing research study designs that reflect an embedded PPIE approach, as seen in PICCS1 and PICCS2.

7.3.2 The impact of COVID-19

During the timeline of the PICCS1 and PICCS2 studies, the COVID-19 pandemic (see glossary) was a significant challenge to the delivery, focus, and completion of the study. The researcher encountered particular challenges caused by the pandemic, in trying to complete the study within the agreed timescales and ensuring that recruitment was still possible within all stakeholder groups.

PICCS1 and PICCS2 included participation of HCPs based within primary and secondary care, many of whom were re-deployed to areas of clinical need during COVID-19. The researcher, as a midwife by profession, was also re-deployed to the clinical area, and academic studies were placed on hold. This led to a pause in all study related activity for three months. Ethical approval was extended to allow for this and also a substantial amendment submitted to the HRA ethics committee (see Appendix 8). One member of the expert panel was

unable to participate due conflicting demands on their workload caused by the pandemic. The remaining members of the PICCS2 panel reported an desire to continue with the research, reinforcing the need for CAYA cancer survivorship research.

Struggles with mental well-being, anxiety caused by the pandemic and trying to avoid burn out during the clinical re-deployment of the researcher were particular personal challenges. The adjustment of returning to full-time study after being in the clinical space was also identified as a difficulty, which had an impact on the timeline of the studies and the productivity of the researcher. Regular supervisory meetings and one-to-one meetings with the director of studies helped to mitigate some of the concerns and helped to re-focus and re-engage a positive mindset. Despite the challenges of the COVID-19 pandemic, the researcher was able to return to studies after three months and complete the research within the timeframe allowed. Ethics were supportive of the extension to the timeline and the university were also supportive with a non-detriment policy for students. Likewise, funding for the researcher was extended for three months, allowing for continued full-time study.

7.3.3 Contribution to new knowledge (theory)

The adoption of a dual-paradigm philosophical framework, based upon the critical realist method of enquiry is a novel approach adopted for PICCS1 and PICCS2. The findings from PICCS1 and PICCS2 have provided evidence to support the use of critical realism in health care research. It demonstrates how scientific data can be complemented by the personal beliefs and experiences of

those affected by the issue. The same merit is given to both data that can be measured and validated and the patient voice/experience, providing a balanced view that is inclusive of the patient/parent voice.

The adoption of a critical realist philosophical framework to address the issue of unmet informational needs of female CAYA cancer survivors, provides an example for addressing issues in health care that are not easily solved by using traditional research designs, such as RCTs. In circumstances where a purely quantitative or qualitative methodology are not sufficient, critical realism aims to bridge the gap between the two paradigms, providing a richer and more translatable method to improve patient outcomes. RCTs by design, provide little indication as to how an intervention will work in specific populations, or how the effect of cultural or socioeconomic circumstances will impact the overall outcome (Clark, MacIntyre, and Cruickshank 2007). This creates an issue for the generalisability and confirmation of similar effect when replicating studies on a wider scale and in different populations (Clark, MacIntyre, and Cruickshank 2007).

Critical realism as a means to address both the scientific and external contextual factors surrounding a problem has been encouraged by the MRC in their *Framework for the Development and Evaluation of Complex Healthcare Interventions* (Dieppe et al. 2006). However, as yet, critical realism has not been widely adopted or is evident in reported funding applications of large health research funders (such as NIHR and Wellcome) (Corry, Porter, and McKenna 2019). Therefore more studies using this approach are needed to effectively validate its use and application of methods in health care research.

PICCS1 (systematic review) provided a robust and transparent review process with PPIE oversight embedded throughout. Despite wide heterogeneity of population cohorts and measured outcomes of the included studies the findings from the literature provided sufficient evidence to guide the methods and content for PICCS1 (questionnaires and interviews). A limitation to the systematic review was several iterations of the study protocol to reflect the change in scope (to all late effects) and to reflect delays caused by COVID-19. Despite this, the use of the PRISMA reporting guidelines and risk of bias assessment provided an acceptable level of rigour to the review. The research question for the systematic review was broad to include communication of all late effects, rather than a focus on future fertility and reproductive health. By changing the focus of the review to a broader inquiry (all late effects) this allowed for future iteration to determine the statements used in PICCS2, which may not have been related to future fertility or reproductive health risks.

Data from the online questionnaires provided the researcher with a deeper insight into the identified gaps from the published literature and explored the gaps from the insight of female CAYA cancer survivors, parents, and HCPS. There was a notable disparity in the number of responses between the two questionnaires, with more CAYA cancer survivors and parents than HCPs taking part. This outcome was predicted by the researcher, due to the increased time demands of HCPs and the difficulties in accessing this group without active recruitment via the NHS. However, the questionnaires were able to provide a dual perspective of patient/parent and HCP, which has rarely been reported in the field of communication of late effects with CAYA cancer survivors.

PICCS1 (interviews) were designed and approached by the researcher with caution, reflective of recommendations by Davies et al. (2020) that advise sensitive conduct and design of interviews with cancer survivors, to avoid potentially distressing content and memory triggers. Best practice for discussing sensitive and possibly triggering topics is to use a face-to-face method for interviewing (Fox and Ward 2008). However, this was not feasible due to time and financial constraints of the PhD and the wide geographical locations of interviewees (n.b. interviews were conducted pre COVID-19). Despite the use of an application to aid the transcript process, *Otter* (Otter AI 2021), manual transcription was also needed as the software did not capture all data or recognise specific terminology relating to cancer and reproductive health. The overall interview process and transcription activity was viewed positively by interviewees and the researcher, with adequate support, guidance and resources available for use.

A notable limitation to the interviews was sample size of eight. This was purposely small as the researcher wanted to capture a ‘snapshot’ of the deeper personal experiences of CAYA cancer survivors, parents and HCPs. Data saturation or the point at which no new data arises, is usually determined as the place to stop data collection in qualitative inquiry and guides the sample size choices of the researcher. Often in-depth topics attract a smaller sample size, with larger samples used for broader themes. The PICCS1 interviews did not reach data saturation, however the eight interviews represented a broad range of views from a multi-stakeholder background. The findings enriched the online questionnaire and systematic review findings and did not form the main body of

PICCS1. The addition of the interviews provided an additional layer of robustness and reflected the critical realist approach used by the researcher that upholds science informed by real-life experience.

The triangulation of data from PICCS1 was a challenging process due to the breadth and depth of data to be synthesised. Selection of the correct triangulation theory was paramount; however the choice of in-between methodological triangulation facilitated the collation of data without compromise of data integrity. In-between methodological triangulation upheld the philosophical underpinning of the study (critical realism) and demonstrated how the findings from PICCS1 had been appraised and integrated into the design of PICCS2.

7.3.4 Contribution to new knowledge (practice)

The expert guidance document from PICCS2 (Appendix 13), and the novel primary data reported in PICCS1 (questionnaires and interviews) adds new evidence to the field of CAYA cancer survivorship and communication needs. PICCS2 presented a co-produced guidance tool, setting out recommendations for:

- the optimal timing of information delivery for late effects (fertility and reproductive health)
- the HCP considered to be most appropriate to deliver and discuss this information
- a definition of fertility post-cancer treatment

- recommendations for how to best support parents of female CAYA cancer survivors when communicating key future fertility and reproductive health risks to their child

The guidance tool addresses the key issues identified within PICCS1, that did not have a defined answer or solution in the existing published evidence. The tool (Appendix 13) provides an opportunity for HCPs to directly implement an evidence-based resource, formed from expert opinion in this field. Prior to this document, a resource for the communication of future fertility and reproductive health late effects risk for female CAYA cancer survivors and their families did not exist. The tool is intended to be a starting point for education and awareness of HCPS. However, a notable limitation is that the guidance is not officially ratified by an official health care body or organisation. Despite this, there is potential for the output to be evaluated and adopted through a process of peer review and further iterations. Equally, data collected in PICCS1 from CAYA cancer survivors and parents is reflective of communication that happened >11 years ago for most participants. This suggests that more experiences are needed that are reflective of current communication in more recently diagnosed patients. For example, female CAYA cancer survivors wanting to know their fertility status or consider pregnancy now, will have very different informational needs to those that are currently being treated for cancer.

A measure of quality for the recommendations is reflected in the stakeholder representation of the Delphi panel, who reflect experts in this field with experience of creating clinical guidelines. The inclusion of CAYA cancer survivors, their parents and PPIE oversight of PICCS1 and PICCS2 also adds a

level of transparency to the research process, maximising the potential for patient impact on a wider scale. The recruitment process, although subject to a certain level of selection and researcher bias, represented a wide stakeholder group that included HCPs, academics and CAYA cancer survivors and their parents and provided a balanced and inclusive view of the issues.

The method chosen of three rounds, email, email, and web-based meeting was adapted from the original design of email, email, face-to-face, due to the nationwide restrictions caused by the COVID-19 pandemic. This prohibited meeting of groups in person, however, benefitted the study design as it allowed panel members to attend the web-based meeting who might have not been able to due to home or work commitments. Caveats to the recommendations that included consideration of age, stage of cancer, and maturity of the CAYA cancer survivor were evident; but serve to highlight the need for further research in this area. The final expert guidance is a platform for development and iteration based on emerging evidence and expert advice.

7.4 Implications for practice

PICCS2 produced a set of expert recommendations for the optimal communication of future fertility and reproductive health risks with female CAYA cancer survivors and/or parents, the first of its kind in the UK. The guidance document can be directly implemented into clinical practice and be used for education and awareness by HCPs working in the field of CAYA cancer survivorship.

However, there is a need for further research to validate findings from PICCS1 and PICCS2 on a larger scale to ensure that recommendations can be implemented on a national level. PICCS1 provided a deeper insight into the personal experiences, values and communication needs of female CAYA cancer survivors, parents and HCPs during key late effects communication exchanges. PICCS1 further reiterated the need to address the high risk of adverse psychological outcomes linked to unmet informational needs of CAYA cancer survivors.

An extended set of future recommendations, based upon the findings from PICCS1 and PICCS2 have been tabulated below. They demonstrate the scope of investigation and breadth of exploration that is needed to fully understand this complex issue but is not an exhaustive list, but an evolving research field within CAYA cancer survivorship care (Table 47).

Table 47 - Recommendations for future research

Recommendations
Further investigation of safe toxicity thresholds for reproductive organs (reflective of current treatment protocols)
Further exploration into the optimal time point for delivery of late effects risk communication (including fertility and reproductive advice)
Analysis of a causal link between adverse psychological and social outcomes of CAYA cancer survivors and informational unmet need
Further evaluation of the PICCS2 guidance with an interventional study to test level of unmet informational need before and after the intervention or acceptability of guidance by HCPs
Further research examining parents' experiences of communicating late effects risk information to their children (including future fertility and reproductive health risks)

Recommendations
Investigation of factors that affect psychological well-being of female CAYA cancer survivors and interventions to address this in the CAYA with cancer population

The tabulated recommendations above, could adopt various forms and levels of inquiry. For example, further investigation of toxicity thresholds of the uterine tissue and the long-term consequences of damage could be explored in an in-vivo environment using retrospective tissue collection of CAYA with cancer who have donated specimens to a tissue bank as part of their treatment. Funding for this type of research would be available from institutions such as the Wellcome Trust and would be suitable for post-doctoral research.

Ethnographic inquiry using interviews and observations of clinical settings could be used to explore the relationship between the parent and the CAYA cancer survivor and the manner that late effects risk is communicated. This could reveal more about assumptions such as information shielding by parents and miscommunication between the HCP and parent in the initial information exchange (if the child is too young to receive personally).

Psychological well-being of CAYA cancer survivors is a topical issue at present and the focus of enquiry by European organisations such as PANCARE. A retrospective cohort study of CAYA cancer survivors, stratified by age at diagnosis would provide a basis of investigation to explore the impact of unmet future fertility and reproductive late effect risks information on long-term psychological well-being. Substantial consideration of well-being for this patient group would be needed for this work to ensure that referral pathways and

signposting was in place due to the sensitive nature of enquiry. Likewise an interventional approach such as the HOPE programme, used for adult cancer survivors would be suitable to test in a group of CAYA cancer survivors, tailored to address issues related to unmet informational needs (Martin et al. 2020). Analysis of psychological well-being before and after the intervention could provide key insights into the scale and depth of the problem, alongside a possible solution that is easily transferable into direct patient care and impact.

7.4.1 Measuring impact of PICCS2

Evaluation of success or the impact of research is often something that is not planned for when forming recommendations for future research (NIHR 2012). Measurement of impact and translatability into patient care is needed to ensure that (a) an intervention works, (b) that the impact is positive for the patient and the HCP, and (c) that the acceptability of the intervention will be high. An example of a tool that could be used to measure the impact of the PICCS2 recommendations is The Action to Support Practices Implementing Research Evidence tool (ASPIRE). ASPIRE is an evidence-based tool used in health care settings that evaluates clinical service performance following an intervention (Uy, Lizarondo, and Atlas 2016). Originally developed to address the challenges faced by HCPs in evaluating the impact of patient-outcome focused interventions, the tool could be used to test a variety of interventions aimed at improving CAYA cancer survivorship care (Table 48).

Table 48 - ASPIRE framework for evaluation of health care services (adapted from Uy, Lizarondo and Atlas 2016)

ASPIRE for quality framework	
Area for evaluation*	The evaluation team identifies and prioritises the clinical area for performance evaluation
Set goals*	Based on the identified clinical area, the evaluation team sets the goals for performance evaluation
Performance indicators**	The evaluation team, assisted by experienced researchers, identifies performance measures or indicators
Information sources*	The evaluation team maps the performance measures to information sources
Report results**	The researchers and evaluation team collaboratively analyses the results and report to stakeholders
Evaluate**	The researchers and evaluation team collaboratively evaluates the performance evaluation system
* Tasks are responsibilities of allied health practitioners ** Tasks are shared responsibilities of researchers and practitioners	

Digitization of the PICCS2 expert guidance document, could be an additional method of ensuring dissemination and adoption of the recommendations on a national level. Digitization offers benefits such as ability to implement new research and iterations of the guidance easily, without having to manually amend paper copies or recall versions from clinical settings. Digitization would also offer a lost-cost option for sharing the guidance with a variety of HCPs from different disciplines, who may encounter female CAYA cancer survivors. This also includes those who do not normally have access to clinical guidance such as charities and trusted third parties (e.g., local CAYA cancer support networks).

Likewise, adoption of the guidance by professional health care bodies such as CCLG, or NICE would encourage future development and iterations of the guidance with in-built mechanisms to record patient and parent feedback and HCP acceptability. An annual review and clinical updates from a multi-stakeholder expert group, would also ensure the longevity of the guidance to ensure it reflects the most up-to-date research and continues to meet the needs of female CAYA cancer survivors and families.

The PICCS2 guidance, although intended to be used as a resource for HCPs, adds to the current information resources that exist for cancer survivors. The website *Cancer, fertility, and me,* produced by a collective of fertility and psychological HCPs working in the field of cancer survivorship (University of Edinburgh 2020) is a rich resource that acts as a decision aid for women that have had cancer and their fertility and reproductive health needs following treatment. Although not CAYA specific, it covers adults that may have had cancer some time ago and those that my have had it recently. The PICCS2 expert guidance for communication of risk, would sit alongside this evidence resource well and input for development could be gained from cancer survivors that access the site. However, a noted caveat to the site is the omission of pregnancy and birth specific information for survivors, that may have a high-risk of complications.

The guidance could also be adopted within the European CAYA cancer survivorship networks, including PANCARE. However, as the example of the *SurPass* survivorship passport (Haupt et al. 2018) demonstrated, there may be unknown challenges with the adoption of the guidance on a country-based level

due to variation in health care systems and language.

Chapter Eight – Conclusion

PICCS1 provided novel data to support findings within existing literature, but also provided a unique and in-depth view of unmet informational needs from the point of view of the female CAYA cancer survivors, parents and HCPs. PICCS1 amplified the value of including the patient voice/experience alongside traditional scientific findings by using a critical realism methodology to address the many complexities of addressing the needs of CAYA cancer survivors. This approach to critical realism, provides an example of how a dual-paradigm methodology can be used in health care research, illustrating it's translatability to other health research study designs.

PICCS1 (systematic review) revealed that CAYA cancer survivors had significant unmet informational needs relating to the communication of late effects risks (Vetsch et al. 2017, Wakefield et al. 2012, Wright et al. 2014). Female CAYA cancer survivors in particular reported unmet informational needs pertaining to their future fertility and reproductive health risks following treatment for cancer. A strong link between unmet informational needs and long-term psychological distress was evident in the published literature (van Dorp et al. 2018, Gianinazzi et al 2014, Crawshaw et al. 2009) and was a strong theme throughout the PICCS1 (interview) transcripts from CAYA cancer survivors and parents.

The long-term negative emotional impact over ambiguity surrounding future fertility status and the importance of communicating future fertility risks early on at diagnosis and again at key timepoints (e.g. treatment completion), is underestimated by HCPs working in CAYA cancer survivorship care (Signorelli

et al. 2019b, Wright et al. 2014). This view was supported by female CAYA cancer survivors and their parents in the PICCS1 interviews. Evidence to explore who is the most appropriate HCP to communicate late effects risk information, particularly sensitive information (such as future fertility) is largely underreported in the published literature and mirrored the PICCS1 questionnaire findings, demonstrating a lack of consensus in who or when this type of information should be discussed with families. Similarly, with format for communication of information, and appropriate timing of conversations about late effects, future fertility and reproductive health risks. Published and anecdotal evidence was lacking or ambiguous, leading to the inability to make recommendations that can be easily applied to the wider CAYA cancer survivor population. Verbal communication of late effects risk with a written 'back-up' was the preferred format for communication of late effects information, however this finding was reported before the COVID-19 pandemic. Therefore preferences may have now changed to digital/online and requires further investigation.

HCPs demonstrated a sound knowledge of future fertility risks for female CAYA cancer survivors such as an inability to conceive and the risk of early menopause (PICCS1 questionnaires). However, despite over 10 years of evidence to demonstrate increased risk of adverse outcomes in pregnancy and birth for female CAYA cancer survivors treated with radiotherapy (Reulen et al. 2009, Polanco et al. 2021), HCPs did not discuss this risk in clinical consultations with families. Similarly, HCP awareness and acknowledgement of level of treatment received and the higher risk of late effects linked to

combination therapies when compared to chemotherapy or surgery alone needs to be addressed in communication guidance.

CAYA cancer survivorship services in the UK are not yet meeting the standards recommended by health regulatory bodies such as NICE and the NHS (NICE 2014, NHS England 2019a). Likewise fertility preservation services for paediatric oncology patients are not yet aligned with standards set out by NICE (NICE 2014). The HCPs in PICCS1 (interviews) suggested that there may be scope to develop a 'code of practice' for paediatric oncology MDTs in the UK and this should be investigated further to help the standardisation of CAYA cancer services to meet the needs of CAYA with cancer.

Expert recommendations from PICCS2 are directly applicable to HCPs working in the field of CAYA cancer survivorship in the UK (Appendix 13). Guidance for the optimal communication of future fertility and reproductive health risks has not been addressed previously in the literature (e.g. Mulder et al. 2021, van der Kooi et al. 2021), or in clinical practice guidelines. The manner and sensitive delivery of late effects risk information was a key finding from the PICCS1 (interviews), therefore guidance for optimal methods of communication are warranted.

Despite this, how, when, and who is the most appropriate HCP from the clinical team to deliver future fertility and reproductive health risks is dependent upon the age-appropriate needs and maturity of the CAYA with cancer. An individualised approach, fully involving the young person in their care and offering the opportunity to discuss information with or without the parent present is recommended to meet the holistic needs of the CAYA. Level of informational

need should also be assessed at regular intervals to accommodate for the broad age range of CAYA with cancer, ensuring that informational needs are met at the correct time for the CAYA.

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Appendices

Appendix 1 - PICCS1 Online questionnaire (CAYA cancer survivors/parents)

PICCS (Pregnancy Information for Childhood Cancer Survivors) Online Survey

Start of Block: Default Question Block

Start of Block: Default Question Block

Q1 Thank you for agreeing to take part in this online questionnaire.

We want to have a better understanding about what information is given to childhood/teenage/young adult cancer survivors and their families regarding future pregnancy risk following treatment for childhood cancer (which included radiotherapy to the tummy).

We would like to ask patients/parents and also health care professionals to complete this questionnaire to get balanced view of what currently happens in the UK.

We are interested to hear about any conversations, audio, video, printed information or internet resources you might have been given in relation to future pregnancy risks following treatment, in particular if you/your child received radiotherapy to the tummy. This information must have been given to you as part of your cancer care from a professional and not from third parties such as charities or websites, e.g. Google.

As part of a PhD funded by Coventry University, Angela Polanco (Research midwife and childhood cancer parent/advocate) will be looking at published articles about what information is currently given to childhood/teenage/young adult cancer patients and their families about long- term health risks following treatment in the UK. This information will then be compared with results from this questionnaire and with some interviews with childhood cancer survivors/their parents and health care professionals. The aim of the project is to see if there are any recommendations that can be made for communication of future pregnancy risks for childhood/ teenage/young adult cancer survivors and their families.

You may stop taking this questionnaire at any point. After you complete your answers, you may withdraw the information, without reason, by contacting the researcher by email at polanco2@uni.coventry.ac.uk within two weeks. If you choose

to do this, there is no risk of affecting your/your child's care or future care in any way. All results will be made anonymous, and answers used for the research project and scientific publications only. Any questions or personal issues that may arise from taking part in this questionnaire can be directed to your long-term follow up care team, GP, or to the organisation links at the end of this questionnaire.

Many thanks for your time.

Q2 We would like you to take part as a parent/patient if:

- [ ] You/your child are a female childhood cancer survivor (diagnosed between 0-24 years old) (1)
- [ ] You/they received radiotherapy to the tummy as part of your/their cancer treatment (2)
- [ ] Your/their cancer treatment ended more than a year ago (3)

Q3 What is your background...

- ○ Parent of a child that had cancer (1)
- ○ Female survivor who hasn't had a child (2)
- ○ Female survivor who has had a child (3)

Q4 How long ago did you/your child complete treatment for childhood cancer?

- ○ 5 years ago (1)

- 6-10 years ago (2)
- >11 years ago (3)

Q5, Do you know how much radiation you/your child received?

- Yes (1)
- Maybe (2)
- No (3)

Display This Question:

If Do you know how much radiation you/your child received? Yes

And Do you know how much radiation you/your child received? Maybe

Q6 If you do know how much radiotherapy was given, please write below (total Gy)

Q7 At what age did you/they receive radiotherapy?

- 0-4 years (1)
- 5-10 years (2)
- 11-16 years (3)
- 17-24 years (4)

Q8 At what age did you/they complete treatment for childhood/teenage/young adult cancer?

- 0-5 years old (1)
- 6-12 years old (2)
- 13-17 years old (3)
- 18-23 years old (4)
- 24 years old and over (5)

Q9 Have you been told that your/your child's treatments for cancer are likely to affect fertility (ability to have a baby) or future pregnancy?

- Yes (1)
- Maybe (2)
- No (3)
- I don't remember (4)

Q10 If you do remember discussing or reading anything regarding future pregnancies or ability to have a baby after treatment for cancer? (please select below anything that might have been mentioned which may be more than one answer)

- [ ] Difficulty becoming pregnant (1)

- [ ] The risk of early menopause (9)
- [ ] Possible risk of miscarriage (2)
- [ ] Possible risk of a small baby (3)
- [ ] Possible risk of premature baby (born early) (4)
- [ ] What the risk of cancer in the baby might be (5)
- [ ] Possible pregnancy risks to the mother (e.g. bleeding at birth, high blood pressure during pregnancy, thyroid issues) (6)
- [ ] Possible risks of abnormalities in baby (7)
- [ ] Something else (8)

Display This Question:

If you do remember discussing or reading anything regarding future pregnancies or ability to have...

Something else

Q11 If you selected 'something else' to the last question, please write below what you remember:

Q12 If you were given/told about any information for you/your child, please indicate how this was given to you (you can select more than one answer):

- [ ] Spoken conversation (1)

- [ ] Leaflet (2)
- [ ] Audio (sound or recording) (3)
- [ ] Link to internet resource (4)
- [ ] other (please specify) (5)

Q13 At what point in the treatment journey was any information given/discussed with you/your family regarding future fertility or long-term effects of treatments for future pregnancy?

- [ ] Diagnosis (1)
- [ ] During treatment (2)
- [ ] When treatment finished (3)
- [ ] When thinking about starting a family (4)
- [ ] When pregnant (5)

Q14 Thank you for taking the time to participate in this questionnaire.

Your responses will be used for a PhD project looking into the best way to communicate information to childhood cancer survivors about future pregnancy risks related to treatments. *The information collected will be made anonymous and is confidential. If by doing this questionnaire, you feel you would like to talk to someone or have any questions, please contact your local paediatric/adult oncology long-term follow up team or your GP. You can also contact the following organisations for more*

support and information: https://www.clicsargent.org.uk/
https://www.macmillan.org.uk/

Thank you for taking part. If you have changed your mind and wish to withdraw you answers, please enter a 4-digit code below and email polanco2@uni.coventry.ac.uk with the code and your answers will be removed. You may do this up to two weeks after completing your answers and this will not affect you/your child in any way.

○ 4-digit code (1) _____

Q17 We would also like to invite a selection of participants who have completed this questionnaire to take part in more in-depth telephone interviews to gain a better understanding of your/your child's experience. If you would like to take part in this part of the project, which involves a 10–15-minute telephone interview, please click on the link below which will take you to a form to complete your details.

As a thank you for taking part in the interview we can offer a gift voucher for £10. This will be sent to you by the researcher following completion of the interview.

https://coventryhls.eu.qualtrics.com/jfe/form/SV_5jLpXE1FmWEUSPj

Many thanks for your time.

Appendix 2 - PICCS1 Online questionnaire (HCPs)

PICCS (Pregnancy Information for Childhood Cancer Survivors) Online survey Health Care Professionals

Q2 Thank you for agreeing to take part in this online questionnaire.

We want to have a better understanding about what information is given to childhood/TYA cancer survivors and their families regarding future pregnancy risk following treatment for childhood cancer. In particular those which were treated with radiotherapy to the abdomen/flank or pelvis.

We would like to ask patients/parents and also health care professionals involved in the care of childhood and TYA cancer patients to complete this questionnaire to get balanced view of what currently happens in the UK. As a health care professional, we are interested to hear about any consultations, conversations, audio, video, printed information or internet resources you have provided to patients and their families in relation to future pregnancy risks following treatment. This information must have been given as part of routine cancer care from a professional working in the field of paediatric/TYA oncology, not from third parties or charities or external organisations, websites, e.g. Google.

As part of a PhD funded by Coventry University, Angela Polanco (Research midwife and childhood cancer parent/advocate) will be undertaking a review of available evidence to understand what information provision currently exists in the UK for childhood/TYA cancer survivors with regards to long term health risks. This literature review will then be compared with results from this questionnaire and will be further explored with semi-structured interviews with selected childhood cancer survivors/their parents and health care professionals. The aim of the research is to produce evidence-based recommendations for communication of potential future pregnancy risk for childhood/TYA survivors.

You may discontinue taking part in this questionnaire at any point. After submitting your answers, you may withdraw the information, without reason by contacting the researcher by email at polanco2@uni.coventry.ac.uk within two weeks.

If you choose to withdraw your information, this will not affect any opportunities, communications or have any future implications for you as an individual. All results will be pseudo-anonymised, and data will be used for the research project and scientific publications only. Any questions can also be directed to the researcher at polanco2@uni.coventry.ac.uk,

Many thanks for your time.

*

Q1 We would like you to take part in this questionnaire as a health care professional if any of the following apply: (please select one or more)

- [ ] You provide care of children/TYA's with cancer (diagnosed between 0-24 years) (1)
- [ ] You provide long-term care of children/TYA's with cancer once treatment has been completed (2)
- [ ] You provide care for children/TYA's with cancer that need radiotherapy to the flank, abdomen or pelvis as part of their treatment (3)
- [ ] You discuss long-term health risks related to treatment for childhood/TYA cancer with patients and their families (4)

Q2 What is your background...

- [ ] Paediatric Oncologist (1)
- [ ] Paediatric Radiotherapy specialist (2)
- [ ] Paediatric Oncology Nurse (3)
- [ ] Paediatric Haemotologist (4)

Q3 Fertility preservation has been identified as a key concern for childhood/TYA cancer patients and their families. At what point might any information be provided about this in the cancer pathway in your experience?

- [ ] At diagnosis (1)
- [ ] During treatment (6)
- [ ] Before high dose chemotherapy/radiotherapy (2)
- [ ] At end of treatment (3)
- [ ] At relapse (5)
- [ ] None of these (7)

Q4 Are you aware of any long-term risks following treatment for childhood/TYA cancer in relation to future pregnancy?

- ○ Yes (1)
- ○ No (2)

Display This Question:

If Are you aware of any long term risks following treatment for childhood/TYA cancer in relation to...

Yes

Q5 If you selected 'Yes', what potential risks would you feel comfortable with discussing with childhood/TYA cancer patients and their families? (You can select more than one answer)

- ☐ Risk of small baby (1)
- ☐ Difficulty becoming pregnant (2)
- ☐ Risk of premature menopause (3)
- ☐ Risk of not being able to carry a baby to full term (4)
- ☐ Risk of cancer in the baby (5)
- ☐ Risk of abnormalities in the baby (6)
- ☐ Something else (7)
- ☐ None of these (8)

Display This Question:

If you selected Yes , what potential risks would you feel comfortable with discussing with child... Something else

Q6 If you have selected 'something else' please explain your answer here:

_____

Q7 What type of information would normally be provided to patients and their families regarding future pregnancy risks following treatment? (you can select more than one)

- [ ] Verbal discussion (1)
- [ ] Printed information (2)
- [ ] Audio (3)
- [ ] Internet resource (4)
- [ ] Other (please specify) (5)
- [ ] None (6)

Q8 At what point in the cancer treatment pathway would this information be provided to patients and families?

- [ ] Diagnosis (1)
- [ ] During treatment (2)
- [ ] At the point of radiotherapy or following radiotherapy treatment (3)
- [ ] At the end of treatment (4)
- [ ] In long-term follow up clinic (5)
- [ ] When pregnancy is being considered (6)

Q9 Who would normally discuss this information with families?

- ☐ Paediatric Oncologist (1)
- ☐ Paediatric Radiotherapy specialist (2)
- ☐ Paediatric Haematologist (10)
- ☐ Paediatric Oncology Nurse (3)
- ☐ Clic Sargent or Macmillan liaison individual (4)
- ☐ Advanced Clinical Nurse Specialist (11)

Q10 With regard to information and knowledge about the risks of future pregnancy after completing treatment for childhood/TYA cancer, in your opinion... (please respond below)

	Click to write Column 1		
	Disagree (1)	Neither disagree or agree (2)	Agree (3)
The information you provide to patients and their families is sufficient (1)	○	○	○
The timing of communicating any risks is optimal (2)	○	○	○
You, as a health professional, know enough about these complications (3)	○	○	○

Patients and families can understand and retain the information provided (4)	○	○	○

Q11 If there are any further comments regarding the information provided to patients and their families that you would like to add, please explain below:

Q14 Thank you for taking part. If you have changed your mind and wish to withdraw you answers, please enter a 4-digit code below and email polanco2@uni.coventry.ac.uk with the code and it will be removed. You may do this up to two weeks after submitting your information, without reason and without it affecting you in any way as an individual.

○ 4-digit code (1) _____

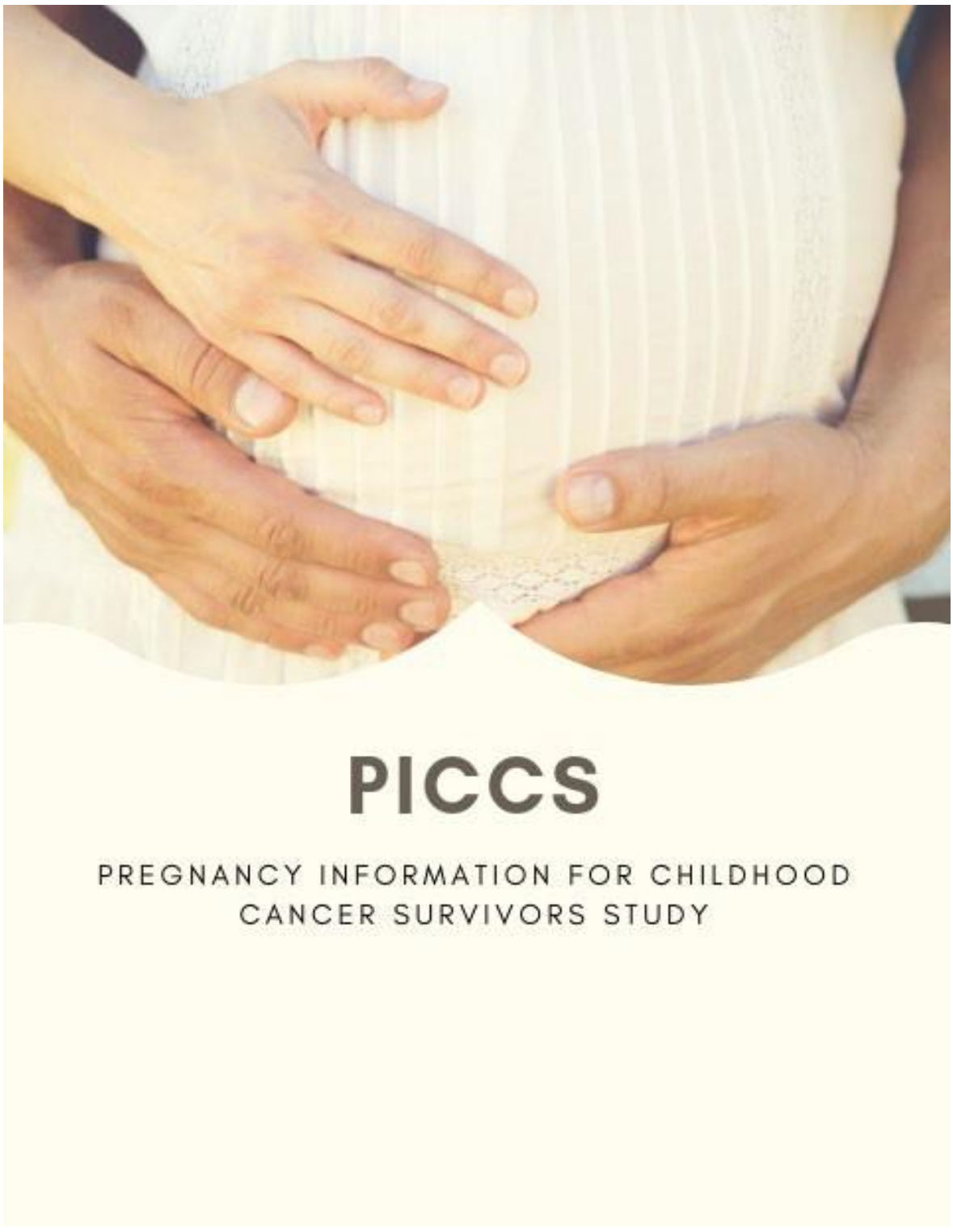
Q15 We would also like to invite a selection of participants who have completed this questionnaire to take part in more in-depth telephone interviews to gain a better understanding of the health care professionals view on information provision of long- term risks for childhood/TYA cancer survivors.

If you would like to take part in this part of the project, which will feature a 10–15-minute telephone interview, please click on the link below, which will take you to a form to complete your details. As a thank you for taking part in the interviews, we can offer a £10 voucher which will be sent to you by the researcher following completion of the interview.

https://coventryhls.eu.qualtrics.com/jfe/form/SV_5jLpXE1FmWEUSPj

Many thanks for your time.

Appendix 3a - PICCS1 Interviews Participant Information Sheet (CAYA cancer survivors/ parents)



PARTICIPANT INFORMATION LEAFLET

Study title: Pregnancy Information for Childhood Cancer Survivors (PICCS1)

Ethics approval number: P87230

You are invited to take part in a research study. Before you decide, it is important for you to understand why the study is being done and what it will involve for you. Please take time to read the following information carefully. Discuss it with friends, relatives or your hospital care team if you wish. It is up to you to decide whether to take part in this study. Whatever you decide, the standard of care you receive will not be affected. If there is anything that is unclear, or you would like more information, please do not hesitate to ask.

About the project

We want to find out more about the information that was given to children/teenagers/young adults with cancer or their parents whilst undergoing treatment or once treatment was completed. We would like to know about the information you were told about future pregnancy risks related to the treatment you or your child received for cancer.

The aim of the research is to ensure that information about possible future risks for female childhood cancer survivors are communicated to families at a time they need it, and, in a way, they understand and can remember.

Why is this important?

In the past 40 years, earlier diagnosis and new treatments for childhood cancer have increased long term survival rates to 82%. More adult survivors of cancer are now able to explore having a family of their own and treatments given as a child for cancer such as radiotherapy, chemotherapy and surgery may carry risks for future pregnancies. It is important that survivors are told about any risks that may affect them, so they can make choices when it comes to choosing their care for pregnancy and birth and so that health care professionals can monitor pregnancies that may be at risk of complications.

Why have I been chosen?

We would like to interview childhood/teenage/young adult cancer survivors (over 18 years old) and/or their parents to take part. We are asking you to take part because you have told us that you/your child is female, has completed treatment for cancer more than one year ago and that you remember being told about future pregnancy risks.

We would like you to answer a few questions about what information you or your child were told and what you can remember now. The questions will be asked over the telephone at a time and day to suit you.

Do I have to take part?

Your participation is voluntary, and you are free to withdraw at any time without giving any reason. Your/your child's care or future care, access to any information or support, or any advice offered by medical teams will not be affected in any way if you choose not to take part in this study.

What do I have to do?

If you would like to take part, you will be asked to read this information sheet and sign a consent form, this will then be emailed to the researcher. The researcher will then contact you to arrange a suitable time and date to do the interview over the telephone to suit you using the details you provided at the end of the online questionnaire. You will be asked if you are happy to still take part and you can discuss any questions you may have.

The interviews will be 10-15 minutes in length and will be audio recorded by using a recording device. Answers will be recorded and then written down. The information will be made anonymous by giving you a false name (pseudonym) or a letter (e.g. participant A). Direct quotations may be used for the project but will not be identifiable to you. No personal information will be directly linked to you or shared with anyone but the researcher.

What are the risks associated with this project?

The study will be approved by an ethics committee before any patients are recruited. The topic of childhood/teenage/young adult cancer survival and future implications for health may cause some distress, memories or worry for the cancer survivor or their parents. Resources for further support and further discussion relating to anything in or relating to this study are available from the research team or can be directed to your care team or GP.

What are the benefits of taking part?

Information gained from this study will provide researchers with valuable information that can be used for other parts of the research project and for future research, helping to improve the communication of long-term risks for future pregnancy for childhood/teenage/young adult cancer survivors and their families. We can offer participants a £10 voucher as a thank you for taking part, which will be sent out by the researcher following completion of the interview. There are no health care or treatment benefits from taking part in this study.

What happens if I don't want to take part anymore?

You may stop taking part in the study at any point. After you complete the interview, you can still choose to withdraw your responses, without reason, by contacting the researcher by email at polanco2@uni.coventry.ac.uk within two weeks of taking part. If you choose to do this, there is no risk of affecting your/your child's care or future care in any way. After two weeks, the information from the interviews will be made anonymous. Once this has taken place, then withdrawal of your information will not be possible.

Will I receive reimbursement any payment for taking part?

We are not able to provide any reimbursement for participants for taking part in the study. However, we can offer a voucher of £10 as a thank you for your participation.

Data protection & confidentiality

Your personal data will be processed in accordance with the Data Protection Act 1998 ("the Act") and General Data Protection Regulation 2016 ("GDPR") and will be kept confidential. It will be stored within the UK, by the researcher on a secure computer programme. Your personal data will only be seen by the researcher. Once the data has been made anonymous, other members of the research supervisory team will be able to view the data, but this will not identify you in any way. Your data will be disposed of securely in accordance with "the Act" and GDPR after five years, as recommended by Coventry University.

What if things go wrong?

In the very unlikely event of you being harmed in any way by taking part in this research project, there are no special compensation arrangements. If you are harmed due to someone's negligence, then you may have grounds for legal action, but you may have to pay for it. If you wish to complain or have any concerns about any aspect of the way you have been approached or treated during this study, please visit the website www.ico.org.uk. Questions, comments or requests about your personal data can be sent to the Data Protection Officer - enquiry.ipu@coventry.ac.uk.

What will happen with the results of the study?

All results will be reported anonymously and used for a PhD publication and possible scientific publications. Information published will be readily available and accessible to participants and shared at conferences/events suitable for childhood cancer survivor/ pregnancy research discussions for professionals.

The researcher will also use results from this part of the project to shape professional guidance recommendations for long-term risks following treatment for cancer in childhood, helping to make sure information is communicated at the right time and in the right way for patients and their families.

Who has reviewed this study?

This study has been reviewed and approved by Coventry University Ethics on 3rd April 2019 (P87230)

Who can I contact for further information?

You can contact the researcher Angela Polanco (lead researcher) at polanco2@uni.coventry.ac.uk for more information about the study or to ask any questions about this information sheet.

Data Protection Rights

The Data Protection Act 1998 ("the Act") gives you the right to access information held about you. Your right of access can be exercised in accordance with the Act. You also have other rights including rights of access, correction, erasure, objection, and data transferability. For

more details concerning these and your other rights including the right to lodge a complaint with the Information Commissioner's Office, please visit website www.ico.org.uk

Questions, comments or requests about your personal data can be sent to the Data Protection Officer - enquiry.ipu@coventry.ac.uk

Thank you for considering taking part in this research study. Whilst we would obviously be delighted if you can help us, there is no obligation to do so.

Appendix 3b - PICCS1 Interviews Participant Information Sheet (HCPs)

PICCS

PREGNANCY INFORMATION FOR CHILDHOOD CANCER SURVIVORS STUDY

HEALTH CARE PROFESSIONAL INFORMATION LEAFLET

Study title: Pregnancy Information for Childhood Cancer Survivors (PICCS1)

Ethics approval number: P87230

You are invited to take part in a research study. Before you decide, it is important for you to understand why the study is be ng done and what it will involve for you. Please take time to read the following information carefully. Discuss it with friends, colleagues and relatives if you wish.

It is up to you to decide whether to take part in this study. Whatever you decide, the decision you make will have no impact or affect upon you as an individual. If there is anything that is unclear, or you would like more information, please do not hesitate to ask.

About the project

We want to find out more about the information or advice that you normally give to childhood/TYA cancer patients and their families during treatment, or once treatment has been completed. We would like to know, more about the information you provide regarding future pregnancy risks related to treatments for childhood cancer.

The aim of the research is to ensure that information about possible future risks for female childhood cancer survivors are communicated to families at a time they need it, and, in a way, they understand and can remember.

Why is this important?

In the past 40 years, earlier diagnosis and new treatments for childhood cancer have increased long term survival rates to 82%. More adult survivors of cancer are now able to explore having a family of their own and treatments given evidence shows that there are links with treatments such as radiotherapy to the abdomen with future pregnancy risk. It is important that survivors are told about any risks that may affect them, so they can make choices when it comes to choosing their care for pregnancy and birth and so that health care professionals can monitor pregnancies that may be at risk of complications.

Why have I been chosen?

We would like to interview health care professionals that are involved in the care of childhood/TYA cancer patients and their families. We are asking you to take part because you have told us that you work in this field and provide information about long-term risks to patients and their families as part of your job.

We would like you to answer a few questions about what information you would give to patients and their families and your experiences of doing so. We would also like to know your thoughts about your knowledge of these risks and your thoughts about care plans for survivors

in future pregnancies. The questions will be asked over the telephone at a time and day to suit you.

Do I have to take part?

Your participation is voluntary, and you are free to withdraw at any time without giving any reason. Your rights will not be affected in any way by not taking part and will have no effect upon you as an individual if you choose not to take part in this study.

What do I have to do?

If you would like to take part, you will be asked to read this information sheet and sign a consent form, this will then be emailed to the researcher. The researcher will then contact you to arrange a suitable time and date to do the interview over the telephone to suit you using the details you provided at the end of the online questionnaire. You will be asked if you are happy to still take part and you can discuss any questions you may have.

The interviews will be 10-15 minutes in length and will be recorded by using a recording device. Answers will be recorded and then written down. The information will be made anonymous by giving you a false name (pseudonym) or a letter (e.g. participant A). Direct quotations may be used for the project but will not be identifiable to you. No personal information will be directly linked to you or shared with anyone but the researcher.

What are the risks associated with this project?

The study will be approved by an ethics committee before any patients are recruited. The topic of childhood/teenage/young adult cancer survival and future implications for health may cause some distress, memories or worry for the cancer survivor or their parents. Resources for further support and further discussion relating to anything in or relating to this study are available from the research team.

What are the benefits of taking part?

Information gained from this study will provide researchers with valuable information that can be used for other parts of the research project and for future research, helping to improve the communication of long-term risks for future pregnancy for childhood/TYA cancer survivors and their families. We can offer participants a £10 voucher as a thank you for taking part in the interviews, which will be sent out following completion of the interview. There are no direct health or treatment benefits from taking part in this study.

What happens if I don't want to take part anymore?

You may stop taking part in the study at any point. After you complete the interview, you can still choose to withdraw your responses, without reason, by contacting the researcher by email at polanco2@uni.coventry.ac.uk within two weeks of taking part. If you choose to do this, there is no risk of this decision affecting you in any way. After two weeks, the information from the interviews will be made anonymous. Once this has taken place, then withdrawal of your information will not be possible.

Will I receive reimbursement any payment for taking part?

We are not able to provide any reimbursement for participants for taking part in the study. However, we can offer a voucher of £10 to participants as a thank you for taking part.

Data protection & confidentiality

Your personal data will be processed in accordance with the Data Protection Act 1998 ("the Act") and General Data Protection Regulation 2016 ("GDPR") and will be kept confidential. It will be stored within the UK, by the researcher on a secure computer programme. Your personal data will only be seen by the researcher. Once the data has been made anonymous, other members of the research supervisory team will be able to view the data, but this will not identify you in any way. Your data will be disposed of securely in accordance with "the Act" and GDPR after five years, as recommended by Coventry University.

What if things go wrong?

In the very unlikely event of you being harmed in any way by taking part in this research project, there are no special compensation arrangements. If you are harmed due to someone's negligence, then you may have grounds for legal action, but you may have to pay for it. If you wish to complain or have any concerns about any aspect of the way you have been approached or treated during this study, please visit the website www.ico.org.uk. Questions, comments or requests about your personal data can be sent to the Data Protection Officer - enquiry.ipu@coventry.ac.uk.

What will happen with the results of the study?

All results will be reported anonymously and used for a PhD publication and possible scientific publications. Information published will be readily available and accessible to participants and shared at conferences/events suitable for childhood cancer survivor/ pregnancy research discussions for professionals. The researcher will also use results from this part of the project to shape professional guidance recommendations for long-term risks following treatment for cancer in childhood, helping to make sure information is communicated at the right time and in the right way for patients and their families.

Who has reviewed this study?

This study has been reviewed and approved by Coventry University Ethics on 3rd April 2019 (P87230)

Who can I contact for further information?

You can contact the researcher Angela Polanco (lead researcher) at polanco2@uni.coventry.ac.uk for more information about the study or to ask any questions about this information sheet.

Data Protection Rights

The Data Protection Act 1998 ("the Act") gives you the right to access information held about you. Your right of access can be exercised in accordance with the Act. You also have other

rights including rights of access, correction, erasure, objection, and data transferability. For more details concerning these and your other rights including the right to lodge a complaint with the Information Commissioner's Office, please visit website www.ico.org.uk

Questions, comments or requests about your personal data can be sent to the Data Protection Officer - enquiry.ipu@coventry.ac.uk

Thank you for considering taking part in this research study. Whilst we would obviously be delighted if you can help us, there is no obligation to do so.

Appendix 4a - PICCS1 Interview schedule (CAYA cancer survivor/parents)

Semi-Structured interview questions – Parent/Survivor

(Participant will be welcomed, and confirmation of consent and audio recording will be confirmed by the researcher. The researcher will make an introduction and will outline that the interview can be paused, stopped or rescheduled if required. If the participant would like to receive extra help and support, then the researcher will signpost to appropriate organisations).

(prompts for researcher as bullet points)

1. Would you feel comfortable telling me about your/your child's cancer diagnosis?
    - When did treatment finish?
    - Did you/they have radiotherapy?
2. Tell me more about what you remember being told about long-term effects of treatments on future fertility and pregnancy?
    - Feelings/worries
    - Talking with others
    - Recall/understanding
    - Timing of discussion
    - Person who discussed information
3. How does knowing this information make you feel now?
    - Thinking about the future
    - Impact on everyday life?
    - Family planning
    - Pregnancy choices?
    - Have they told the child?
4. What do you think is important to know or understand about future pregnancy risks as a patient/parent?
    - Any key points
    - Timing of information
5. Is there anything else you would like to discuss in relation to this project or the previous questions?

(Participant will be thanked for their time, reminded that they have the option to discuss any feelings or worries with signposted organisations and contact information given for withdrawal and confirmation that voucher will be posted to them as a thank you for their time.)

Debrief for the researcher will also take place following the interview with the supervisory team members.

Appendix 4b - PICCS1 Interview schedule (HCPs)

Semi-structured interview questions – Health Care Professionals

(Participant will be welcomed, and confirmation of consent and audio recording will be confirmed by the researcher. The researcher will make an introduction and will outline that the interview can be paused, stopped or rescheduled if required. If the participant would like to receive extra help and support, then the researcher will signpost to appropriate organisations).

(prompts for researcher as bullet points)

1. Can you tell me more about what you normally discuss with patients and their families during a consultation about future pregnancy risk following treatments?
   - Timing in treatment
   - Directed at parent or child?
   - Who does it?
2. In your opinion do you think what you currently tell families and young people is enough?
   - Long-term recall
   - Knowledge of professional
3. Have you ever been faced with any questions you could not answer in a discussion about future pregnancy risks?
   - Referral to obstetric professional?
   - Possible treatment implications?
   - Multi-disciplinary examples of shared care
4. In your opinion is the issue of future pregnancy risk for childhood/TYA cancer survivors an issue for maternity services?
5. Is there anything else you would like to discuss or feel that is important to share or mention?

(Participant will be thanked for their time, reminded that they have the option to discuss any feelings or worries with signposted organisations and contact information given for withdrawal and confirmation that voucher will be posted to them as a thank you for their time.)

Debrief for the researcher will also take place following the interview with the supervisory team members.

Appendix 5 - PICCS2 draft documents/ Round one

Delphi consensus document package –
PICCS2 study

Dear Participant,

Many thanks for agreeing to take part in the Delphi consensus stage of the Pregnancy Information for Childhood Cancer Survivors Study 2 (PICCS2) study.

What is PICCS2?

The PICCS2 study follows on from PICCS1 which looked at all the available evidence for communication of late effects. We then compared this evidence to real-life patient/parent and professional experiences to create a complete picture of how communication of late effects is currently done.

We then focused more on communication of future fertility and pregnancy risks. From this evidence we were able to see what the common issues were, good examples of communication and what the next steps we needed to address were.

What will happen next?

PICCS2 will aim to produce 'expert' recommendations for the communication of risk for future pregnancy for female childhood/adolescent/young adult (CAYA) cancer survivors. These recommendations will be specific to future pregnancy risk and will be formulated by the expert panel of patients/parents and professionals using a method called 'Delphi'. This method is used to gain consensus or 'agreement' in areas where there is no concrete evidence.

We will send out a set of statements and will ask you to rank them on a scale of 1-9 (1=strongly disagree, 9= strongly agree). A statement is said to have reached consensus or 'agreement' if 70% of participants rank from 7-9. If a statement does not reach the consensus level, then feedback and comments from participants will be used to re-frame or discard the statement. Following each round of the Delphi, ranking and feedback will be shared in an anonymous way prior to the next round.

There will be 2 email rounds and 1 web-based meeting round.

The final web-based meeting will then finalise agreed recommendations which will be shared and published widely, with the aim to produce guidance for open and honest communication of late- effects related to future pregnancy for female CAYA cancer survivors.

Why focus on reproductive risk?

Communication of late effects related to future pregnancy has been selected as the focus as I am a midwife by background and the evidence has suggested that future fertility and

reproductive health risks are the biggest areas of unmet late effects need for CAYA cancer survivors.

Can I see the results from PICCS1?

The results from PICCS1 are still being put together but the key features are as follows:

- Future fertility and future pregnancy outcomes are of great importance to both female CAYA cancer survivors and their parents
- Communication of late-effect risks is not done in a standardised way and is not understood very well by the majority of survivors or parents
- There is a need to create a communication method that is individual, that is revisited throughout the cancer journey, and which can be shared with health care professionals outside of oncology once treatment ends
- An open, honest and inclusive communication method is wanted to meet unmet information needs
- CAYA cancer survivors and parents want to be an active part of how future risk is communicated and want to be involved in the survivorship plan

Background reading around the topic has been provided with the inclusion of the studies used for the systematic review. **You do not need to read these, but if you wish to then they are included.**

How long do I have to read and send back the statements?

The first two rounds of the method will involve the email ranking of statements. These will be sent out to participants by email and then you will be asked to email your ranking back to me within 14 days.

When will the 1st round start?

The first two rounds of email ranking will commence on **June 29th and then 27th July**. The final meeting (which was scheduled to be face-to-face but will now be online), will take place on the **4th of September (time TBC)**. The final face-to-face meeting will last approximately 40 minutes.

Will the expert group know who is taking part?

Participants will remain anonymous during the email rounds and will not know who is in the expert panel. Feedback and results from the email rounds will be anonymised and all email communication will be conducted via this email address (polanco2@uni.coventry.ac.uk).

The face-to-face meeting and webinar will not be anonymous, and participants will be asked to introduce themselves and their background. If this is not something that you want to happen then please inform me before the meeting and a random pseudonym will be arranged and/or webcam disabled. Participants will also be thanked by name in any publication of results of the study. If this is not something you wish to happen, then please just let me know in advance of the final round.

What if I have a question?

Any questions about the project, draft statements or the evidence file then please just ask. If you require hard copies of any of the documents this can also be arranged.

Thank you for taking part and I will be in contact in approximately 4 weeks with round one. Please return draft statement feedback and any queries to me within 2 weeks to allow for edits and a reply.

Best wishes,

Angela Polanco

Polanco2@uni.coventry.ac.uk

Delphi consensus draft statements – PICCS2 study/Round one

Based upon the evidence from PICCS1, the following key areas have been identified for communication of late effects related to future fertility and pregnancy. Please rank the following key themes for importance using the scale below.

Please add any suggestions or comments in the free text box below if needed.

Theme	Not important	Unsure of importance	Important
Communicating specific pregnancy and birth risks to female survivors and families	1 2 3	4 5 6	7 8 9
Identifying a key professional to communicate the information	1 2 3	4 5 6	7 8 9
Identifying the best time to communicate information	1 2 3	4 5 6	7 8 9
Creating a plan for communication of information that can be assessed and revised easily	1 2 3	4 5 6	7 8 9
Identifying terminology to use for communication that can be understood by All	1 2 3	4 5 6	7 8 9
Defining what is meant by future fertility (survivor and health care professionals view of the term)	1 2 3	4 5 6	7 8 9
Managing expectations for future fertility and pregnancy	1 2 3	4 5 6	7 8 9
Communicating risks to health care professionals from outside of paediatric oncology	1 2 3	4 5 6	7 8 9

Appendix 6 - PICCS2 participant information sheet

PICCS

PREGNANCY INFORMATION FOR CHILDHOOD CANCER SURVIVORS STUDY

PARTICIPANT INFORMATION LEAFLET

Study title: Pregnancy Information for Childhood Cancer Survivors 2 (PICCS2)

Ethics approval number: IRAS 266234
Chief Investigator: Dr Elizabeth Bailey

You are invited to take part in a research study. Before you decide, it is important for you to understand why the study is being done and what it will involve for you. Please take time to read the following information carefully. Discuss it with friends, relatives or your hospital colleagues or care team if you wish.

It is up to you to decide whether to take part in this study. Whatever you decide, the this will not affect you in any way. If there is anything that is unclear, or you would like more information, please do not hesitate to ask.

About the project

The aim of the research is to provide 'expert' guidance for the communication of possible future pregnancy risks for female childhood, teenage and adolescent cancer survivors following treatment for cancer. We would like to see that information is communicated to families at a time they need it, by the most appropriate professional, and, in a way, they understand and can remember.

Part one of this study (PICCS) investigated the current evidence and experiences of survivors, families and health care professionals. We would now like to complete a group communication exercise called a 'Delphi technique' to come up with group agreement about key statements relating to what should be communicated to families, who should be responsible for this and when this communication should take place in the cancer journey.

The Delphi technique is a widely recognised tool used in research where little or no evidence currently exists. The Delphi technique involves selecting a group or panel of people and features several rounds to gain 'agreement' for a list of statements or professional guidance, which can then be taken forward for use in clinical care. This leaflet gives you information about the study and the Delphi technique so that you can see what will be involved if you choose to take part.

Why is this important?

In the past 40 years, earlier diagnosis and new treatments for childhood, teenage and young adult cancers have increased some long-term survival rates to 82%. More adult survivors of cancer are now able to explore having a family of their own, however treatments given for cancer in childhood or adolescence may carry risks for future pregnancies. It is important that survivors are told about any risks that may affect them, so they can make choices when it comes to choosing their care for pregnancy and birth and so that health care professionals are also aware and can monitor pregnancies that may be at risk of complications.

Why have I been chosen?

You have been selected as a potential participant for this study because of your professional or personal experiences and/or knowledge of this area. You may have also participated in the first part of this study.

We would like to form an 'expert' group of:

- Female childhood, teenage and young adult cancer survivors and/or their parents
- Nurses, midwives and obstetricians
- Paediatric oncologists and GP's
- Researchers

To take part in three rounds of decision making (Delphi technique) to produce a final 'agreement' about key issues (called statements) that can then be taken forward for use in clinical care. We would like to invite approximately 20 'experts' to take part and will only require 2-3 participants from each of the groups above. Participants will need to reside in England to take part and if we receive too many consent forms, then the researcher will select 2-3 participants from each group and inform you by email if you have not been selected to take part.

The Delphi technique chosen by the researcher will involve 2 rounds of email communication and 1 face-to-face meeting. The email communication rounds will be anonymised with only the researcher being able to see the participants email address. Any feedback or results from the email rounds sent between participants, will be anonymous. Email addresses will not be shared or circulated and will only being seen by the researcher.

Details of the face-to-face meeting will be sent upon receipt of your consent form. Names and profession/background will be disclosed at the final meeting unless you do not wish for this to happen. Instructions for the rounds and examples will be sent to participants to help guide you on how to take part and any questions can be directed to the researcher at polanco2@uni.coventry.ac.uk

Do I have to take part?

Your participation is voluntary, and you are free to withdraw at any time without giving any reason. If you choose to withdraw, this will not affect you in any way, now or in the future.

What do I have to do?

If you would like to take part, you will be asked to read this information sheet and sign a consent form. You can then print, scan and email, electronically sign and email the form or request a hard copy and/or print and post back to the researcher. A hard copy of the consent form and a stamped addressed envelope can be requested by emailing the researcher at polanco2@uni.coventry.ac.uk

Once the form has been received, the researcher will then contact you by email with key information and dates for the 3 rounds of the process including the details for the face-to-face meeting (round 3). At each round, you will be asked if you are happy to still take part and you

can discuss any questions you may have by emailing the researcher at polanco2@uni.coventry.ac.uk

Each round will require approximately 1 hours' worth of your time to complete, and all resources, additional information and instructions will be provided by the researcher. You will have 2 weeks to complete each round, and a reminder will be sent by email after 1 week. The face-to-face meeting will take 1 hour and will take place at a venue in London. The face- to-face meeting will be facilitated and may involve the taking of notes from the meeting. If you do not wish for your notes to be used, please let the researcher know in advance and make this clear on the consent form.

Answers from each round will be received by email by the researcher and will then be put together, recorded and analysed. Notes from the face-to-face meeting and key discussions will be noted down by the researchers and the facilitators and used to produce the final set of agreed statements. The researcher would like to thank participants from this study in future scientific publications and professional guidelines, however you have the option to not be named if you wish. No personal information provided to the researcher will be shared.

The researcher will inform your GP of your participation in the research project if you wish. If you do wish for this to happen, please email the researcher at polanco2@uni.coventry.ac.uk

What are the risks associated with this project?

The study has been approved by an ethics committee at Coventry University and The Health Research Authority. The topic of childhood, teenage or young adult cancer survival and future implications for health may cause some distress, memories or worry for the cancer survivor, their parents or health care professionals. Resources for further support and further discussion relating to anything in or relating to this study are below and available from the research team by emailing polanco2@uni.coventry.ac.uk. If you have any worries or clinical questions about anything that arises from taking part in this study please contact your GP, your primary treatment centre or long-term follow up care team. A list of primary treatment centres can be provided by the researcher by emailing polanco2@uni.coventry.ac.uk.

Organisations for support and advice

Macmillan: www.macmillan.org.uk or 0808 281 3000 (information and support) Cancer Research UK www.cancerresearchuk.org/support-organisations (information) Children's Cancer and Leukaemia Group: www.cclg.org.uk (information and support) Clic Sargent: www.clicsargent.org.uk or 0300 330 0803 (information and support)

What are the benefits of taking part?

Information gained from this study will provide researchers with valuable information that can be used for the next part of the research project and future research, helping to improve the communication of future pregnancy risks for female childhood/teenage/young adult cancer survivors and their families. There are no health care or treatment benefits from taking part in this study.

What happens if I don't want to take part anymore?

You may stop taking part in the study at any point. At any point, you can choose to withdraw your responses, without reason, by contacting the researcher by email at polanco2@uni.coventry.ac.uk within two weeks of taking part in each round. If you choose to do this, there is no effect to you or your child in any way now or in the future.

Will I receive reimbursement any payment for taking part?

We can offer funding of up to £50 per participant for standard rate travel expenses for childhood, teenage or young adult female cancer survivors or their parents for the face-to-face meeting in London. Travel bookings must be made in advance and be standard class travel. Receipts will be needed and applications for reimbursement will be given at the meeting by the researcher. We are not able to provide any reimbursement for health care professionals or researchers taking part in this study.

Data protection & confidentiality

This research will be conducted to meet legislation which protects the way that your data is used, stored, disposed of and details of who has access to your data and why. This legislation is called the General Data Protection Regulation (GDPR). The new EU General Data Protection Regulation (GDPR) came into force in the UK on 25 May 2018. The detail of its application in the UK is set out in the new Data Protection Act (2018). Further details about how your data will be used can be found in the supplementary page to this participant information sheet (version 1.0 1st October 2019).

Questions, comments or requests about your personal data can also be sent to the Data Protection Officer at Coventry University by emailing enquiry.ipu@coventry.ac.uk.

Your personal data will be kept confidentially by the researcher on a secure computer system based at Coventry University. Your personal data will only be seen by the researcher, however once the data has been made anonymous, other members of the research supervisory team will be able to view the data, but this will not identify you in any way. Your data will be disposed of securely in accordance with The Data Protection Act 2018 and destroyed after five years, as recommended by Coventry University.

What if things go wrong?

In the very unlikely event of you being harmed in any way by taking part in this research project, there are no special compensation arrangements. If you are harmed due to someone's negligence, then you may have grounds for legal action, but you may have to pay for it. If you wish to complain or have any concerns about any aspect of the way you have been approached or treated during this study, please visit the website www.ico.org.uk. Questions, comments or requests about your personal data can be sent to the Data Protection Officer - enquiry.ipu@coventry.ac.uk.

What will happen with the results of the study?

All results will be reported anonymously and used for a PhD publication and possible scientific publications. Participants in the Delphi study will be thanked by name, unless specified that you do not wish for this to happen. Information published will be readily available and accessible to participants and shared at conferences/events suitable for childhood cancer survivor/ pregnancy research discussions for professionals.

The researcher will use results from this part of the project to produce professional guidance recommendations for the communication of future pregnancy risks following treatment for female childhood, teenage and young adult cancer survivors. Participants will be emailed after the study has been completed with a link to the results. Email addresses will be kept for a period of five years following the end of the trial on a secure computer system and only accessible to the researcher.

Who has reviewed this study?

This study has been reviewed and approved by Coventry University Ethics on 23rd July 2019 with the approval number P93106. This study has also been approved by a Research Ethics Committee with the approval number IRAS 266234.

Who can I contact for further information?

You can contact the researcher Angela Polanco (lead researcher) at polanco2@uni.coventry.ac.uk for more information about the study or to ask any questions about this information sheet.

Thank you for considering taking part in this research study. Whilst we would obviously be delighted if you can help us, there is no obligation to do so.

Appendix 7 - PICCS2 consent form

PICCS2 CONSENT FORM

Project Title: Pregnancy Information for Childhood Cancer Survivors Study **2.**

Participant identification number:
IRAS number: 266234
Chief Investigator – Dr Elizabeth Bailey
Principal Investigator - Angela Polanco (Research Midwife)

Please Initial

I confirm that I have read and understood the participant information sheet version no. 1.2 dated 8th November 2019 for the above study and have had the opportunity to ask questions.	☐
I agree to take part in the three rounds of the above study	☐
I understand that notes will be taken at the face-to-face meeting as part of the research project (please see the 'what do I have to do' section of the participant information sheet for further information)	☐
I give permission to be contacted by email by the named researcher for the purpose of study	☐
I give permission for my GP to be contacted to inform them that I am taking part in this research study	☐
I understand that my email address and name will be held and processed for the purposes of the above study for a period of five years after taking part	☐

I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason without being penalised or disadvantaged in any way, subject to my personal or sensitive personal data being anonymised ☐

I understand that my data will communicated anonymously between the group in the first two rounds of the study with only the researcher able to see my identity. I understand that the final results will be shared with members of the research team at Coventry University and used for publication purposes ☐

I give permission for my responses or notes to be used in direct quotations for publications and PhD work and understand that these will be given a pseudonym or 'fake name' by the researcher ☐

I consent to be named as a participant in the final publication of the results of the Study (If you do not want this then participants will be thanked as a 'panel') ☐

Name of Participant	**Date**	**Signature**
Name of Researcher	**Date**	**Signature**

Version 1.2 8TH November 2019

ONE copy of the Participant Information Sheet and ONE copy of the signed consent form to be given to the participant. ONE copy of the signed consent form to be filed in the investigator file

Appendix 8 - Full ethics approval documents (PICCS1 and PICCS2)

Certificate of Ethical Approval

Applicant:

Angela Polanco

Project Title:

Pregnancy after malignancy in childhood: Communication and information needs of female survivors and recommendations for optimal care

This is to certify that the above named applicant has completed the Coventry University Ethical Approval process and their project has been confirmed and approved as Medium Risk

Date of approval:

03 April 2019

Project Reference Number:

P87230

Certificate of Ethical Approval

Applicant:

Angela Polanco

Project Title:

Pregnancy Information for Childhood Cancer Survivors 2 (PICCS2)

This is to certify that the above named applicant has completed the Coventry University Ethical Approval process and their project has been confirmed and approved as High Risk

Date of approval:

23 July 2019

Project Reference Number:

P93106

Ymchwil Iechyd a Gofal Cymru
Health and Care Research Wales

NHS
Health Research Authority

Dr Elizabeth Bailey
University Hospitals Coventry and Warwickshire
Clifford Bridge Road
cv2 2dx

Email: hra.approval@nhs.net
HCRW.approvals@wales.nhs.uk

06 December 2019

Dear Dr Bailey

HRA and Health and Care Research Wales (HCRW) Approval Letter

Study title:	**Pregnancy Information for Childhood Cancer Survivors 2 (PICCS2)**
IRAS project ID:	**266234**
REC reference:	**19/LO/1442**
Sponsor	**Coventry University**

I am pleased to confirm that **HRA and Health and Care Research Wales (HCRW) Approval** has been given for the above referenced study, on the basis described in the application form, protocol, supporting documentation and any clarifications received. You should not expect to receive anything further relating to this application.

Please now work with participating NHS organisations to confirm capacity and capability, in line with the instructions provided in the "Information to support study set up" section towards the end of this letter.

How should I work with participating NHS/HSC organisations in Northern Ireland and Scotland?

HRA and HCRW Approval does not apply to NHS/HSC organisations within Northern Ireland and Scotland.

If you indicated in your IRAS form that you do have participating organisations in either of these devolved administrations, the final document set and the study wide governance report (including this letter) have been sent to the coordinating centre of each participating nation.

The relevant national coordinating function/s will contact you as appropriate.

Please see IRAS Help for information on working with NHS/HSC organisations in Northern Ireland and Scotland.

How should I work with participating non-NHS organisations?

HRA and HCRW Approval does not apply to non-NHS organisations. You should work with your non-NHS organisations to obtain local agreement in accordance with their procedures.

What are my notification responsibilities during the study?

The standard conditions document "*After Ethical Review – guidance for sponsors and investigators*", issued with your REC favourable opinion, gives detailed guidance on reporting expectations for studies, including:

- Registration of research
- Notifying amendments
- Notifying the end of the study

The HRA website also provides guidance on these topics, and is updated in the light of changes in reporting expectations or procedures.

Who should I contact for further information?

Please do not hesitate to contact me for assistance with this application. My contact details are below.

Your IRAS project ID is **266234**. Please quote this on all correspondence. Yours

sincerely,

Christie Ord

Approvals Specialist

Email: hra.approval@nhs.net

Copy to: *Professor Alpaslan Ozerdem*

IRAS project ID	266234

Information to support study set up

The below provides all parties with information to support the arranging and confirming of capacity and capability with participating NHS organisations in England and Wales. This is intended to be an accurate reflection of the study at the time of issue of this letter.

Types of participating NHS organisation	Expectations related to confirmation of capacity and capability	Agreement to be used	Funding arrangements	Oversight expectations	HR Good Practice Resource Pack expectations
All sites will perform the same research activities therefore there is only one site type.	Research activities should not commence at participating NHS organisations in England or Wales prior to their formal confirmation of capacity and capability to deliver the study.	An Organisation Information Document has been submitted and the sponsor is not requesting and does not expect any other site agreement to be used.	No study funding will be provided to sites as per the Organisational Information Document	A Principal Investigator should be appointed at study sites	No Honorary Research Contracts, Letters of Access or pre-engagement checks are expected for local staff employed by the participating NHS organisations. Where arrangements are not already in place, research staff not employed by the NHS host organisation undertaking any of the research activities listed in the research application would be expected to obtain a Letter of Access based on standard DBS checks and occupational health clearance.

Other information to aid study set-up and delivery

This details any other information that may be helpful to sponsors and participating NHS organisations in England and Wales in study set-up.
The applicant has indicated that they do not intend to apply for inclusion on the NIHR CRN Portfolio.

List of Documents

The final document set assessed and approved by HRA and HCRW Approval is listed below.

Document	Version	Date
Confirmation of any other Regulatory Approvals (e.g., CAG) and all correspondence		
Confirmation of any other Regulatory Approvals (e.g., CAG) and all correspondence [ETHICS CU]		23 July 2019
Copies of advertisement materials for research participants [ADVERT HCP]	1.0	01 Oct 2019
Copies of advertisement materials for research participants [ADVERT PUBLIC]	1.0	01 Oct 2019
Costing template (commercial projects) [COSTS]		01 May 2019
Costing template (commercial projects)		01 May 2019
Evidence of Sponsor insurance or indemnity (non-NHS Sponsors only) [INDEMNITY]		01 Aug 2019
GP/consultant information sheets or letters [GP LETTER]	1.0	01 May 2019
Interview schedules or topic guides for participants [Draft statements for participants]	1.0	01 May 2019
IRAS Application Form [IRAS_Form_12082019]		12 Aug 2019
Letter from sponsor [SPONSOR LETTER]		29 July 2019
Letters of invitation to participant [EOI]	1.0	05 June 2019
Organisation Information Document [OID]	V1.4	21 Aug 2019
Participant consent form [CONSENT CO-CREATION TRACKED]	1.2	08 Nov 2019
Participant consent form [CONSENT DELPHI TRACKED]	1.2	08 Nov 2019
Participant consent form [CONSENT DELPHI CLEAN]	1.2	08 Nov 2019
Participant consent form [CONSENT CO-CREATION CLEAN]	1.2	08 Nov 2019
Participant information sheet (PIS) [PIS SUPPLEMENTATION GDPR]	1.0	01 Oct 2019
Participant information sheet (PIS) [PIS DELPHI CLEAN]	1.2	08 Nov 2019
Participant information sheet (PIS) [PIS DELPHI TRACKED]	1.2	08 Nov 2019
Participant information sheet (PIS) [PIS CO-CREATION CLEAN]	1.2	08 Nov 2019
Participant information sheet (PIS) [PIS CO-CREATION TRACKED]	1.2	08 Nov 2019
Referee's report or other scientific critique report		03 April 2019
Referee's report or other scientific critique report [ETHICS WP1]		03 April 2019

Document	Version	Date
Research protocol or project proposal [PROTOCOL]	1.1	01 Oct 2019
Response to Additional Conditions Met		
Schedule of Events or SoECAT [SOE]	1.0	21 Aug 2019
Summary CV for Chief Investigator (CI) [CVCI]		29 July 2019
Summary CV for student		29 July 2019
Summary CV for student [CV AP]	1.0	29 July 2019
Summary CV for supervisor (student research) [DB CV]		01 July 2019
Summary CV for supervisor (student research) [CV JC]	1.0	22 Aug 2019
Summary of any applicable exclusions to sponsor insurance (non- NHS sponsors only)	N/A	29 July 2019
Summary, synopsis, or diagram (flowchart) of protocol in non-technical language [RECRUITMENT FLOW CHART]	1.0	01 May 2019

TO WHOM IT MAY CONCERN QRS/Ethics/Sponsorlet

Tuesday, 23 July 2019

Dear Sir/Madam

Researcher's name: **Angela Polanco Project**

Reference: **P93106**

Project Title: **Pregnancy Information for Childhood Cancer Survivors 2 (PICCS2)**

The above named researcher has successfully completed the Coventry University Ethical Approval process and received authorisation for their project to proceed.

I should like to confirm that Coventry University is happy to act as the sole sponsor for this researcher and attach details of our Public Liability Insurance.

Yours faithfully

[redacted]

Olivier Sparagano

Associate Pro-Vice-Chancellor – Research

Enc

London - Camden & Kings Cross Research Ethics Committee

NHSBT Newcastle Blood Donor Centre

Holland Drive
Newcastle upon Tyne

NE2 4NQ

Tel: 0207 104 8277

Please note: This is the favourable opinion of the REC only and does not allow the amendment to be implementedat NHS sites in England until the outcome of the HRA assessment has been confirmed.

17 November 2020

Mrs Angela Polanco
[redacted]

Dear Mrs Polanco

Study title:	**Pregnancy Information for Childhood Cancer Survivors 2 (PICCS2)**
REC reference:	**19/LO/1442**
Amendment number:	**P93106**
Amendment date:	**11 November 2020**

IRAS project ID: 266234

The above amendment was reviewed on 13 November 2020 by the Sub-Committee in correspondence.

Ethical opinion

The Sub-Committee did not raise any ethical issues. The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents

The documents reviewed and approved at the meeting were:

Document	*Version*	*Date*
Completed Amendment Tool [Amendment tool]	1.0	11 November 2020

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

Working with NHS Care Organisations

Sponsors should ensure that they notify the R&D office for the relevant NHS care organisation of this amendment in line with the terms detailed in the categorisation email issued by the lead nation for the study.

Amendments related to COVID-19

We will update your research summary for the above study on the research summaries section of our website. During this public health emergency, it is vital that everyone can promptly identify all relevant research related to COVID-19 that is taking place globally. If you have not already done so, please register your study on a public registry as soon as possible and provide

the HRA with the registration detail, which will be posted alongside other information relating to your project.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

HRA Learning

We are pleased to welcome researchers and research staff to our HRA Learning Events and online learning opportunities– see details at: https://www.hra.nhs.uk/planning-and- improving-research/learning/

IRAS Project ID - 266234:	**Please quote this number on all correspondence**

Yours sincerely

On behalf of

Mrs Rosie Glazebrook Chair

E-mail: CamdenandKingsCross.REC@hra.nhs.uk

London - Camden & Kings Cross Research Ethics Committee Attendance at

Sub-Committee of the REC meeting on 13 November 2020

Committee Members:

Name	*Profession*	*Present*	*Notes*
Mrs Rosie Glazebrook	Consumer Marketing	Yes	
Dr Jacqueline Maxmin	Retired GP	Yes	

Also in attendance:

Name	*Position (or reason for attending)*
Saira Adil	Approvals Administrator

Appendix 9 - PICCS2 full results (all rounds)

Questions	Not important			Unsure			Agree							
Theme	1	2	3	4	5	6	7	8	9	Missing	Total participants	Mean score	Total votes 7-9	70% consensus rate
Communicating specific pregnancy and birth risks to female survivors and families					2		2	3	11		**19**	7.73	**16**	pass
Identifying a key professional to communicate the information			1	1	1	1	5	2	8		**19**	7.42	**15**	pass
Identifying the best time to communicate information							6	5	7	n=1	18	8.05	**18**	pass
Creating a plan for communication of information that can be assessed and revised easily					2	1	7	6	3		**19**	7.36	**16**	pass
Identifying terminology to use for communication that can be understood by all						1	5	5	8		**19**	8.05	**18**	pass

Questions	Not important			Unsure			Agree							
Theme	1	2	3	4	5	6	7	8	9	Missing	Total participants	Mean score	Total votes 7-9	70% consensus rate
Defining what is meant by future fertility (survivor and health care professionals view of the term)						2	1	9	7		19	8.1	17	pass
Managing expectations for future fertility and pregnancy		1					2	8	7	n=1	18	7.94	17	pass
Communicating risks to health care professionals from outside of paediatric oncology				1	1	1	6	4	6		19	7.52	16	pass
How to assess if unmet need still exists and ways to address this within survivorship care		1	1			2	3	4	7	n=1	18	7.38	14	pass
Helping parents to communicate information to survivors					3	2	2	5	7		19	7.57	14	pass

Q1 Which of the following late-effect risks for future pregnancy do you think are HIGH PRIORITY for communication to the female child/teen/adolescent (CAYA) with cancer and/or their parents?														
Questions	Not important			Unsure			Agree							
Theme	1	2	3	4	5	6	7	8	9	Missing	Total participants	Mean score	Total votes 7-9	70% consensus rate
Difficulty becoming pregnant						1	4	4	10		19	8.21	18	pass
Success rates and risks associated with pregnancy using artificial fertility treatments (IVF)			2	4	1	4	3	1	4		19	6.1	8	fail
Miscarriage		1	1		2		7	4	4		19	6.9	15	pass
High risk pregnancy care	2		1			3	1	3	8	n=1	18	7	12	borderline
Likelihood of being able to have a normal birth (birth plan expectations)	1		2	2		2	5	3	4		19	6.42	12	fail
Early labour (<37 weeks)	1		1	1	4		7	2	3		19	6.31	12	fail
Small baby (<2.5kgs or clinically small for dates)	1		1	1	2	2	6	2	4		19	6.52	12	fail
Stillbirth		1	1	1	1	2	5	1	7		19	6.94	13	pass
Risk of abnormality in baby				1	1	3	5	1	8		19	7.47	14	pass
Risk of cancer in the baby					2	1	4	2	10		19	7.89	16	pass
Bleeding after delivery or other complications with the birth	1		2	3	1	4	2		6		19	6.1	8	fail

Q2 What STAGE in the cancer journey do you think is the most appropriate TIME to FIRST communicate any future PREGNANCY or FUTURE FERTILITY risks related to treatments?														
Questions	Not important			Unsure			Agree							
Theme	1	2	3	4	5	6	7	8	9	Missing	Total participants	Mean score	Total votes 7-9	70% consensus rate
At diagnosis		1	3	2	2		3		7	n=1	18	6.11	10	fail
During active treatment	2	1	2	3	3	1	2	2	2	n=1	18	5.05	6	fail
During last 6 months of treatment or maintenance	5	1	1	2	2	1	4		2	n=1	18	4.44	6	fail
Upon completion of treatment	3		1	3	1	1	4	1	4	n=1	18	5.6	9	fail
<6 months after treatment	4		1		3	1	2	1	6	n=1	18	5.77	9	fail
>5 years after treatment	6		1		1		2	1	7	n=1	18	5.5	10	fail
At relapse	4		1	1	2	1	4	1	4	n=1	18	5.5	9	fail
Upon wanting to start a family	4	2	1		1		1	2	7	n=1	18	5.66	10	fail
Upon becoming pregnant	5	1	1	1	1		1	4	4	n=1	18	5.22	9	fail

Q3 What STAGE in the cancer journey do you think is the most appropriate TIME to REINTRODUCE information about any future PREGNANCY or FUTURE FERTILITY risks related to treatments?														
Questions	Not important			Unsure			Agree							
Theme	1	2	3	4	5	6	7	8	9	Missing	Total participants	Mean score	Total votes 7-9	70% consensus rate
At diagnosis	12	2	1	1			1		2		19	2.52	3	fail
During active	4	1	3		4	2	2	1	2		19	4.57	5	fail

Q3 What STAGE in the cancer journey do you think is the most appropriate TIME to REINTRODUCE information about any future PREGNANCY or FUTURE FERTILITY risks related to treatments?														
Questions	Not important			Unsure			Agree							
Theme	1	2	3	4	5	6	7	8	9	Missing	Total participants	Mean score	Total votes 7-9	70% consensus rate
treatment														
During last 6 months of treatment or maintenance	3		2		3	2	4	2	3		19	5.63	9	fail
Upon completion of treatment	2			1	1	1	6	3	5		19	6.73	14	pass
<6 months after treatment	1		1	1	1	1	4	2	7	n=1	18	7	13	pass
>5 years after treatment	4				1	1		4	9		19	6.73	13	pass
At relapse	4		3		3	1	1	2	5		19	5.36	8	fail
Upon wanting to start a family	4						2	3	10		19	6.94	15	pass
Upon becoming pregnant	5						1	3	10		19	6.63	14	pass

Q4 What STAGE in the cancer journey do you think is the most appropriate TIME to speak DIRECTLY to the female CAYA cancer survivor and REINTRODUCE information about any future PREGNANCY or FUTURE FERTILITY risks related to treatments?														
Questions	Not important			Unsure			Agree							
Theme	1	2	3	4	5	6	7	8	9	Missing	Total participants	Mean score	Total votes 7-9	70% consensus rate
At diagnosis	4	2	1	1	2	1	2		4	n=2	17	4.76	6	fail
During active treatment	1	2	3	2	2		4	2	2	n=1	18	5.22	8	fail
During last 6 months of treatment or	1	2	1		3	1	5	2	3	n=1	18	5.94	10	fail

Q4 What STAGE in the cancer journey do you think is the most appropriate TIME to speak DIRECTLY to the female CAYA cancer survivor and REINTRODUCE information about any future PREGNANCY or FUTURE FERTILITY risks related to treatments?														
Questions	Not important			Unsure			Agree							
Theme	1	2	3	4	5	6	7	8	9	Missing	Total participants	Mean score	Total votes 7-9	70% consensus rate
maintenance														
Upon completion of treatment	1			1	2		3	5	6	n=1	18	7.22	14	pass
<6 months after treatment		1	1	1	4		4	1	6	n=1	18	6.61	11	fail
>5 years after treatment	2	1			1	1	4	3	6	n=1	18	6.77	13	pass
When the female survivor reaches age 16 years	2				2	1	3	2	7	n=2	17	6.55	12	pass
At relapse	2	1	1		3	2	1	3	5	n=1	18	6.11	9	fail
Upon wanting to start a family	1	1			1		1	8	6	n=1	18	7.38	15	pass
Upon becoming pregnant	2				1	1	4	1	9	n=1	18	7.22	14	pass

Q5 WHO do you think is the most appropriate professional to FIRST DISCUSS information with the CAYA with cancer and/or their parents?														
Questions	Not important			Unsure			Agree							
Theme	1	2	3	4	5	6	7	8	9	Missing	Total participants	Mean score	Total votes 7-9	70% consensus rate
Paediatric oncology consultant				1	1	1	5	2	9		19	7.73	16	pass
Paediatric oncology nurse	2				1	1	3	1	9	n=2	17	7.23	13	pass
Macmillan or CLIC support worker	3	1	4	1	3	3	2		2		19	4.52	4	fail
Midwife	9	2	2	1	3		1		1		19	2.84	2	fail

Q5 WHO do you think is the most appropriate professional to FIRST DISCUSS information with the CAYA with cancer and/or their parents?														
Questions	Not important			Unsure			Agree							
Theme	1	2	3	4	5	6	7	8	9	Missing	Total participants	Mean score	Total votes 7-9	70% consensus rate
Fertility specialist	3	1	2	2			5	1	5		19	5.63	11	fail
Obstetrician	7	2	2	3	1	1	1	1	1		19	3.36	3	fail
Long-term follow up doctor	4		3	1	2		1	2	6		19	5.47	9	fail
Paediatric Radiotherapy consultant	1			2	3		5	2	4	n=2	17	6.52	11	borderline
Other (please specify in box below)														

Q6 WHAT is meant by being FERTILE following cancer treatment?														
Questions	Not important			Unsure			Agree							
Theme	1	2	3	4	5	6	7	8	9	Missing	Total participants	Mean score	Total votes 7-9	70% consensus rate
Being able to have a period	4	1	1	1	2	3	6	1			19	4.78	7	fail
Being able to conceive a pregnancy naturally					2		1	3	13		19	8.31	17	pass
Being able to conceive a pregnancy by using fertility treatments (IVF)	1				4	1	10		3		19	6.52	13	pass
Being able to carry a pregnancy to full term (37 completed weeks)	1	4			2		4	4	4		19	6.05	12	fail

Q6 WHAT is meant by being FERTILE following cancer treatment?														
Questions	Not important			Unsure			Agree							
Theme	1	2	3	4	5	6	7	8	9	Missing	Total participants	Mean score	Total votes 7-9	70% consensus rate
To be able to have a live baby	2	3	1			1	1	2	8	n=1	18	5.89	11	fail

Q7 A summary of treatments received, and late effects related to future fertility and pregnancy should be COMMUNICATED to the following professionals outside of paediatric oncology upon treatment completion:														
Questions	Not important			Unsure			Agree							
Theme	1	2	3	4	5	6	7	8	9	Missing	Total participants	Mean score	Total votes 7-9	70% consensus rate
GP							1	4	14		19	8.68	19	pass
Obstetrician	4				3	1		1	10		19	6.47	11	fail
GP practice nurse or advanced practitioner	3	1			6	2		2	5		19	5.68	7	fail
Midwife/Health Visitor	4		1		3	2			9		19	6.05	9	fail
Hospital based MDT team	1	1			1	1	4	1	10		19	7.36	15	pass
Local NHS fertility services	2	2	1		2	2	2	2	6		19	6.05	10	fail
Other (please specify below)														

Q8 The FORMAT of a treatment summary with late-effect risk information for FUTURE FERTILITY and PREGNANCY should be available for CAYA cancer survivors and health care professionals as an:														
Questions	Not important			Unsure			Agree							
Theme	1	2	3	4	5	6	7	8	9	Missing	Total participants	Mean score	Total votes 7-9	70% consensus rate
Online resource				2	1	2	2	2	9	n=1	18	7.55	13	pass

Q8 The FORMAT of a treatment summary with late-effect risk information for FUTURE FERTILITY and PREGNANCY should be available for CAYA cancer survivors and health care professionals as an:														
Questions	Not important			Unsure			Agree							
Theme	1	2	3	4	5	6	7	8	9	Missing	Total participants	Mean score	Total votes 7-9	70% consensus rate
Written leaflet					1	1	9	2	6		19	7.57	17	pass
Electronic record on the health care professional computer system						1	4	3	11		19	8.26	18	pass
Given orally in the clinical conversations				1			6	3	9		19	7.94	18	pass
Via an App or similar patient resource	2		1	2	3	1	6	1	3		19	5.84	10	fail
Inserted into the pregnancy held records when pregnant		1		1	1	1	3	4	8		19	7.47	15	pass
A combination of written information and online resource						1	2	2	14		19	8.52	18	pass

Q9 PARENTS should be offered a session with a health professional at treatment completion about HOW to communicate late-effects to female CAYA cancer survivors regarding FERTILITY and PREGNANCY with:														
Questions	Not important			Unsure			Agree							
Theme	1	2	3	4	5	6	7	8	9	Missing	Total participants	Mean score	Total votes 7-9	70% consensus rate
Face-face session with the paediatric oncologist			2	1	2	5	2	2	5		19	6.57	9	fail
Face to face session with the					4		3	3	8	n=1	18	7.61	14	pass

Q9 PARENTS should be offered a session with a health professional at treatment completion about HOW to communicate late-effects to female CAYA cancer survivors regarding FERTILITY and PREGNANCY with:														
Questions	**Not important**			**Unsure**			**Agree**							
Theme	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**Missing**	**Total participants**	**Mean score**	**Total votes 7-9**	**70% consensus rate**
nurse or other health care practitioner														
Online course module or guidance					3	6	5	3	2		19	6.73	10	fail
Written information to read						4	6	6	3		19	7.42	15	pass
Joint face to face session with the female CAYA cancer survivor and parent				1	5		5	3	5		19	7	13	pass
A community- based session with other parents led by the community nursing team or other professional	3		1	2	4	1	5		3		19	5.36	8	fail
Other (please specify below)														

Q10 A glossary of terms or lay summary which helps to EXPLAIN information used in relation to late effects of treatment and FUTURE FERTILITY and PREGNANCY should be included in the treatment summary plan														
Questions	**Not important**			**Unsure**			**Agree**							
Theme	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**Missing**	**Total participants**	**Mean score**	**Total votes 7-9**	**70% consensus rate**
Printed glossary of terms (written)			3		2	3	3	2	6		19	6.73	11	fail

Q10 A glossary of terms or lay summary which helps to EXPLAIN information used in relation to late effects of treatment and FUTURE FERTILITY and PREGNANCY should be included in the treatment summary plan														
Questions	Not important			Unsure			Agree							
Theme	1	2	3	4	5	6	7	8	9	Missing	Total participants	Mean score	Total votes 7-9	70% consensus rate
Online resource					1	3	2	3	10		19	7.94	15	pass
Added electronically to patient held records	2		1	1	2	1	4	2	6		19	6.47	12	fail
Given to parents in written format		1	1	1	3		5	2	6		19	6.78	13	pass
Oral explanation of terms during consultations					2	1	7	1	8		19	7.63	16	pass
Oral explanation to female CAYA cancer survivor when reaches age of maturity					1	1	2	2	13		19	8.31	17	pass

Q11 UNMET NEEDS for late effects regarding FUTURE FERTILITY and PREGNANCY of female CAYA cancer survivors and/or parents should be re-evaluated at the following TIME points:														
Questions	Not important			Unsure			Agree							
Theme	1	2	3	4	5	6	7	8	9	Missing	Total participants	Mean score	Total votes 7-9	70% consensus rate
During active treatment	1	2		2	4	3		3	4		19	5.84	7	fail
Upon treatment completion				2	2	2	3	3	7		19	7.26	13	pass
<6 months following treatment	1	1		1	2		4	1	9		19	7.05	14	pass
>5 years following treatment	1				1	2	1	4	10		19	7.73	15	pass

Q11 UNMET NEEDS for late effects regarding FUTURE FERTILITY and PREGNANCY of female CAYA cancer survivors and/or parents should be re-evaluated at the following TIME points:														
Questions	Not important			Unsure			Agree							
Theme	1	2	3	4	5	6	7	8	9	Missing	Total participants	Mean score	Total votes 7-9	70% consensus rate
When accessing fertility services		1			1		2	3	12		19	8.05	17	pass
When pregnant	2				1		2	4	10		19	7.52	16	pass

Q12 The UNMET NEEDS of female CAYA cancer survivors for late effects related to FUTURE FERTILITY and PREGNANCY should be evaluated BY:														
Questions	Not important			Unsure			Agree							
Theme	1	2	3	4	5	6	7	8	9	Missing	Total participants	Mean score	Total votes 7-9	70% consensus rate
Paediatric oncology consultant	1	1		1	1	1	4	4	6		19	6.94	14	pass
Paediatric oncology nurse	1	1		1		2	6	3	5		19	6.84	14	pass
Macmillan or CLIC support worker	2	2	1	2		3	7		2		19	5.36	9	fail
Midwife	2	3	1	1		4	1	2	5		19	5.63	8	fail
Fertility specialist	1		1			2	2	1	12		19	7.68	15	pass
Obstetrician	1	1			2	1	2	3	8		18	6.78	13	pass
Long-term follow up doctor (not oncology)	1				1		1	5	11		19	8	17	pass
Paediatric Radiotherapy consultant	1		1	3	4	3	4		3		19	5.73	7	fail

Q13 The UNMET NEEDS of female CAYA cancer survivors for late effects related to FUTURE FERTILITY and PREGNANCY should be evaluated WITH the following resources/tools:														
Questions	**Not important**			**Unsure**			**Agree**							
Theme	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**Missing**	**Total participants**	**Mean score**	**Total votes 7-9**	**70% consensus rate**
Anxiety/depression scales (validated tools)		1		1	5	1	3	3	5		19	6.68	11	fail
Needs analysis similar to care planning in healthcare					3	1	7	2	5	n=1	18	7.27	14	pass
Questionnaire (written)		1		3	4	3	4	1	3		19	6.05	8	fail
Questionnaire (online)				1	2	2	6	2	5	n=1	18	7.16	13	pass
Face to face consultation with professional					1	1	3	2	12		19	8.21	17	pass
Interview (telephone or face to face) with an independent person outside of oncology care	1	2			5	2	6		3		19	5.84	9	fail
Online tool to assess need or satisfaction with information received		1	1		2		9	2	4		19	6.84	15	pass

Round 2 - PICCS2

Q1 Health Care Professionals should communicate the following future fertility and pregnancy risks to female CAYA cancer survivors and/or parents (risks vary depending on treatment received):														
Questions	Not important			Unsure			Agree			Total	Mean	Total 7-9	70% consensus	Other
	1	2	3	4	5	6	7	8	9					
Difficulty becoming pregnant					1		3	2	13	19	8.36	18	pass	
Higher risk of miscarriage	1				2	3	5	2	6	19	7.05	13	fail	
The need for high-risk pregnancy care		1			1	1	4	5	7	19	7.57	16	pass	
Higher risk of stillbirth	1			2	2	2	5	1	6	19	6.73	12	fail	
Low risk of abnormality in baby			1	1	1	2	4	2	8	19	7	14	pass	
Low risk of cancer in the baby			1	1	1	2	3	2	9	19	7.47	14	pass	

Q2 Health Care Professionals should FIRST communicate (either to the CAYA cancer survivor and/or parent) potential future fertility and pregnancy late-effects:														
Questions	Not important			Unsure			Agree			Total	Mean	Total 7-9	70% consensus	Other
	1	2	3	4	5	6	7	8	9					
At diagnosis	1	1		1	1	1	3	2	9	19	7.15	14	pass	
>5 years after treatment	9		1		2	3	1		3	19	3.89	4	fail	
At end of treatment	6					3	4	2	4	19	5.47	10	fail	
Upon wanting to start a family	11		1	1	2	1	1		2	19	3.1	3	fail	

Q3 Health Care Professionals should RE-INTRODUCE potential future fertility and pregnancy late-effects:														
Questions	**Not important**			**Unsure**			**Agree**			**Total**	**Mean**	**Total 7-9**	**70% consensus**	**Other**
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**					
Upon completion of treatment				1	2		3	2	11	19	7.89	16	pass	
<6 months after treatment	3	1		1	3	1	3	4	3	19	5.78	10	fail	
At regular intervals during diagnosis, treatment, and remission	3		2	1		3	2	2	6	19	6.05	10	fail	
>5 years after treatment	2		1	2	1	1	3	3	6	19	6.47	12	fail	
Upon wanting to start a family	2	1					5	2	9	19	7.15	16	pass	
Upon becoming pregnant	2		1			1	4	2	9	19	7.15	15	pass	

Q4 The most appropriate age to discuss future fertility and pregnancy late-effects with the female CAYA cancer survivor is:														
Questions	**Not important**			**Unsure**			**Agree**			**Total**	**Mean**	**Total 7-9**	**70% consensus**	**Other**
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**					
When the female CAYA cancer survivor reaches 11 years old	3		4	3	3	2	1		3	19	4.63	4	fail	
When the female CAYA cancer survivor reaches age 12 years	2		1	4	4	1	3	2	2	19	5.36	7	fail	
When the female CAYA cancer survivor reaches age 16 years	2		1		1		1	4	10	19	7.31	15	pass	
When the parent is happy for this to be discussed with the	3		1	2	4	3		4	2	19	5.36	6	fail	

Q4 The most appropriate age to discuss future fertility and pregnancy late-effects with the female CAYA cancer survivor is:														
Questions	Not important			Unsure			Agree			Total	Mean	Total 7-9	70% consensus	Other
	1	2	3	4	5	6	7	8	9					
female CAYA cancer survivor														

Q5 Health Care Professionals should talk directly to the female CAYA cancer survivor about future fertility late-effects:														
Questions	Not important			Unsure			Agree			Total	Mean	Total 7-9	70% consensus	Other
	1	2	3	4	5	6	7	8	9					
Upon completion of treatment (if deemed age appropriate)				1		1	4	1	12	19	8.1	17	pass	
>5 years after treatment (if deemed age appropriate)	2						4	3	10	19	7.57	17	pass	
Upon the female CAYA cancer survivor wanting to start a family							3	4	12	19	8.47	19	pass	
Upon the female CAYA cancer survivor becoming pregnant	2		1			1	2	2	11	19	7.36	15	pass	

Q6 The most appropriate Health Care Professional to discuss future fertility and pregnancy late-effects is:														
Questions	Not important			Unsure			Agree			Total	Mean	Total 7-9	70% consensus	Other
	1	2	3	4	5	6	7	8	9					
Paediatric oncology consultant	1			1			4	7	6	19	7.52	17	pass	
Paediatric oncology nurse	1	1				1	6	7	3	19	7.05	16	pass	
GP	4	5	2	1	1	1	3		2	19	3.89	5	fail	
Fertility specialist	2			1	2	2	1	2	9	19	6.94	12	fail	
Paediatric	4		2				6	4	2	18	5.66	12	fail	n=1

Q6 The most appropriate Health Care Professional to discuss future fertility and pregnancy late-effects is:														
Questions	Not important			Unsure			Agree			Total	Mean	Total 7-9	70% consensus	Other
	1	2	3	4	5	6	7	8	9					
Radiotherapy consultant														missing

Q7 Being fertile following cancer treatment can be defined as:														
Questions	Not important			Unsure			Agree			Total	Mean	Total 7-9	70% consensus	Other
	1	2	3	4	5	6	7	8	9					
Being able to conceive a pregnancy naturally	1		2				2	3	11	19	7.57	16	pass	
Being able to conceive (either natural or via ART methods)	1		1		3	3	3	5	3	19	6.57	11	fail	

Q8 A summary of treatments received and late-effects risk for future fertility and pregnancy following treatment should be sent to:														
Questions	Not important			Unsure			Agree			Total	Mean	Total 7-9	70% consensus	Other
	1	2	3	4	5	6	7	8	9					
GP						1	1	2	15	19	8.63	18	pass	
The female CAYA cancer survivor and/or parents						1		3	15	19	8.68	18	pass	
Long-term follow up doctor	1		1					3	14	19	8.1	17	pass	

Q9 The most appropriate format for a treatment summary with future fertility and pregnancy late-effect risk information is:														
Questions	Not important			Unsure			Agree			Total	Mean	Total 7-9	70% consensus	Other
	1	2	3	4	5	6	7	8	9					
Online resource	2			2	4	1	7	2	1	19	5.78	10	fail	
Written leaflet	1		1	1	3	1	8	3	1	19	6.21	12	fail	
Via patient electronic medical record	1				2	1	4	3	8	19	7.42	15	pass	

Q9 The most appropriate format for a treatment summary with future fertility and pregnancy late-effect risk information is:														
Questions	**Not important**			**Unsure**			**Agree**			**Total**	**Mean**	**Total 7-9**	**70% consensus**	**Other**
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**					
Verbally during consultations	2		3		2		4	3	3	**18**	**5.66**	**10**	**fail**	**n=1 missing**
Inserted into the pregnancy held records	3		1	1	2	1	4	1	6	**19**	**6.1**	**11**	**fail**	
A combination of written information and online resource	2				2		3	4	8	**19**	**7.21**	**15**	**pass**	
A combination of written, verbal, and signposting to trusted online resources	1							5	13	**19**	**8.31**	**18**	**pass**	

Q10 The most appropriate format to assist parents with the communication of potential future fertility and pregnancy late-effects is:														
Questions	**Not important**			**Unsure**			**Agree**			**Total**	**Mean**	**Total 7-9**	**70% consensus**	**Other**
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**					
Face to face session with a Health Care Professional						1	2	8	8	**19**	**8.21**	**18**	**pass**	
Written information to read	1	1	1	1	1	1	6	5	2	**19**	**6.36**	**13**	**fail**	
Joint face to face session with the female CAYA cancer survivor and parent	1		1		1		4	5	7	**19**	**7.36**	**16**	**pass**	

Q11 The most appropriate way to explain medical terms and provide a lay summary of treatment received including future fertility and pregnancy late-effect risks is:														
Questions	Not important			Unsure			Agree			Total	Mean	Total 7-9	70% consensus	Other
	1	2	3	4	5	6	7	8	9					
Online resource	2			1		1	7	5	3	19	6.73	15	pass	
Given to parents in written format	1					3	3	6	6	19	7.47	15	pass	
Verbally during consultations	1			2	1	1	2	3	9	19	7.31	14	pass	
Verbally when the female CAYA cancer survivor reaches age of maturity	1	1	1		2	1	4	2	7	19	6.78	13	fail	

Q12 Unmet informational late effects needs of female CAYA cancer survivors should be re-evaluated at:														
Questions	Not important			Unsure			Agree			Total	Mean	Total 7-9	70% consensus	Other
	1	2	3	4	5	6	7	8	9					
Treatment completion				1			4	4	10	19	8.1	18	pass	
<6 months following treatment	1		1		2		4	1	10	19	7.36	15	pass	
>5 years following treatment	1			1			1	4	12	19	8	17	pass	
When accessing fertility services			1			1	2	4	11	19	8.1	17	pass	
When pregnant	1		1			2	3	4	8	19	7.42	15	pass	

Q13 The most appropriate Health Care Professional to assess unmet informational needs of female CAYA cancer survivors relating to future fertility and pregnancy is:														
Questions	Not important			Unsure			Agree			Total	Mean	Total 7-9	70% consensus	Other
	1	2	3	4	5	6	7	8	9					
Paediatric oncology consultant	1	1	1		2		6	6	2	19	6.52	14	pass	
Paediatric oncology		1		1	1	1	8	4	3	19	6.94	15	pass	

Q13 The most appropriate Health Care Professional to assess unmet informational needs of female CAYA cancer survivors relating to future fertility and pregnancy is:														
Questions	**Not important**			**Unsure**			**Agree**			**Total**	**Mean**	**Total 7-9**	**70% consensus**	**Other**
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**					
nurse														
Fertility specialist	2		1	2	1		2	3	7	18	6.61	12	fail	n=1 missing
Obstetrician	2		2	1	1	2	5	2	4	19	6.1	11	fail	
Long term follow up doctor (not-oncology)	2			1	2		1	5	8	19	7.1	14	pass	
GP	2	3	4		5	2		1	2	19	4.36	3	fail	

Q14 The best format to assess unmet informational needs for female CAYA cancer survivors regarding future fertility and pregnancy late-effects is:														
Questions	**Not important**			**Unsure**			**Agree**			**Total**	**Mean**	**Total 7-9**	**70% consensus**	**Other**
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**					
Needs analysis (similar to nursing)	1				3	1	4	4	6	19	7.15	14	pass	
Questionnaire (online)	2	2		1	1	5	3	3	2	19	5.68	8	fail	
Face to face consultation with fertility counselling specialist				3	1	1	4	2	8	19	7.31	14	pass	
Online survey	2		1	3	1	4	4	1	1	19	6.26	6	fail	

Round 3 - PICCS2 Final statements

1) Health Care Professionals should communicate the following future fertility and reproductive health risks to female CAYA cancer survivors and/or parents (N.B. risks vary dependent upon level of treatment received):
• You may have difficulty becoming pregnant
• You will need high-risk pregnancy care and pre-pregnancy counselling
• There is a low risk of abnormality in baby
• There is a low risk of cancer in the baby

2) Health Care Professionals should FIRST communicate (either to the female CAYA cancer survivor and/or parent) future fertility and reproductive health risks:
• At diagnosis

3) Health Care Professionals should RE-INTRODUCE future fertility and reproductive health risks to female CAYA cancer survivors/parents at the following time points:
• When treatment is complete (Paediatric or LTFU team)
• Upon wanting to start a family (Fertility services or GP)
• Upon becoming pregnant (Obstetrics/fertility teams)

4) The most APPROPRIATE AGE to discuss future fertility and reproductive health risks directly with the female CAYA cancer survivor is:
• At an appropriate age as defined by the female CAYA with cancer/parent or health care professional ***(N.B. This should be no later than 16 years of age)***

5) The most APPROPRIATE Health Care Professional to discuss future fertility and reproductive health risks with female CAYA cancer survivors/parents is:
• The health care professional with the most knowledge in this area and with the best relationship with the female CAYA cancer survivor and/or parents ***(N.B. This may not be within the paediatric or LTFU teams)***

6) Being 'Fertile' following treatment for cancer is best defined as:
• Being able to conceive a pregnancy naturally (not requiring fertility services)

7) A treatment SUMMARY including information about future fertility and reproductive health risks should be sent to: (N.B. This should also be in a 'lay' format to ensure adequate comprehension)
• The General Practitioner
• The female CAYA cancer survivor and/or parents
• The long-term follow up team (if still involved in the care of the patient)

8) The most appropriate FORMAT to provide a treatment summary that includes future fertility and reproductive health risk is:
• Via input onto the electronic patient medical record
• Through a combination of written and oral information, with signposting to trusted online resources

9) The best method to support parents of female CAYA with cancer to communicate future fertility and reproductive health risks is a combination of:
• An information session (face-to-face) with a Health Care Professional (without the patient)
• **AND/OR** A joint face-to-face session with the female CAYA cancer survivor and their parent ***(N.B. dependent on age and understanding/willingness of the patient to have their parent present)***

10)Unmet future fertility and reproductive health informational needs of female CAYA cancer survivors should be EVALUATED at the following times (N.B. dependant on the age and maturity of the patient) :
• At treatment completion
• At 5 years following treatment completion
• When thinking about becoming pregnant

11)The most appropriate Health Care Professional to EVALUATE unmet future fertility and reproductive health informational needs of female CAYA cancer survivors is:
• The health care professional with the best relationship with the patient
• The health care professional with the most knowledge of future fertility and reproductive health risks ***(N.B. This may not necessarily be the paediatric or LTFU team)***

12)The best FORMAT to evaluate unmet future fertility and reproductive health informational needs of female CAYA cancer is:
• By using a needs-based analysis questionnaire
• **THEN** If deemed necessary or there are concerns voiced, a face-to-face consultation with a fertility specialist is recommended

Appendix 10 - PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	149
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	14 (see note p153)
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	150
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	158
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	159
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	161

Section/topic	#	Checklist item	Reported on page #
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	162
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	163-4
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	164
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	165
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	166
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	166-7
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	167
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I2) for each meta-analysis.	167
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	171-2
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	173

Section/topic	#	Checklist item	Reported on page #
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	172
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	175
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	177
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	177-182
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	201
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	222
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	n/a
DISCUSSION			
Summary of evidence	24	Summarise the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	224
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	234

Section/topic	#	Checklist item	Reported on page #
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	237
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	152

Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *PLoS Med* 6(7): e1000097.

Appendix 11 - PICCS1 Included studies summary table

Title	**Brand, Fasciano, and Mack 2017**
Study type	Qualitative, content analysis
Key words	Paediatrics, Oncology, Communication, Child, Adolescent, Prognosis
Study setting	USA, Hospital setting
Source	Journal
Purpose	How young cancer patients experienced communication around their illness and outcomes from disease and treatment
Sample/Population	n=16 (80% of 20) n=9 Female, n=7 Male, age at participation 8.3-17.8 years, no data for age at diagnosis or time since completing treatment No socio-demographics n=13 haematological cancer n=3 solid tumour Purposeful sampling from previous study
Data collection	Semi structured interviews, 3rd party trained interviewer, audiotaped, and transcribed Direct content analysis, Independent coding and group review

Title	Brand, Fasciano, and Mack 2017
Major findings	Themes: Participant expectations about what will happen because of the illness, Affective response to this information, The process of information exchange. Young people want prognostic information and be direct participants in care, participants valued open and honest communication with HCPs, who were the most frequent source of information Certain health information may not want to be heard by survivors Parents are important communicators and holders of information There is a reliance on parents to filter information to free them of the burden of difficult conversations Additional sources of information (online)can cause confusion and distress Overall survivors were satisfied with level of information but wished they understood some issues better, HCPs must balance information provision with ambivalence and individualised information needs Health care providers need to be intuitive, explore concerns, and have regular check ins

Title	Cox et al. 2019
Study type	Quantitative, questionnaire
Key words	cancer; oncology; survivors; childhood cancer; health-related needs
Study setting	USA, posted
Publication	Journal
Purpose	Describe the prevalence and predisposing factors for potentially modifiable unmet emotional, care/support, and information needs among adult survivors of childhood cancers
Sample/Population	Stratified sample of participants from the CCSS (n=1189; mean [SD] current age, 39.7 [7.7], range=26–61 years; 60.9% women; mean [SD] years since diagnosis, 31.6 [4.7]). Survivors self-reported demographic information, health concerns, and needs; diagnosis/treatment data were obtained from medical records. Adjusted proportional risk (PR) ratios were used to evaluate 77 separate needs (St Jude patients and survivors younger than 25 years as of December 31, 2009, excluded from sample) total eligible sample (n=4454) Purposeful sampling
Data collection method	CCSS-Needs Assessment Questionnaire (CCSS-NAQ) booklets Insurance status and health care access were assessed by using index items from the National Health Interview Survey Data related to childhood cancer (diagnosis, date of diagnosis, interval since diagnosis, treatment exposures) were obtained from the medical records of the CCSS database Common Terminology Criteria for Adverse Events (CTCAE) Health-related concerns and cancer-related fear/anxiety items were derived from the most recent CCSS cohort follow-up survey completed during the same time interval as the CCSS NAQ.
Major findings/ Conclusions/ Themes	54% of survivors reported unmet psycho-emotional needs. 41% reported coping needs and 35% reported care/support needs. 51%, 35%, and 33%, respectively, reported unmet information needs related to cancer/treatment, the health care system, and surveillance. Being female and an annual income <$60K were associated with multiple needs. Fewer needs linked to diagnosis/years since/or age at diagnosis. Cancer-related

Title	Cox et al. 2019
	anxiety/fear was associated with all needs, including a >6-fold increased prevalence for help dealing with “worry” (PR=6.06; 95% CI, 3.79 – 9.69), anxiety (PR=6.10; 95% CI, 3.82–9.72), a >5-fold increased prevalence for “needing to move on with life” (PR=5.56; 95% CI, 3.34–9.25), and dealing with “uncertainty about the future” (PR=5.50; 95% CI, 3.44–8.77). Radiation exposure and future health status were related to 42 and 29 needs. Demographic factors, disease/treatment characteristics, and intrapersonal factors can be used to profile survivors’ unmet emotional, care/support, and information needs. Concern about the ability to have children was associated with 1 surveillance, 11 of 20 care/support, 6 of 10 health-care system, and 8 cancer-related information needs. Compared to survivors diagnosed more than 31 years ago, survivors diagnosed more recently had needs related to physician communication and the need to make sense of their illness. A patient’s age is associated with the preferred style of patient-provider interaction: older patients are more accepting of an authoritative physician interaction style, whereas younger patients expect a more consultative style with more shared decision making. Patients want providers to ask about their health-related needs, but assessment is often unsystematic, and providers frequently focus only on specific presenting problems. Professionals’ varying ability to elicit relevant information, and patients’ inability or reluctance to volunteer their needs and concerns all contribute to poor documentation of needs. Clinician awareness of the risk groups identified, and the nature of the many survivor needs that may go “unspoken” should be included as potential focal points during the clinical encounter.

Title	**Crawshaw et al. 2009**
Study type	Qualitative, grounded theory
Key words	Teenage cancer, fertility preservation, sperm banking, decision making, gender, parental involvement
Study setting	UK, place of participants choosing
Publication	Journal
Purpose	To map the range of experiences of being advised that treatment might affect fertility
Sample/ Population	n=38 (35% recruitment rate), age at study 16-30 years, n=21 female, n=17 men, age at diagnosis 11-20 years, time since diagnosis 1-15 years Socioeconomic data provided 37% sarcoma, lymphoma 16%, leukaemia 16%, 13% germ cell, central nervous system tumour 11% n=5 were parents and n=11 were in stable relationships
Data collection method	Grounded theory Theoretical and purposeful sampling In depth interviews, tape recorded, and transcribed Coding frame used and qualitative software Data presented in narrative form Participants given a copy of the transcript, study report and summary

Title	Crawshaw et al. 2009
Major findings/ Conclusions/ Themes	Strong support for being told about fertility status around diagnosis Women more likely to have lower levels of comprehension, have later distress and need to revisit decisions about fertility preservation Men found decision making straight forward regarding sperm banking and reported satisfaction at choice offered Suggests young people can cope with fertility discussions around diagnosis especially when parental and professional support is proportionate to impact Consultant oncologists were key professionals in discussing fertility matters with limited involvement from nurses Little knowledge surrounding fertility impairment as a side effect of treatment Majority of participants told about fertility at diagnosis Possible assumptions by professionals that fertility matters would be of little consequence Giving final decision-making choice to patient welcomed Strong support for conversations to be directed to patients and not through parents Counselling not offered although a requirement by UK fertility preservation services

Title	Gianinazzi et al. 2014
Study type	Quantitative, Cohort study
Key words	Childhood cancer survivors, cohort study, information needs, information provision, questionnaire, survey
Study setting	Switzerland, cancer registry
Publication	Journal
Purpose	To assess the information survivors reported to have received on disease, treatment, follow up and late effects, their information needs, and the format preferred. Also, the association with psychological distress and quality of life
Sample/Population	n=319 (45% response rate, n=3 excluded), n=179 56% female, n=140 44% male, age at diagnosis <21 years (mean 8.9), time since diagnosis >5 years (mean 12.5) n=113 Leukaemia, n=59 Lymphoma, n=37 Central nervous tumour, n=106 other Socio-demographics analysed from registry data but not provided Comparator group n=388, n=165 female, n=223 male, mean age at diagnosis 8.9 years, mean time since diagnosis 12.8 years 375 non-responders and 13 who did not participate
Data collection method	Questionnaire, available in 2 languages. Demographic data and treatment data taken from registry Brief symptom inventory-18 used and Global severity index HRQoL (SF-12) used for quality-of-life measurement Analysis performed with statistical software Multivariable linear regression analysis for associations

Title	**Gianinazzi et al. 2014**
Major findings/ Conclusions/ Themes	Most survivors received verbal information only (late effects verbal 68%, written 14%). Most survivors who had not previously received information rated it as 'important' for late effects (71%). 44% would like personalised information on late effects Improving information provision allows survivors to have better control of health and to become better decision makers Survivors with an increased need for information had significantly higher depression scores (p=0.005) Information on follow up and late effects is lacking Suggestion for official online resources

Title	Greenzang, Dauti and Mack 2018
Study type	Qualitative
Key words	Communication, decision making, information, late effects of cancer treatment, parent, paediatric, oncology
Study setting	USA, Hospital setting
Publication	Journal
Purpose	To explore how parents of children with cancer consider late effects in initial treatment decision making and during active cancer treatment
Sample/Population	n=12 (86% recruitment rate), n=9 female, n=3 male, age at diagnosis for child 0.2-15.7 years, time from diagnosis for child 3.6-10.5 months n=5 haematological malignancy, n=2 brain tumour, n=5 extra-cranial solid tumour Screening undertaken prior to recruitment Recruited from hospital clinic - purposeful Gift card given for participation Socio-demographics measured
Data collection method	Semi-structured interviews by trained professional researcher Audio recorded, transcribed and coded Continuous analysis with thematic saturation Framework by Pope et al. used for analysis
Major findings/ Conclusions/ Themes	All parents wanted to know about risk of late effects and that this information is important 7 parents preferred early information regarding late effects Ambivalence at wanting and not wanting to know Parents wanted information on actionable late effects Many parents satisfied with quality and quantity of information Fertility information provision lacking Providing information, even if upsetting, is critically important and does not diminish hope What information does the parent need? What does the parent want to know and when? How do they want to learn about it? 50% of parents considered risk of late effects to be a key factor for treatment decision making

Title	**Greenzang et al. 2018**
Study type	Quantitative, questionnaire
Key words	Health communication, late effects of cancer treatment, paediatric oncology, risk communication
Study setting	USA, hospital clinic
Publication	Journal
Purpose	To better understand the communication process about risks of potential long-term effects of cancer and cancer treatment by evaluating parents' perceptions of their child's risk of future limitations Secondary aim - whether parents of children whom physicians considered to be at the highest risk of future limitations recognized this risk, and whether parents' desires for information about late effects varied based on their child's risk.
Sample/ Population	382/565 participants completed the survey within 12 weeks of child's diagnosis. Participation rates did not differ by diagnosis group, parents of children with brain tumours were slightly less likely to participate when compared with parents of children with hematologic malignancies or extracranial solid tumours (p=0.07). Paired physician surveys were obtained for 361/382 parent surveys (95%). 94 physicians participated; 34 (36%) had a single patient enrolled, 33 (35%) physicians had two to three patients enrolled, and 27 (29%) had four or more patients enrolled. Sociodemographic data collected Purposeful sampling

Title	Greenzang et al. 2018
Data collection method	n=9 surveys were excluded due to incomplete items for the primary outcome (n=6 parents and n=3 physicians). n=352 parents of children with cancer and their children's physicians used for analysis. Survey was pilot tested with parents and physicians prior to implementation English and Spanish and paper/online format available 5-point Likert scale used options for primary outcome “extremely likely (>90%)”, “very likely (75–90%)”, “moderately likely (50–74%),” “somewhat likely (25–49%),” “unlikely (10–24%),”and “very unlikely (<10%).” Additional outcomes - prognosis, communication quality, information quality, emotional impact of information, and trust in physicians Statistical analysis with Kappa statistic and tests of symmetry and univariate and multivariable mixed-effects logistic regression. Fisher's exact test was used to compare concordance of parent and physician predictions
Major findings/ Conclusions/ Themes	Parents more likely to understand their child's risk of future limitations when child at low risk of future impairment (odds ratio [OR] 3.01; 95% confidence interval [CI], 1.62–5.60). Parents who found information about future limitations less upsetting, were more likely to understand their child's risk, when compared to parents who found the information upsetting (OR 1.75; 95% CI 1.08–2.82). Parents less likely to understand their child's risk of future impairment when their child had a lower likelihood of cure (OR 0.63. Primary outcome - parent understanding of his/her child's risk of future limitations, which was defined as agreement between parent and physician estimations of risk, secondary outcome parent information preferences about possible future limitations Overall, 92% of parents felt it was extremely or very important to receive information about the likelihood of their child experiencing future effects of cancer treatment

Title	Greenzang et al. 2018
	There were no statistically significant differences in parent information preferences between those whose children were at high, moderate, or low risk of future impairment 86% of parents preferred receiving detailed information about the likelihood of their child experiencing future limitations from cancer or cancer treatment. Although most parents want information about life after cancer, most parents of children at high risk of future impairment do not recognise this risk Strategies to improve communication about late effects throughout paediatric cancer treatment should prioritise meeting information needs and improving parent understanding of the risk of impairment Physicians considered 22% of children at high risk of physical impairments, 9% at high risk for impaired intelligence, and 6% at high risk for impaired QOL. Among high-risk children, 38% of parents recognized this risk in physical abilities, 21% in intelligence, and 5% in QOL

Title	Hess et al. 2011
Study type	Quantitative, questionnaire
Key words	Not given
Study setting	Norway, Hospital setting
Publication	Journal
Purpose	To assess knowledge of diagnosis, treatment, and late effects in adult survivors of childhood malignant lymphoma
Sample/ Population	n=128 (58% response rate, n=2 excluded for misdiagnosis) Cancer registry data used for medical and social demographics n=69 male, n=59 female, age at diagnosis 0-18 years, time since diagnosis 7-37 years, n=84 Hodgkin's lymphoma, n=44 Non-Hodgkin's lymphoma. Purposeful sampling from registry data
Data collection method	Semi structured interviews with questionnaire filled at home. Questions based on previous study sample Descriptive statistics using SPSS Health related QoL, health, education and work measured but instrument not named Closed questions
Major findings/ Conclusions/ Themes	121 reported their diagnosis correctly, 7 reported they had had cancer but not Hodgkin's Lymphoma. 123 reported treatment modalities correctly, 85 (66%) were not aware of any risk of late effects, 43 could name at least one late effect. 37 provided additional information about receiving information about late effects Age at diagnosis and education level not associated with level of knowledge of late effects Survivors are insufficiently aware of their risks of late effects 15 (12%) confirmed they had received a written summary of treatment Survivors diagnosed before 1990 have less knowledge of late effect risk Asymptomatic survivors at high risk of late effects should be offered regular aftercare

Title	Keats et al. 2019
Study type	Qualitative, content analysis
Key words	Childhood cancer, Survivorship care plan, Surveillance, Needs
Study setting	Canada
Publication	Journal
Purpose	To explore the individual needs, preferences, and perceived utility of a personalized, algorithm-driven, automatically generated Survivorship Care Plan for Childhood Cancer Survivors
Sample/Population	Survivors were diagnosed between the ages of 3–15 years (mean = 9, SD = 4.7) and ranged in age from 14 to 29 years (mean = 23; SD = 5.6) at the time of interview. Family practitioners reported practicing family medicine for an average of 26.3 (SD = 10.1) years (range 9–39 years) and had an average of 2.8 (SD = 1.5; range 1–5) CAYA cancer survivors in their current practice Socioeconomic data collected and used for analysis (education, employment)
Data collection method	24 interviews were conducted with survivors, parents/guardians, and Family practitioners. 74 letters of invitation were sent to both survivors and their parents/guardians. Of these 74, 11 survivors and 15 parents/guardians consented to participate. 8 survivors and 10 parents/guardians completed the interviews. Demographic and medical information were summarised using descriptive statistics using *IBM SPSS Statistics for Windows Version 23.* Participant interviews were transcribed verbatim, and the resulting data was imported into *NVivo* software to facilitate the development and comparison of categories Semi-structured telephone interviews with a purposefully selected sample of survivors, parents/guardians, and family practitioners. Data included responses to stakeholder cancer care information needs, concerns with or gaps in communication, the perceived role of the family practitioner in the long-term management of survivors care, utility of the Survivorship Care Plan, preferred format, and suggestions for improvement. A deductive content analysis was conducted

Title	Keats et al. 2019
Major findings/ Conclusions/ Themes	Themes from data: (1) informative reference, (2) coordination of follow-up, (3) barriers to follow-up care, and (4) suggestions for improvement and future implementation. 4 survivors reported that they did not have any cancer-specific health concerns, while others expressed some uncertainty about fertility, cancer recurrence, and treatment-related late effects. Several survivors noted that they were not aware of the late effects and need for long-term follow-up. Survivors expressed concerns about a lack of confidence in the family practitioner to meet the unique health care needs of a survivor. 6/10 parents/guardians received documentation outlining their child's diagnosis and treatment history at discharge from active treatment. Others noted that while they did not recall having received a written summary, they felt well informed of their child's cancer history upon discharge. Some parents indicated that the survivorship care plan provided little or no added information, but it was a useful and concise summary of their child's cancer history and an important reminder for the need for long-term surveillance. Parents were concerned about non-dependent children and their willingness or motivation to follow up with a family physician about future cancer care needs. HCPs - the majority (5/6) noted a lack of information and/or sufficient knowledge about paediatric cancer treatments, potential late-effects, and recommended guidelines for surveillance and follow-up testing. Despite not having received a detailed Survivorship Care Plan, most family practitioners reported having initiated some type of cancer-related health care discussions with their survivor patients. The Survivorship Care Plan was viewed as a useful resource to empower the survivor and to facilitate communication with family practitioners, ultimately improving the survivors' approach and engagement in their own cancer care. Physicians also noted that while the physical repercussions of the disease and associated treatments were well- described, the psychological impact. Many physicians discussed the need to address the underlying fear and

Title	Keats et al. 2019
	distress that many survivors continue to feel as a result of their childhood cancer experience—which may deter some from seeking/adhering to additional follow-up and testing. In addition to the treatment summary, a comprehensive follow-up timeline, personalised lifestyle information, and details on how to access additional psychosocial support were highlighted as important components.

Title	Lee et al. 2019
Study type	Quantitative, questionnaire
Key words	adolescent; cancer survivor; health self-management; late effects. pediatric oncology; self-management; young adult
Study setting	USA
Publication	Journal
Purpose	To examine the level and predictors of knowledge of late effects risks from childhood cancer treatment in adolescent and young adult (AYA) survivors
Sample/Population	73 AYAs, aged 14–21, completed measures of knowledge of late effect risks, executive functioning, and responsibility for health self-management. 67 parents of these AYA survivors (91.7%) also participated. The 73 participants ranged in age from 14 years to 21 years (mean 17.16, SD 2.23) and included 56.2% males. Parent participants (n=67) included 91.0% mothers and 9.0% fathers. The parents of 6 AYAs did not participate due to the young adult living and/or attending the appointment independently. The study included patients who were treated for cancer before 18 years of age that were >2 years off-treatment. Exclusion criteria for participants included intellectual disability or inability to speak or read English fluently. Patients with history of central nervous system tumours were also not included in this study, as they are followed up separately. Compensation for study participation was provided in the form of a $20 gift card

Title	Lee et al. 2019
Data collection method	Sociodemographic data collected The patient's electronic medical record was accessed to gather information related to the patient's medical diagnosis, time since diagnosis, treatment exposures, and risks for late effects. The Survivor Knowledge Questionnaire (SKQ) used to evaluate AYAs' knowledge of their risk for 11 different late effects of childhood cancer treatment. The Readiness for Transition Questionnaire (RTQ) used, AYA self-report (AYA-RTQ) and parent proxy-report (P-RQT). Behaviour Rating Inventory of Executive Functioning (BRIEF) was used to assess AYA survivors' self- and parent proxy-reported executive functioning. Parents completed the BRIEF-Parent Form (patients ages 14–18) or BRIEF A-Informant Report (patients ages 19+ years). AYAs completed the BRIEF Self-Report (ages 14–18) or BRIEF-A Self-Report (ages 19+years). Linear regression analyses
Major findings/ Conclusions/ Themes	The recruitment rate was 74.6%. Reasons for declining included lack of time/not interested in participating (n=23), desire not to participate in any research (n= 5), and caregiver belief that AYA was too young to participate in the study (n=1). Of the 85 families who provided consent to participate, one family withdrew from the study (1.2%) and 73 families returned complete data (85.9%). Overall, AYAs demonstrated low knowledge of their risks for late effects with a mean knowledge score of 54.29% (SD 24.19%). Only four participants (5.5%) identified their risk level correctly for all 11 late effect risks. Knowledge across specific late effects was variable, with rates of accuracy ranging from 0% to 100%. As standard of care in this clinic, providers review a personalized survivorship care plan, detailing diagnosis, treatment history, and risk for specific late effects based on treatment exposure with patients, and a recommended surveillance schedule. Survivors demonstrated poor knowledge of their unique risks for treatment-related late effects, with a mean accurate knowledge score of 54.29% (SD

Title	Lee et al. 2019
	24.19%). The number of late effects for which survivors were at risk was negatively correlated with risk knowledge ($p < .01$). Survivors' executive functioning was not related to risk knowledge. In regression analyses, survivor age positively predicted accurate knowledge of late effects risks, and the number of late effects risk was a negative predictor. In separate models, survivor self-report of AYA responsibility for health self-management did not predict knowledge ($p < .01$), but parent proxy-report was a significant positive predictor ($p < .01$). Parental involvement was not a significant predictor in either model. There are significant knowledge gaps among AYA survivors of childhood cancer, which appear to be related to younger AYA age and lower levels of AYA responsibility for health self-management. Additional intervention is critical to increase AYA knowledge of their risk for late effects in order to promote continued engagement in long-term follow-up care and surveillance across the lifespan
	AYAs who had already transitioned to adult care, those who had participated in health self-management focused programming as part of their pediatric care (e.g., communicating with medical staff in person) evidenced higher knowledge of their treatment and their risk of late effects This sample had already received individualised education regarding late effects as a part of standard of care, demonstrating that despite efforts to provide education, knowledge remained low. This carries significant clinical implications for AYAs for LTFU. This study also suggests that while knowledge and self-management are related, they are not equivalent. It is possible that separate interventions will be needed to bolster both knowledge of late effects and skills for the subsequent self-management one's health care.

Title	Lie et al. 2015
Study type	Qualitative, thematic analysis
Key words	Childhood cancer survivors, providing information, Late effects, Patient perspective, patient education
Study setting	Norway, Hospital setting
Publication	Journal
Purpose	How and when adult, long-term survivors prefer to receive information about late effects
Sample/ Population	n=34 (50% participation rate), age at diagnosis 3-18 years, time since diagnosis 12-39 years, n=19 female, n=15 male, year of diagnosis 1970-2000 Purposeful sampling from previous study participants n=21 Hodgkin lymphoma, n=13 Non-Hodgkin lymphoma No socio-demographics Comparator group n=93, age at diagnosis 0-18, time since diagnosis 9-36-year, n=40 female, n=53 male, year of diagnosis 1970-2000 Data from previous follow up study, cohort did not participate in focus groups
Data collection method	Focus group interviews (5 groups of 4-8 survivors) Facilitated groups Audio recorded and transcribed Semi structured interview guide used Thematic analysis and coding software Summary sent to participants

Title	Lie et al. 2015
Major findings/ Conclusions/ Themes	Six themes - Experiences on receiving information about late effects, experiences on finding information, what information they want (and why), how to inform about late effects, when to inform about late effects, ambivalence about receiving information about late effects The survivors want information about late effects Information should be tailored, carefully timed, given 'face-to-face' and in written format Many survivors expressed ambivalence to receiving the information but thought it was 'essential to know' A re-information session around age 25 was suggested as beneficial Information about late effects is an on-going process which may change over time, but helps survivors understand health risks and aids better health self-management Difficult to find information and sometimes only told when late effects happen Primary care professionals 'unaware' or insufficient knowledge

Title	**Signorelli et al. 2019b**
Study type	Qualitative, mixed methods (cross-sectional)
Key words	Primary care, Childhood cancer, Follow-up care, Confidence, Barriers, Transition
Study setting	Australia and New Zealand
Publication	Journal
Purpose	To evaluate the primary care practitioner's role and confidence in providing follow-up care to survivors of childhood cancer
Sample/Population	Survivors who were diagnosed with cancer before 16 years of age and were treated at one of 11 participating Australian and New Zealand hospitals; were diagnosed at least 5 years prior; had completed active treatment; were English speaking; and were in remission. We invited parents of young survivors under the age of 16 to complete the interview on behalf of their child. We invited Australian primary care Practitioners nominated by survivors, by post. Of 612 respondents, 358 (58.5%) opted to be interviewed. We interviewed participants until we reached data saturation in each group at 57 adult CAYA cancer survivor (48%; average age: 25.6 years, standard deviation [SD] = 6.2; average time since diagnosis: 18.6 years, SD = 7.8) and 63 parents of survivors under 16 years (53%; average child age: 12.7 years, SD = 2.0; average time since diagnosis: 10.2 years, SD = 2.1). Of 160 eligible and contactable primary care professionals nominated by Stage 1 survivors/parents, 74 opted-in for an interview (46%). We reached data saturation after interviews with 51 HCPs determined by two authors (C.S., J.F.) conducting analysis alongside data collection. 29 (57%) HCPs were male, 33 (65%) worked in practices in major cities, and on average had 28.3 years' experience (range = 8–60, SD =11.7) at the time of study participation. On average, HCPs had cared for 2.3 CAYA cancer survivors in their career (range = 1–11, SD =2.1).
Data collection method	Electronic hospital records to identify sample Invitations for HCPs sent by post Interviews were audio-recorded and transcribed verbatim. Statistical Analysis performed by SPSS 24.0 (IBM, Armonk, NY) to conduct

Title	Signorelli et al. 2019b
	descriptive analysis and chi-square tests and t test analyses for respondent/nonrespondent and group comparisons. NVivo 11 used for qualitative analysis. Thematic content analysis by Miles and Huberman methodology, matrix coding to explore themes across participant groups and characteristics
Major findings/ Conclusions/ Themes	There is a high prevalence of unmet emotional, care/support, and information needs among adult survivors of pediatric malignancies. 39% of older survivors (>16 years) and 81% of young survivors (<16 years) were engaged in oncologist-led follow-up. Survivors and parents reported similar reasons for not accessing primary care follow-up including lack of cancer knowledge and low confidence in primary care HCPs. CAYA cancer survivors and their parents have low confidence in primary care professionals' ability to manage their survivorship care. Engagement in primary care is important to promote holistic follow-up care, continuity of care, and long-term surveillance. Survivors'/parents' confidence in physicians may be improved by better involvement throughout treatment and early survivorship. Staged transition of care to adult and primary services advised. Although physicians are willing to deliver childhood cancer survivorship care, their confidence in doing so may be improved through better communication with tertiary services and more appropriate training Participants preferring oncologist-led care (26%) occasionally even delayed seeking medical advice from a primary care professional (n = 4), instead "saving" it for their next clinic appointment. Other barriers to seeking primary care follow-up included having an aversion to doctors after treatment (n = 4), perceiving primary care professionals as too busy (n = 11) for their complex needs, or due to out-of-pocket expenses (n = 3). Many (67%) recalled receiving letters from the survivor's treating oncologist about their cancer history and current medical needs. A few

Title	Signorelli et al. 2019b
	primary care professionals recalled receiving a treatment summary for their patients (12%). All primary care professionals felt confident providing care to adult cancer survivors, but only 54% felt confident to care for CAYA cancer survivors. Low confidence appeared to be related to poor knowledge about late effects surveillance for survivors. Collaborative working between multidisciplinary team may improve survivors' confidence and reduce potential anxiety induced by transition to adult (often primary) care, when many survivors become disengaged from any follow-up.

Title	Sisk et al. 2018
Study type	Quantitative, questionnaire
Key words	Communication, late effects, parent, paediatric oncology, survivorship
Study setting	USA, hospital setting
Publication	Journal
Purpose	To assess whether parental preferences for late effects information change over the year after diagnosis.
Sample/ Population	n=565 eligible parents, n=382 (68%) completed the baseline questionnaire, 211 (69%) completed the 4-month questionnaire, and 168 (82%) completed the 12-month questionnaire. n=3 excluded from n=168 parents due to missing values. Final cohort n=165 parents No formal consent process Comparator group - Primary oncologists for each patient were given the physician survey at each time point Socio-demographic data collected Hematologic malignancies (51%), solid tumours (38%) and brain tumours (12%) Parents of children between 1 and 6 weeks after diagnosis. Further sample contacted 4 months and 12 months after diagnosis to complete follow-up questionnaire
Data collection method	Multiple choice based on Likert agreement scales Mc Nemar's test used for baseline and follow-up Bivariable logistic regression to evaluate factors associated with parental report of wanting Analyses were conducted using the SAS statistical package Most parents found information related to late effects of cancer therapy to be very or extremely important at baseline (94%,153/162), 4 months (91%, 147/162), and 12 months (96%, 156/163)
Major findings/ Conclusions/ Themes	Most parents preferred to receive as many details as possible related to late effects at diagnosis (85%,141/165),4 months (87%,144/165), and 12 months (83%,137/165) Wanting as many details as possible about late effects at diagnosis was associated with having a favourable outcome from cancer (OR 2.94, 1.18–

Title	Sisk et al. 2018
	7.31, P=0.02), but not significantly at 4 months (OR2.20,1.18– 7.31, P=0.12) or 12 months (OR 1.94, 0.82–4.59, P=0.13)

Title	Vetsch et al. 2017
Study type	Qualitative, mixed methods
Key words	Childhood cancer survivors, parents, information needs, mixed methods study, paediatric oncology
Study setting	Australia, questionnaire
Publication	Journal
Purpose	To assess survivors and parent's information needs and associations between unmet information needs and clinical and socio-demographic characteristics
Sample/ Population	n=485 (n=322 survivors, n=163 parents) for questionnaire. For interviews n=70 (n=39 survivors and n=31 parents). Questionnaire - response rate 59%, Interviews 24.5% Survivors - mean age at study 26.7 years, time since diagnosis mean=19.7 years, inclusion criteria <16 years at diagnosis Parents - child age mean=12.9 years, time since diagnosis mean=9.7 years, Socio-demographics data collected but raw data not available Recruitment through national media and medical records - purposeful Diagnosis - n=131 Leukaemia, n=49 Lymphoma, n=33 Brain cancer, n=107 other
Data collection method	Online questionnaire and semi-structured telephone interviews Questionnaire data piloted before use Interviews conducted by a trained psychologist and piloted before use EuroQoL EQ-5D-5L used for anxiety and depression measurement Descriptive statistics and regression analysis with univariable and multivariable linear regression used Interviews - content analysis and thematic organisation by coding. Matrix coding to cross-analyse

Title	Vetsch et al. 2017
Major findings/ Conclusions/ Themes	Overall information needs for late effects (85% survivors and 90.2% parents). Survivors reported unmet information needs about late effects (57.5%) and parents fertility issues (62.5%). Survivors had more information needs for medical information, and parents had information needs for lifestyle and sexual issues Significant association with unmet needs for being a parent (p=0.001), dissatisfaction with follow up care (p=0.003), lower overall health (p=0.014), higher perceived risk of late effects (p<0.001) and greater anxiety and depression (p<0.001) Many survivors rely on their parents for information, but deficiencies in knowledge transfer occur Tailored information recommended Socio-demographics not associated with information need Treatment summaries not understood and contain too much jargon Difference in information need from survivors and parents suggest a need to revisit discussions

Title	Wakefield et al. 2012
Study type	Qualitative, content analysis
Key words	Childhood cancer, family studies, information, survivorship, treatment completion, unmet needs
Study setting	Australia, telephone/hospital setting
Publication	Journal
Purpose	To explore the information needs of families of childhood cancer survivors in the first-year post-treatment
Sample/ Population	n=112 (34% response rate), n=19 survivors, n=44 mothers, n=34 fathers, n=15 siblings, results from 45 families 76.8% interviewed within 12 months of completing treatment Mean age at diagnosis 13.3 (7-17 years), mean time since treatment complete 12.46 months (1.9-27.7) Diagnosis n=13 Acute Lymphoblastic Leukaemia, n=5 Central Nervous System tumour, n=4 Wilms tumour, n=4 Hodgkin disease, n=3 Ewing's sarcoma, n=3 Germ cell, n=3 Acute Myeloid Leukaemia, n=2 Osteosarcoma, n=2 Rhabdomyosarcoma, n=1 Chronic Myeloid Leukaemia, n=1 Non-Hodgkin lymphoma, n=1 Hepatoblastoma, Socio-demographics (education and employment) provided Purposeful sample
Data collection method	n=108 semi-structured interviews conducted over the phone, n=4 in person at participant request Interview schedule piloted before use Experienced interviewers for study Transcribed and coded with software support, 15% of interviews coded independently Descriptive statistics used for socio-demographics and comparisons

Title	Wakefield et al. 2012
Major findings/ Conclusions/ Themes	Few recalled having a formal meeting for treatment completion. 1/19, 9/44, 9/34, 4/15. Only 8 parents described this as an unmet need Many report receiving insufficient information post-treatment 3/19, 29/44, 17/34, 14/15 Primary source of information is the oncologist 13/19, 32/44, 22/34, 0/15. Other members of medical team infrequently referred to as information resource 11/19, 11/44, 9/34, 0/15 reported receiving information from a newsletter and conference 4/19, 9/44, 5/34, 0/15 reported finding information from the internet but 2/19, 4/44, 4/34, 3/15 describe the internet as a source of fear/concern Fertility most common unmet information need 5/19, 14/44, 15/34, 0/15 Most preferred information source - booklet (mean 7.6/10), online support (mean 7.3/10). Parents preferred booklet to online support

Title	Wright et al. 2014
Study type	Qualitative, mixed methods approach
Key words	Fertility information, reproduction, psychosocial needs, adolescents, teenagers and young adults, cancer
Study setting	UK, Hospital setting
Publication	Journal
Purpose	The fertility information needs of teenagers and young adults with cancer
Sample/ Population	n=40 (n=14 young people, n=6 parents and young partners), age at diagnosis 12-24 years, time since diagnosis 2 months-4.5 years, n=5 female young people, n=9 male young people Sample characteristics presented in additional paper Purposeful sampling
Data collection method	Participant observation and semi-structured interviews Thematic content analysis Coding and software support
Major findings/ Conclusions/ Themes	All but one participant received information about the impact of cancer on their fertility Diagnosis in early teens meant how, when, and from whom, regarding information provision varied Young women tended to receive incomplete information Most participants are unaware of fertility status Participants did not know where to obtain more information from Young people often not included in conversations Standard of information and manner of delivery important to young people Parent's presence in conversations should be an individual choice HCPs need to challenge assumptions of 'normal' family Tailor made information with honest and open discussions Recommended

Appendix 12 - PICCS1 Interviews – Example transcript

AP 0:06

Okay, participant A, this is an interview for the pregnancy information for childhood cancer survivors study. If you could just start by introducing yourself that would be great.

A 0:19

Yes, so my name is participant A and I'm one of the clinical nurse specialists from ##################

Unknown 0:26

Can you just confirm for me that you have had the opportunity to read the information sheet and sign the consent form?

A 0:30

I have yes

AP 0:34

And, that you are happy for me to audio record this conversation.

A 0:36

Yep, that's absolutely fine.

AP 0:39

Great. And I just need to make sure that you're that you understand that you can withdraw anytime, you can stop the conversation at any point and if you want any further support or signposting to any organisations then just let me know.

A: Yep, great that is really helpful, thank you

AP: Okay, so the first question is, can you tell me a bit more about what you would normally discuss with patients and families during the consultation about future pregnancy risk after treatment?

A: 1:14

Erm, so at the minute myself, cos I have a job share with another colleague, and er we have been in the job for seven months and it was a new service that we brought over from ####### and we are kind of still in our infancy, but, the information we are giving out, not necessarily at the minute but any information that we have to give out to a patient about future pregnancies, sorry I don't know if this is as helpful as what you wanted,

AP: No, no it's fine

A: we give information out about how it might affect their fertility, but for the vast majority of them, it might be chemotherapy they've had, it won't necessarily, or it will affect their fertility and it may out them into early menopause, rather than making them infertile there and then.

Some of the treatments do, but a lot of the chemotherapies that we are giving their more inclined to go into early menopause, but we do say to them, we don't know what that will look like for your future, but there is a possibility if you want that looking into further then just get in touch with us and we put them in touch with the gynaecologist over in ######### women's

AP: um, hmm

A: to have further investigations done over there to look into infertility. But as and when patients come to us that would possibly need this information, about future pregnancy, they would be patients that have had radiotherapy, and at the minute, my clinics that I've done, or I've done with my colleague haven't come across anyone that needs that information. So, we've not thought but I don't think it's a widely spoken thing at the hospital if that makes sense

AP: Yeah, sure

A: At the children's hospital, I would say, t hat we are definitely down that holistic role and looking at aftercure, think it's definitely an area that we are lacking, could probably do with perhaps a bit more information to give out to families, you know our patients.

AP: 2:27

Okay, and what, what kind of timing in the treatment pathway do these conversations happen?

A: so, a lot of, particularly for the girls there has been a lot of advancement in fertility preservation, so I know a lot of the patients that have literally in the last 12 months, err a lot of the younger ones have gone for fertility preservation and they've had ovarian tissue taken, so they've already taken tissue of the ovary for storage , so I know that conversation happens at the beginning and usually if they are going to do that then it's before they start treatment, so between diagnosis and doing all the work up and starting treatment, if it's appropriate obviously, depending on how quick the treatment needs to start. I know of a couple of our patients that have gone for fertility preservation, so a conversation… even if they can't have fertility preservation, any treatment that can potentially affect the fertility or the ability to have children that's talked about at the beginning, that it's just one of the side effects, that they go through before they start chemotherapy.

AP 3:19

Okay, and um those clinical conversations who, who starts those conversations or who discusses that with the families,

A: 3:37

That will be the consultant. It will be part of the work up and when they are doing their consent for chemotherapy and they go through the side effects of what the chemotherapy may be, it will be brought up then and they will go through it with them.

AP 3:41

Okay. And, in your opinion, do you think what we currently tell families and young people is enough. In regard to information.

A: 3:49

I think probably, at the beginning I think it is. Because at that stage, especially with the ages of our kids, they're like 5 or 6 years old and the family are like, yeah that's the future, you know we still have a child with cancer, well do whatever we need to do, so I think at that stage then definitely yes. Enough, they get told what they need to get told and basically we won't know how the future looks until the future happens, but I think as far as aftercure goes,so after finishing treatment and where you can say, so for the rest of your life this is your long term thing, I think we are probably lacking and I think that we could be a little bit more clear, and a little bit more direct with what we tell them, so rather than say oh if you've got a problem then well find out in the future, actually we could spend more time saying the problem you might face is that you'll be fertile for a shorter period of time, you know you're going to go into early menopause, don't wait to be having children, I think you definitely need to be a bit more open with that then

AP: Yeah

A: and explore that a little bit more with the families

AP: 4:36 Okay, brilliant and in, in, in the work that you've been doing, do you think you've ever faced any questions that you couldn't answer in a discussion?

A: 4:51

Erm, no I think again since we have come into post, we have started a new thing where we have an MDT meeting which is dedicated to aftercure, where we discuss patients, and we've actually started inviting one of the gynaecologist from the Women's to come. So whenever we have a patient come through and there's a question with fertility, she's been able to, this again this has only happened in the last couple of months really, she's been able to say no that patient is of a category that you can refer to me if you want it, you know I can look into testing and start looking into her fertility and things, so that's a lot better, but previously to that, no we weren't the best.

AP: Oh, ok

A: I think we were lacking with, you know some concerns about what's out there and what's available, given that we would say yeah, we will refer you to the gynae consultant, but I don't know whether we knew exactly what that would entail when they got there if that makes sense

AP: Yeah

A: But now as we've got someone that comes to our MDT we can say, this is what I will do, this is what you need to tell her, and you know this is what the patient wanted but yeah, she, we are getting a lot more information and a lot more accurate information from her rather than just sort of signposting, we kind of know what to tell the patients to expect

AP: 5:48

Yeah. Okay, that's great. And do you think that there's any possible treatment implications for um survivors or children when they're going through treatments? Now that fertility is kind of discussed at the beginning. Do you think it has any implications on their treatment plans at all?

A: 6:05

Erm, so I think a couple of the teenage girls, you know the family will say you know if you want fertility preservation then you would have to not start chemotherapy, but you know I don't think the doctor would allow that if they thought that that would make a difference if that makes sense.

AP: Yep

A: So I think it's done in a we've got time, we can try and do this if you want were as if they didn't have time and they should start treatment I think the consultants would be very direct and say we haven't got time to wait we need to start the chemotherapy now, so I don't think it effects treatment in that way, is that what you meant by that question sorry?

AP: 6:32

Yeah, yeah, it's just whether you've encountered any kind of situations where treatment might have been kind of paused or off because of conversations regarding fertility

A: No, none come to mind at all, all I can think of is if the doctors said we've got time we can do this and if they haven't got time the doctors make that very clear and I have known a family that said no I want to do the fertility preservation before they do chemo and have been advised against that, you know, does that make sense? I don't know of anyone that's done the opposite.

AP: 7:04

Yeah. Perfect. Thank you. And in, in your opinion, is the issue of pregnancy risk for childhood and TYA survivors an issue for maternity services?

A: Say that question again sorry

AP: So, the issue of future pregnancy for survivors, do you think it's an issue for maternity services? So, do you think it's something that maternity professionals like myself would need to be concerned about in future?

A: 7:32

Erm, in all honesty I don't know whether I've got enough knowledge to be answer that one, I think as far as carrying a child I think if there was to be any issues, id hope that they'd been told that and I think with most of them the issue with carrying a child would be if they had radiotherapy to the lower abdomen and I think if that happened then that does get explained to them. I think it would definitely get explained at the time, when they have the radiotherapy that this is a side effect as they can't consent without that being done, err but I would say that the role that I'm in at the minute, cos it's still quite new, I haven't had to deal with anybody that needs that information relaying to them, I haven't been in a clinic where a doctors had to do that. I would speak to a consultant to see exactly what they tell them with regard to actually carrying a child, but I would hope that anyone who was going to have the baby, would be able to inform yourselves at the time and say there is a risk, does that make sense?

AP: Yeah absolutely

A: And not be completely unaware that there is a risk.

AP: 8:21

Yeah, yeah, I think that's why we're trying to do this kind of work. To gauge what we need to be aware of and what we need to say.

A: Yeah.

AP: And is there anything else that you think is important or you'd like to share with me about the topic of fertility and future pregnancy for survivors?

A: 8:50

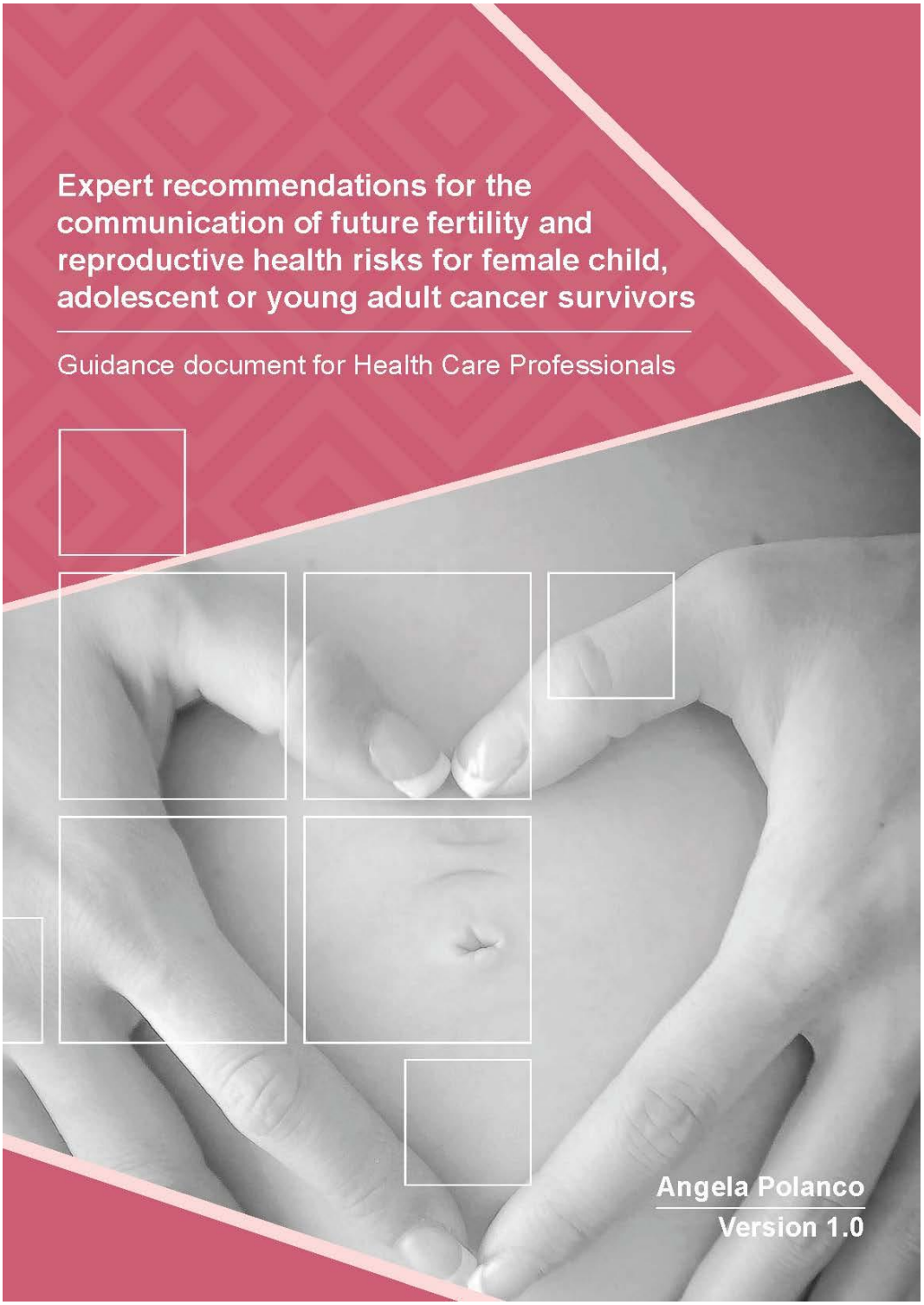
Erm, no I think the questions, those are the questions that would affect people I feel.

AP: Yeah. All right. Okay. Well, that's all the questions I have. So, thank you very much for taking part and as I say, if you decide later that you want to withdraw your answers, or you have any concerns or questions, and you have my email address, and I can give you that information.

A: 9:10

Okay, thank you.

Appendix 13 - PICCS2 Final guideline



Expert recommendations for the communication of future fertility and reproductive health risks for female CAYA cancer survivors – Guidance document for Health Care Professionals

Polanco, A. et al. (2021) version 1.0

"Fertility is one of the biggest issues for young people in cancer survivorship"

Background

Childhood, adolescent and young adult cancer survivors (0-24 years inclusive at diagnosis), are a rapidly growing population with complex and individualised health care needs. Health care providers responsible for their ongoing care need an increased awareness of late-effects of treatments and how best to communicate this to families.

Many female cancer survivors are worried about their future fertility status. Up to 15% of females will be infertile due to treatments with a further 40% at risk of early menopause and primary ovarian insufficiency/ failure.

Female survivors who received radiotherapy to the abdominal area as a child/adolescent or young adult have an increased risk during pregnancy and birth of:

- Premature birth (birth <37 weeks)
- Small for gestational age babies (<2500 grams)
- Miscarriage
- Stillbirth

Information about future fertility, reproductive health and individual risk of complications is an unmet need for survivors and their families. Access to fertility preservation services and lack of awareness of health care professionals about potential risks in adulthood are barriers to effective partnerships between families and professionals. Survivors also describe increased levels of anxiety, depression, and post-traumatic stress disorder caused by not having the information they need to make evidence-based, health-care choices in adulthood.

Clinical guidance for the communication of future fertility and reproductive health late-effects risk for female survivors of childhood, adolescent and young adult cancers.

p2 © Angela Polanco

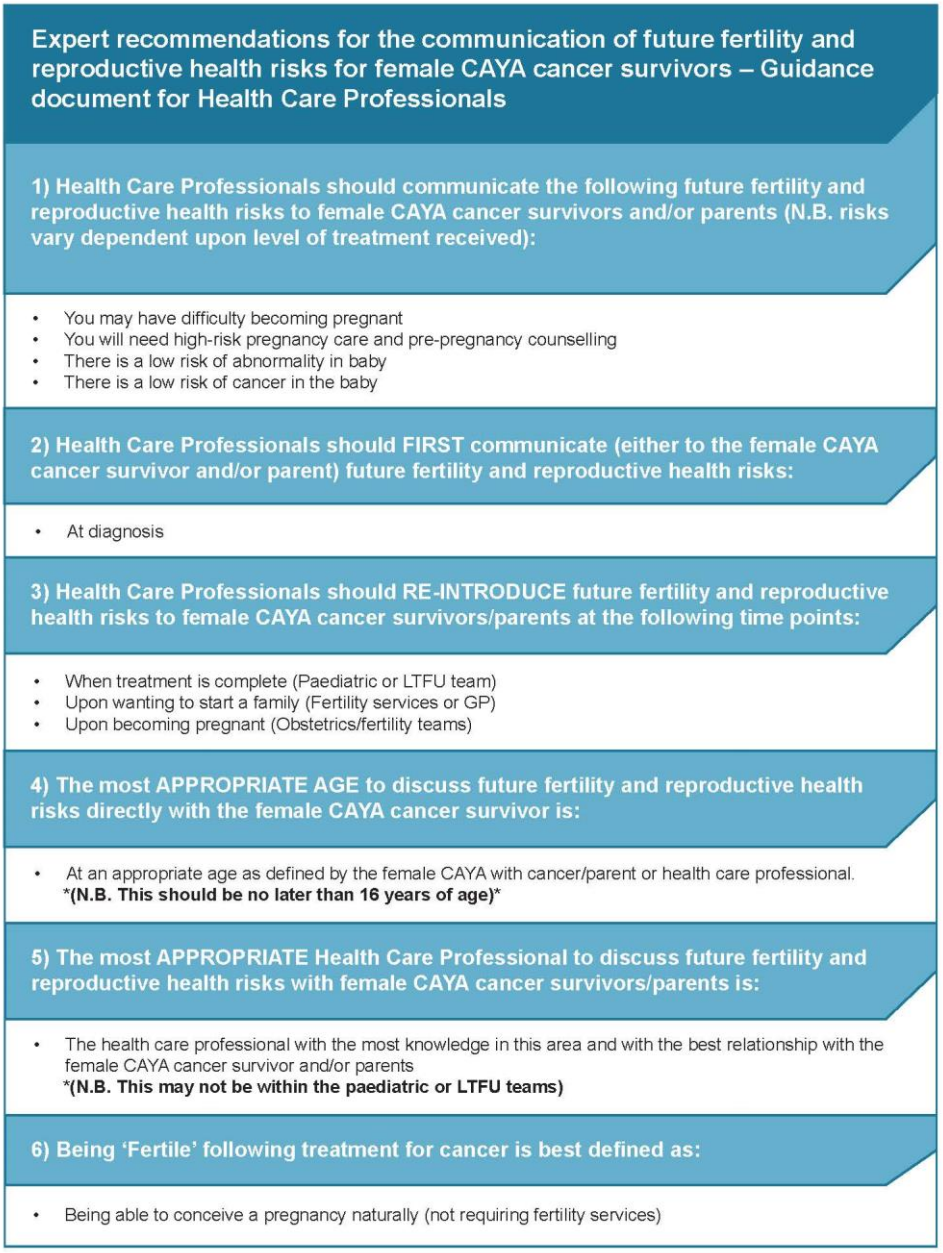
Miscommunication of information can be avoided by using:

- Clear communication
- A format that patients can remember long-term
- Up-to-date evidence
- Being honest and open
- A multi-disciplinary approach
- An individualised risk-assessment

Parents of survivors play a huge part in communication of future health risk. Some survivors may be unaware of their future health risks or even of their original diagnosis. It is important to take this into consideration during clinical consultations, including preferences of the young person with regards to parental involvement in clinical discussions.

PICCS2

Pregnancy Information for Childhood Cancer Survivors Study 2 (PICCS2) recruited an expert panel of 19 health care professionals and 5 patient/parent representatives, using a 3-stage Delphi consensus technique exploring who should communicate future fertility late-effects information, in what detail, and when.


Expert recommendations for the communication of future fertility and reproductive health risks for female CAYA cancer survivors – Guidance document for Health Care Professionals
1) Health Care Professionals should communicate the following future fertility and reproductive health risks to female CAYA cancer survivors and/or parents (N.B. risks vary dependent upon level of treatment received):
• You may have difficulty becoming pregnant
• You will need high-risk pregnancy care and pre-pregnancy counselling
• There is a low risk of abnormality in baby
• There is a low risk of cancer in the baby
2) Health Care Professionals should FIRST communicate (either to the female CAYA cancer survivor and/or parent) future fertility and reproductive health risks:
• At diagnosis
3) Health Care Professionals should RE-INTRODUCE future fertility and reproductive health risks to female CAYA cancer survivors/parents at the following time points:
• When treatment is complete (Paediatric or LTFU team)
• Upon wanting to start a family (Fertility services or GP)
• Upon becoming pregnant (Obstetrics/fertility teams)
4) The most APPROPRIATE AGE to discuss future fertility and reproductive health risks directly with the female CAYA cancer survivor is:
• At an appropriate age as defined by the female CAYA with cancer/parent or health care professional.
(N.B. This should be no later than 16 years of age)
5) The most APPROPRIATE Health Care Professional to discuss future fertility and reproductive health risks with female CAYA cancer survivors/parents is:
• The health care professional with the most knowledge in this area and with the best relationship with the female CAYA cancer survivor and/or parents
*(N.B. This may not be within the paediatric or LTFU teams)
6) Being 'Fertile' following treatment for cancer is best defined as:
• Being able to conceive a pregnancy naturally (not requiring fertility services)
Clinical guidance for the communication of future fertility and reproductive health late-effects risk for female survivors of childhood, adolescent and young adult cancers.
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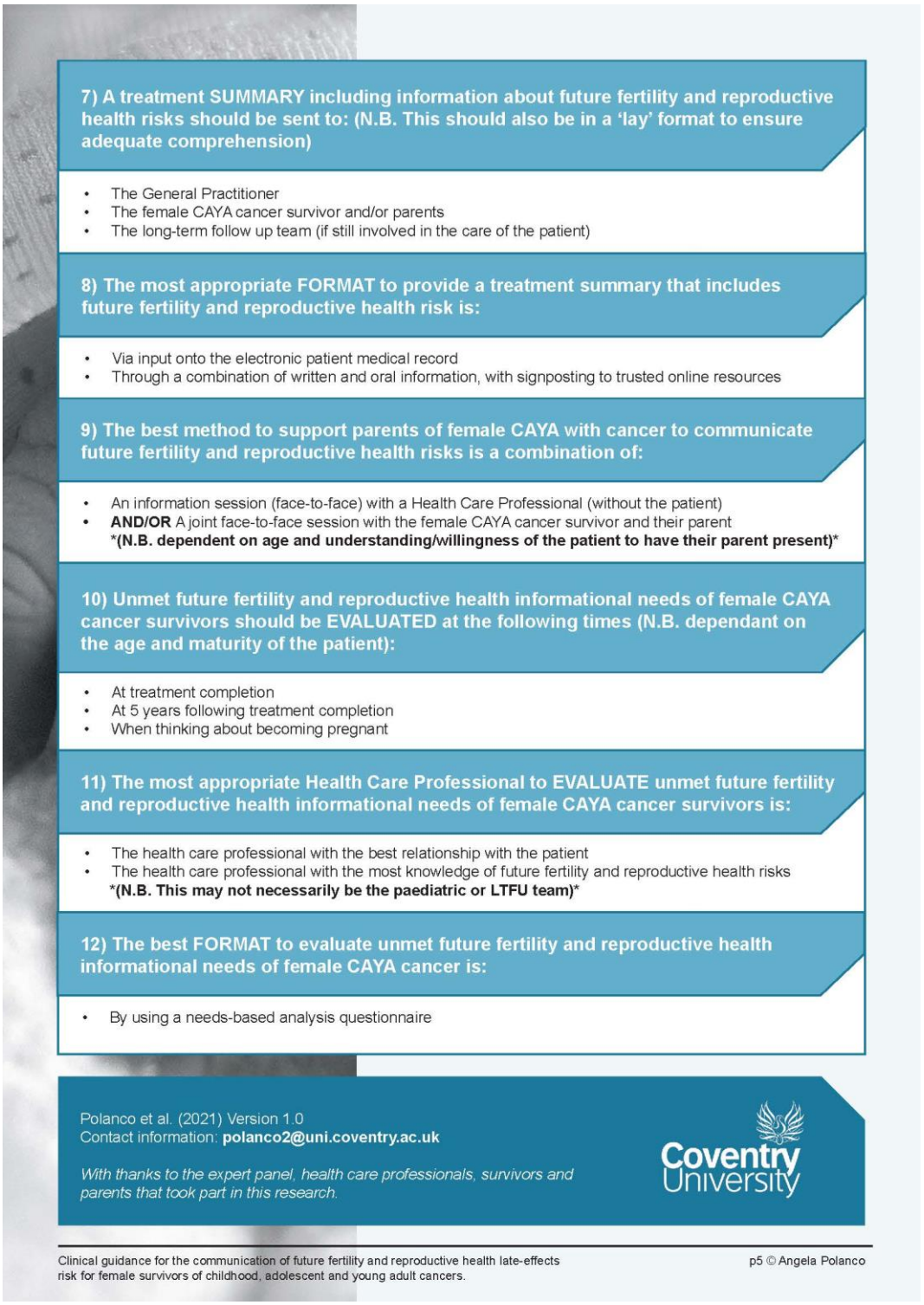
7) A treatment SUMMARY including information about future fertility and reproductive health risks should be sent to: (N.B. This should also be in a 'lay' format to ensure adequate comprehension)
• The General Practitioner
• The female CAYA cancer survivor and/or parents
• The long-term follow up team (if still involved in the care of the patient)
8) The most appropriate FORMAT to provide a treatment summary that includes future fertility and reproductive health risk is:
• Via input onto the electronic patient medical record
• Through a combination of written and oral information, with signposting to trusted online resources
9) The best method to support parents of female CAYA with cancer to communicate future fertility and reproductive health risks is a combination of:
• An information session (face-to-face) with a Health Care Professional (without the patient)
• AND/OR A joint face-to-face session with the female CAYA cancer survivor and their parent
(N.B. dependent on age and understanding/willingness of the patient to have their parent present)
10) Unmet future fertility and reproductive health informational needs of female CAYA cancer survivors should be EVALUATED at the following times (N.B. dependant on the age and maturity of the patient):
• At treatment completion
• At 5 years following treatment completion
• When thinking about becoming pregnant
11) The most appropriate Health Care Professional to EVALUATE unmet future fertility and reproductive health informational needs of female CAYA cancer survivors is:
• The health care professional with the best relationship with the patient
• The health care professional with the most knowledge of future fertility and reproductive health risks
(N.B. This may not necessarily be the paediatric or LTFU team)
12) The best FORMAT to evaluate unmet future fertility and reproductive health informational needs of female CAYA cancer is:
• By using a needs-based analysis questionnaire
Polanco et al. (2021) Version 1.0
Contact information: polanco2@uni.coventry.ac.uk
With thanks to the expert panel, health care professionals, survivors and parents that took part in this research.
Coventry University
Clinical guidance for the communication of future fertility and reproductive health late-effects risk for female survivors of childhood, adolescent and young adult cancers.
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