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Doctoral Thesis

Experiences of Psychological Distress, Uncertainty, and Coping Amongst People with  
Cancer

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### Word Count

	Main Body	Appendices (Including abstract, tables, figures, and references)	Total
Thesis Abstract	n/a	292	292
Section 1: Literature Review	8 000	13 505	21 505
Section 2: Research Paper	7 998	9 660	17 658
Section 3: Critical Appraisal	3 998	780	4 778
Section 4: Ethics Form	5 870	3 997	9 867
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## **Abstract**

The thesis entitled ‘Experiences of Psychological Distress, Uncertainty, and Coping Amongst People with Cancer’ explores the psychological experiences of individuals affected by cancer.

A systematic literature review of the of the relationship between psychological distress and uncertainty amongst younger adults with cancer is presented in section one. Fifteen eligible studies were identified via database and hand searches. Risk of bias assessments were carried out. Findings demonstrated a highly significant relationship between uncertainty and psychological distress, with a number of studies indicating that uncertainty predicts psychological distress. Inconsistency in findings, however, suggests that other variables may influence this relationship. Risks of bias were identified across studies.

A research study exploring patients’ experiences of coping longer-term with cancer of unknown primary (CUP) is presented in section two. Interviews were carried out with ten participants and data was analysed using interpretative phenomenological analysis. Three superordinate themes were identified: (1) “‘Fuss and Bother’”: The Upheaval of Everyday Life’, with subordinate themes of ‘Appointment threats’, and ‘Symptoms and side-effects’; (2) “‘It’s the Unknowing’”: The Enduring Uncertainty of CUP’ with subordinate themes of “‘What the bloody hell’s that?!’”, ‘An uncertain future’, and ‘Hope’; and (3) “‘Just Get on With It’”: Managing and Moving Forwards’ with subordinate themes of ‘Maintaining normality’, ‘Acceptance’, and ‘Support’. Findings highlighted that the experiences of people living longer-term with CUP are comparable to those of other cancer patient populations, however, they also face a number of distinct challenges.

A critical appraisal of the research paper is presented in section three. Within the critical appraisal, consideration is given to the epistemological and ontological assumptions

made within the thesis, the position of the researcher and the importance of researcher reflexivity, and the research process.

The ethics application and associated documentation are presented in section four.

## Declaration

The research reported upon in this thesis was conducted between March 2018 and December 2019 as a requirement of the Lancaster University Doctorate in Clinical Psychology. The work documented here is my own except where due reference has been made within the text. No part of the thesis has been submitted for an award of a higher degree elsewhere.

Signature:

A handwritten signature in black ink, appearing to read 'Hayley Slater', written in a cursive style.

Print name: Hayley Slater

Date: 31/12/2019

## **Acknowledgements**

My sincerest gratitude goes out to all those who have supported me throughout the process of completing this thesis. It has been a long and often challenging undertaking and I couldn't have done it without the help of those around me.

I am grateful in the first instance for the guidance, encouragement, and inspiration provided by my field supervisors. Their passion for and dedication to the work that they do with cancer patients day-in-day-out formed the jumping-off point for the research, but also served as an often-needed reminder of just why I had embarked upon the project. I am also extremely thankful for the erudite and patient support provided by my research supervisors Anna Daiches and Anna Duxbury from the Lancaster University Doctorate in Clinical Psychology, whose wise and motivational words helped me to see the light at the end of the tunnel. Thanks also go to Craig Murray who provided a great deal of methodological guidance as a research supervisor in the early stages.

The research would not have been at all possible without the willing assistance of the wonderful clinical nurse specialists and consultant oncologists who facilitated recruitment. The work that they do for people with cancer of unknown primary and other cancers is remarkable, and I am beyond grateful for the time given by these very busy professionals to support my research.

To the ten individuals with cancer of unknown primary who agreed to give their time to participate in the research, I extend my most heartfelt gratitude. It was my absolute pleasure to about hear their experiences and I was continually moved and humbled by their incredible strength, humour, and vitality.

Finally, my eternal appreciation extends to my wonderful family and friends. Special thanks to: my fiancé Alex for keeping me calm and looking after me through it all; my mum Cath for always believing in me; and my friends for helping me keep things in perspective.

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Section 1: Literature Review

A Systematic Review of the Relationship Between Uncertainty and Psychological Distress  
Amongst Younger Adults with Cancer

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**Abstract**

**Introduction:** Experiences of psychological distress and uncertainty are prevalent amongst cancer survivors. This systematic review aimed to collate and evaluate the available quantitative evidence regarding the relationship between these experiences amongst younger adults with cancer.

**Methods:** Studies were identified through academic database searches and hand searches.

**Inclusion criteria were:** (1) published in English (2) quantitative methodology (3) published in a peer reviewed journal (4) mean sample age of 55 or younger (5) sample with confirmed diagnosis of any cancer (6) and analysis of the association between psychological distress and uncertainty. Studies were assessed for risk of bias.

**Results:** Fifteen studies were identified which demonstrated a statistically significant relationship between psychological distress and uncertainty amongst younger adults with cancer. Several studies suggested that uncertainty is a predictor of psychological distress.

**Findings indicated that a number of other variables may mediate and influence this relationship.**

**Conclusion:** There is a significant association between uncertainty and distress across a range of different cancer survivor populations. However, variability in findings suggested that these experiences were also influenced by other factors which merit further investigation.

**Interpretation of findings was limited by recurrent methodological weaknesses.**

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### **Introduction**

The effects of cancer and its treatments on the physical, social, and emotional wellbeing of individuals following diagnosis has been widely established (Cleeland, 2007; Fan, Filipeczak, & Chow, 2007; Mor, Allen & Malin, 1994; van't Spijker, Trijsburg, & Duivendoorn, 1997). Guidelines for supportive care for adults with cancer from the National Institute for Health and Care Excellence (NICE, 2004) recommend that psychological assessment and support are embedded throughout the care pathway to facilitate the management of cancer-related psychological distress.

Psychological distress in relation to cancer has been defined by The National Comprehensive Cancer Network (NCCN, 2010) as “a multifactorial unpleasant emotional experience of a psychological (cognitive, behavioural, emotional), social, and/or spiritual nature that may interfere with the ability to cope effectively with cancer, its physical symptoms and its treatments”. This definition incorporates a spectrum of experiences ranging from foreseeable reactions, including feelings of fear or sadness, to emotional difficulties meeting criteria for psychiatric diagnoses such as depression or generalised anxiety disorder (NCCN, 2010; NICE 2004). Such experiences are common for people with cancer (NICE, 2004). The shortened term ‘distress’ is used throughout the remainder of the review in reference to psychological distress.

The experience of distress amongst individuals with cancer has been widely researched and reported prevalence rates of diagnosable mental health difficulties vary from 0-49% (Massie, 2004; van't Spijker et al. 1997). It has been suggested that this wide variability of prevalence rates may be attributable to the discrepant conceptualisations and measurements of distress across studies. They may also reflect the divergent experiences of individuals with different diagnoses, stages of disease progression, and treatment pathways. The majority of studies indicate clinical levels of depression or anxiety to impact between

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one-in-five and one-in-three people with cancer (Brintzenhofe-Szoc, Levin, Li, Kissane, & Zabora, 2009; Linden, Vodermaier, MacKenzie, & Greig, 2012.; Singer, Das-Munshi, & Brähler, 2009; Zabora, Brintzenhofe-Szoc, Curbow, Hooker, & Piantadosi, 2001) compared with approximately one in six people in the general population (House of Commons Library, 2018).

Evidence suggests that prevalence of distress may differ depending upon the cancer diagnosis. Systematic literature reviews investigating distress within different cancer populations report prevalence rates of 15-27% for prostate cancer (Watts et al., 2014), 13-27% for ovarian cancer (Watts, Prescott, Mason, McLeod, Lewith, 2015), 9-66% for breast cancer (Maass, Roorda, Berendsen, Verhaak, & de Bock, 2015), and 1-57% for colorectal cancer (Peng, Huang, & Kao, 2019). Several studies comparing rates of distress between cancer populations have found patients with lung cancer to experience greater levels of distress relative to those with other cancers (Carlson et al., 2004; Linden et al., 2012; Zabora et al., 2001). Reasons for this include self-blame, poorer prognosis, later detection, and respiratory symptoms (Akin, Can, Aydiner, Ozdilli, & Durna, 2010; Cataldo & Brodsky, 2013). Gynaecological, haematological, and brain cancers have also been found to lead to greater levels of anxiety when compared with other cancers (Linden et al., 2012). Additionally, cancer of unknown primary is associated with high levels of distress as increased uncertainty in the condition has been shown to amplify difficulties encountered across other cancers (Richardson et al., 2015).

A range of different factors have been associated with cancer-related distress. Disease characteristics, including longer duration of disease presence (Mitchell, Ferguson, Gill, Paul, & Symonds, 2013) and more advanced stage of illness (Couper et al., 2010) may increase distress. Cancer recurrence has also been shown to elicit greater distress than initial diagnosis (Munkres, Oberst, Hughes, 1992). Demographic variables including female gender, lower



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socio-economic status, younger age, and being single have been demonstrated to increase the likelihood of experiencing anxiety or depression in cancer patients (Linden et al., 2012; Montel, Clark, & Loscalzo, 2018; Smith et al., 2018; Watson, Davolls, Mohammed, & Shepherd, 2015). Being younger at the time of diagnosis has also been associated with higher levels of distress (Watson et al., 2015). Possible reasons for this difference may include the greater effects of cancer and treatment side-effects for young people on fertility, social roles, future expectations, and financial stability (Mor, Allen & Malin, 1994; Rosen, Rodriguez-Wallberg, & Rosenzweig, 2009). Treatment factors found to elevate distress include surgical or invasive treatments (Lim, Devi, & Ang, 2011), receiving multiple treatments (Admiraal, Reyners, & Hoekstra-Weebers, 2013), and perceived passive role in treatment decision making (Hack et al., 2010). Frequency of physical symptoms has also been found to be positively correlated with distress (Delgado-Guay, Parsons, Li, Palmer, & Bruera, 2009).

Other predictors of increased distress include personality traits and styles of thinking and coping. Arras et al. (2002) reported individuals employing avoidant coping experience greater anxiety and depression, however, a ‘blunting’ approach to coping, involving avoidance of disease-salient information, may also serve a protective function against distress (Miller 1995). Those described as possessing more ‘neurotic’ personality traits have also been found to experience greater levels of distress (Paika et al., 2010), as well as those of less optimistic disposition (Gustavsson-Lilius, Julkunen, Keskivaara, Lipsanen, & Hietanen, 2012).

### **Uncertainty**

Uncertainty amongst those with acute or chronic illness has been defined as “the inability to determine the meaning of illness-related events” (Mishel, 1988, p. 225). Lazarus and Folkman’s (1984) theoretical model of the relationship between stress, appraisal, and coping posits that uncertainty impacts on appraisal, with high uncertainty theoretically

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causing greater stress and reducing coping capacity. Based on this, Mishel (1988; 1990) developed the theory of uncertainty in illness which postulates that uncertainty occurs in response to illness factors which are ambiguous, vague, unpredictable, unfamiliar, inconsistent, or unknown (McCormick, 2002; Mishel, 1984). The theory provides a four-part framework for understanding the experience of uncertainty. Firstly, interpretation of illness-related experiences (the stimuli frame) is moderated by information and support received (structure providers) and ability make sense of available information (cognitive capacities). These factors are described as antecedents, based on which uncertainty is perceived. Secondly, uncertainty is appraised via a process of either inference or illusion. Inference refers to the process of comparing present experiences to related situations (for example, recalling one's grandmother to have died as a result of cancer), while illusion denotes the construction of usually positive beliefs whereby the absence of information is interpreted as the potential for a positive outcome. This appraisal process leads to the interpretation of uncertainty as either dangerous or a positive opportunity. Thirdly, based upon the nature of this appraisal, different coping strategies are mobilised. Where uncertainty is interpreted as a 'danger', individuals seek to reduce uncertainty (e.g. through seeking information) or use affect regulation strategies to manage the distress which is associated by the uncertainty. Where uncertainty is framed as an opportunity, 'buffering strategies' such as avoidance or minimisation of threatening stimuli are employed to sustain the favoured uncertain state. Finally, where these coping strategies are effective, they facilitate adjustment to the initial illness-related experiences (Mishel, 1988, 1990; Zhang, 2017).

### **Uncertainty and Distress in Cancer**

A literature review by Shaha, Cox, Talman, and Kelly (2008) identified uncertainty as a prevailing experience affecting cancer patients. Sources of uncertainty identified were lack of information, the course of the disease and treatment choices, and everyday life and coping

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with the disease. Given the prevalence of uncertainty across cancer populations, the uncertainty in illness model has been widely applied and tested by studies involving patients with cancer (Zhang, 2017). While distress is not a distinct component of the model, the relationship between uncertainty and distress (generated via the appraisal of danger or threat) is inferred (Mishel, Padilla, Grant, & Sorenson, 1991). A 2017 scoping review by Jabloo et al. investigated antecedents and outcomes associated with uncertainty amongst older adults ( $\geq 65$  years) with cancer. Results showed that uncertainty was positively correlated at a statistically significant level with psychological distress (measured as anxiety and depression) in two studies (Galvin & Watkins, 2012; Lien et al., 2009).

### **Review Rationale and Objectives**

As summarised above, the prevalence of distress and uncertainty are elevated amongst people living with cancer. A scoping review investigating the relationship between these factors reported that amongst older adults with cancer, uncertainty and distress are related at the level of statistical significance (Jabloo et al., 2017). This evidence may suggest that, in accordance with Mishel's uncertainty in illness model, uncertainty is perceived as a potential danger which may lead to distress. No existing review of the literature has assessed how the relationship between uncertainty and distress manifests in younger adults who are prone to greater levels of distress than older cancer patients (Cancer research UK, n.d.; Watson et al., 2015). Therefore, the aim of this review was to collate and appraise the existing quantitative evidence regarding the relationship between distress and uncertainty amongst younger adults with cancer. Reviewing the research in this way can provide a better understanding of the existing data and the scope for subsequent meta-analysis. Qualitative data was not included as the remit of the review was to examine the relationship between uncertainty and psychological distress in as tightly controlled and defined a way as possible. This was

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intended to facilitate consistency with the theoretical and conceptual definitions outlined in the introduction, rather than including subjective experiences and interpretations.

### **Method**

This review follows Preferred Reporting Items for Systematic Reviews and Meta Analyses (PRISMA) statement guidelines where applicable (Moher, Liberati, Tetzlaff, Altman, & The PRISMA Group, 2009) to maximise transparency of reporting. Adherence to reporting guidelines is recommended when conducting systematic reviews as inadequate reporting can prevent accurate interpretation of findings and the corresponding weight carried by the conclusions of the review (Fleming, Koletsi, & Pandis, 2014). Use of PRISMA guidelines have been recommended for the reporting of systematic reviews in clinical and health psychology (Perestelo-Pérez, 2013).

### **Objective**

The PICO (Population, Intervention, Comparison, Outcome[s]) Framework (Richardson, Wilson, Nishikawa, & Hayward, 1995) was employed to frame the review question. This approach is recommended to formulate a specific research question according to systematic criteria which determine the scope of the review (Higgins & Green, 2011; Perestelo-Pérez, 2013). Use of the PICO framework can also optimise the balance between sensitivity and specificity of search results retrieved via electronic database searching (Perestelo-Pérez, 2013; Schardt, Adams, Owens, Keitz, Fontelo, 2007). PICO items are outlined in Table 1-A (p.1-48).

TABLE 1-A HERE

### **Search Strategy**

Searches of relevant electronic databases (PsycINFO, MEDLINE, the Cumulative Index to Nursing and Allied Health Literature [CINAHL], and Web of Science) were conducted on 20<sup>th</sup> January 2019. Prior to this, guidance was sought from a specialist librarian

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regarding the search strategy to optimise retrieval of relevant search results. In each data base the following free text terms, and Boolean operators were searched in study titles and abstracts: (“cancer” OR “neoplasm\*” OR “onco\*” OR “tumour” OR “malign\*”) AND (“uncertainty”) AND (“distress” OR “anx\*” OR “worr\*” OR “depress\*” OR “mood” OR “affect\*” OR “wellbeing” OR “well-being” OR “well being” OR “emotion\*” OR “mental health”). Searches were also trialled with additional cancer type-specific terminology (e.g. carcinoma, melanoma), however, the number of results retrieved was not significantly greater, and as such, on the advice of the specialist librarian, these terms were omitted. The number of results retrieved by these trials are presented in Appendix 1-A (p.1-59). The decision was taken to exclude ‘trauma’ from the searches, as although post-traumatic stress responses to cancer and cancer treatment are widely recognised, diagnosable post-traumatic stress disorder has been shown to impact a relatively small number of patients (approximately 4%). It is acknowledged, however, that there may be overlap in the experiences of post-traumatic stress and broader distress (Palmer, Kagee, Coyne, & DeMichele, 2004). The truncation function (\*) was applied to a number of terms in order to capture relevant terms with variant endings or spellings. Related thesaurus terms for each database were also searched. Age limiters were applied in PsychINFO and CINAHL to exclude papers focusing on populations below the age of eighteen. Equivalent limiters were not available for Web of Science or MEDLINE. Additional filters were also employed on the advice of the specialist librarian where searches retrieved more than 2000 results from a single multi-disciplinary database. This decision was made due to the practical limitations inherent in screening a high volume of search results with potentially decreased relevancy. This applied only to searches in Web of Science where 2472 results were retrieved prior to additional limiters being applied. The ‘web of science categories’ used to refine the search are listed in the full search strategy which is detailed in Appendix 1-B (p.1-60). No date limits were applied to the

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search, allowing papers to be retrieved from any point within each database's temporal range. It was anticipated, however, that relevant papers would have been published from the 1980s onwards following the publication Mishel's uncertainty in illness theory.

Search results were imported using Mendelay referencing software and duplicate results were removed. Results were then screened against inclusion and exclusion criteria as described by Booth, Sutton, and Papaioannou (2016); the title and abstract of each paper was screened initially, followed by the full text. Additional hand searches of references from each eligible study and from key literature reviews (Jabloo et al., 2017; Shaha et al., 2008) were also undertaken. These additional searches are recommended to decrease the probability of relevant studies being omitted from the review (Greenhalgh & Peacock, 2005). A flow diagram of the screening and selection process is presented in Figure 1-A (p.1-58).

FIGURE 1-A HERE

### **Inclusion Criteria**

Studies meeting the following criteria were eligible for inclusion in the review: (1) published in the English language (2) quantitative methodology (3) published in a peer reviewed journal (4) sample population of working age adults (with a mean age of 55 or below) (5) sample with confirmed diagnosis of any cancer, including individuals pre-, during, and post-treatment (6) measure(s) of distress and measure(s) of uncertainty (7) and analysis of the association between distress and uncertainty.

Quantitative observational studies of cross-sectional, correlational, prospective, and case-control design were eligible for inclusion. Intervention trials or studies of experimental design where either distress or uncertainty were manipulated were eligible for inclusion only if data were available for a control group meeting inclusion and exclusion criteria. Studies reporting on samples with multiple life-limiting conditions were eligible for inclusion only where results for the cancer sub-sample were reported separately.

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‘Psychological distress’ was conceptualised broadly, incorporating experience of anxiety and/or depression; measures looking at these individual constructs were eligible for inclusion as well as any measures looking at global distress. This decision was made based on the interchangeable use of these concepts across the relevant literature, and tendency for constructs of anxiety, and depression to overlap and be interpreted generically as distress (Linden et al., 2012; Osman et al., 2012). Previous research has shown that anxiety, depression, and distress are inter-related constructs which are strongly correlated in people with cancer (Pandey et al., 2007). The concept of ‘stress’ was also included as it is understood to be a distress-related construct, with a tendency to co-occur with anxiety and depression, that is widely applied within related literature on coping (Osman et al., 2012). For the sake of this review, ‘stress’ was conceptualised in line with Lazarus and Folkman’s (1984) definition of psychological stress, as opposed to physiological stress responses (Lazarus, 1974). Any quantitative measure of distress and uncertainty was deemed acceptable (e.g. standardised measures, unvalidated Likert scales), as were results of sub-scales forming part of a larger related measure (e.g. quality of life or adjustment) where results for distress or uncertainty were reported and analysed discretely. The decision was made to include studies using the Profile of Mood States (POMS) or short form (POMS-SF) to assess distress as, although described as a measure of transient mood states (McNair, Lorr, & Droppleman, 1989), it has been frequently employed for research purposes as a proxy for distress (Curran, Andrykowski, & Studts, 1995). Measures assessing symptom distress were not included as, although a related concept, the physical symptoms of distress are conceptualised differently to the psychological (Wu et al., 2015).

In the UK, ‘older’ adults are generally conceptualised as people aged 65 and above based on this being the previously recognised state pension age (Banks & Smith, 2006). Although this has now legally altered, this age cut-off continues to represent a significant

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socially recognised transition from mid-life to old age (“Retirement Age”, 2013). While it is acknowledged that this definition is relatively arbitrary, Eurocentric, and not necessarily reflective of the perceptions individuals aged 65 years and older hold about themselves (Westerhof, 2009; World Health Organisation, 2002), for pragmatic purposes it has been used to differentiate ‘older’ and ‘younger’ cancer patients. This also acknowledges that cancer is increasingly likely to affect people from the age of 65 onwards (Cancer Research UK, n.d.). Due to this, the likelihood of mean sample age being skewed towards the upper end of this spectrum was recognised. Accordingly, studies where the mean age of sample participants exceeded 55 years were excluded in order to differentiate the sample from the population reviewed previously by Jabloo et al. (2017), where studies with a mean sample age of 65 and above were included.

### **Exclusion Criteria**

Studies were excluded where they (1) included individuals aged 17 or younger (2) did not report a mean sample age (3) used a qualitative methodology (4) were of single case or case study design (5) contained a sample of over 50% long-term cancer survivors (6) focused exclusively on young adults diagnosed with cancer in childhood or adolescence.

Studies of single-case design and case studies were excluded based on inherent limitations in generalisability (Thomas, 2011) and an absence of group mean data that was of interest in this review. Studies focusing on young adults who had been diagnosed with cancer in childhood and adolescence were excluded based on evidence that their needs and experiences are quite distinct from those of individuals diagnosed with cancer in adulthood (Hudson et al., 2003). For the sake of this study, long-term survivorship was defined as being in remission/cancer free five years post-cancer treatment. This was based on the 5-year point being a significant, widely used clinical marker for survival rates, beyond the period when cancer is most likely to recur (National Cancer Institute, 2019). Again, the needs and



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experiences of this group may be quite different to those of individuals with more recent experiences of diagnosis and treatment (Chambers et al., 2012; Dunn et al., 2012; Helgeson & Tomich, 2005).

### **Data Extraction and Assessment**

Data from studies was compiled using a template based on Booth et al.'s (2016, p.176) data extraction form which is presented in Appendix 1-C (p.1-63). Assessments of reporting quality and methodological quality were undertaken by the author. A second independent reviewer assessed risk of bias in 20% of the studies (n=4), with any discrepancies being discussed to reach consensus, in order to minimise individual reviewer bias, as recommended in the Cochrane Handbook (Boutron et al., 2011). The ratings of the second reviewer are presented in Appendix 1-D (p.1-64) along with a description of discrepancies and resolutions. Due to the range of different statistical analyses employed across studies, it was not possible or within the scope of this review to conduct a meta-analysis of all the findings. However, a meta-analysis was carried out to combine the effects of correlations between uncertainty and distress. The meta-analysis and results are reported in Appendix 1-E (p.1-68).

### **Risk of bias assessment.**

The AXIS quality appraisal tool was used to assess the risk of bias in the included studies (Downes, Brennan, Williams, & Dean, 2016). This tool was selected as it was designed for assessment of cross-sectional studies which were predicted to be the predominant design of included correlational studies. A particular strength of the tool is its inclusion of items to appraise both methodological and reporting quality. A copy of the tool and guidance can be found in Appendix 1-F (p.1-71). The tool uses 'yes', 'no', and 'don't know' ratings. For the purpose of this review, an additional rating of 'partial' was used where criteria were met to some degree, as used in similar assessment tools (Williams, Plassman,

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Burke, Holsinger, & Benjamin, 2010). A rating of ‘not applicable’ was also used where items were irrelevant to the study design. An alternative quality assessment tool developed by the Agency for Health Research and Quality (AHRQ, Plassman, Williams, Burke, Holsinger, & Benjamin, 2010) was also considered. This tool is designed for use with observational studies; however, a number of the criteria were not found to apply for any of the included studies, therefore it was felt that the AXIS was a more appropriate choice. Two items, however, were adopted from the AHRQ tool to supplement the AXIS for assessment of controlled or longitudinal studies.

### Results

A total of 18 studies were eligible for inclusion in the review. Of these, three studies were identified through reference list hand searches<sup>3, 10, 11</sup>. An overview of study characteristics, methods, and results is presented in Table 1-B (p.1-49). Additional study information is outlined in Appendix 1-G (p.1-72). Superscript numerical references throughout the results section correspond to the study number in Tables 1-B and 1-G. Where multiple studies were published by the same author(s) within 5 years, the authors were contacted to clarify whether the same data had been used (if not explicit in the text). Studies where it was confirmed that the same sample had been used have been treated as a single study where data were the same, with results from each paper reported successively in Table 1-B. This applied to two studies, one of which was reported on by two papers<sup>14, 15</sup> and one of which was reported on in three papers<sup>1, 2, 3</sup>. The number of distinct studies included in the review is therefore 15.

TABLE 1-B HERE

## Study Characteristics

### Design.

All included studies were descriptive in nature with 11 employing a cross-sectional design<sup>1,4,5,6,7,11,12,13,14,16,17</sup> and the remaining four using a longitudinal approach<sup>8,9,10,18</sup>. The primary aim of three studies was the psychometric assessment and validation of a measure<sup>2,9,16</sup>.

### Context and sample.

The majority of the included studies took place in either the USA (n=8)<sup>1,6,8,10,11,12,13,16</sup> or Canada (n=3)<sup>7,17,18</sup>, with the remaining studies conducted in Southeast Asia (n=3)<sup>5,9,14</sup> and Spain (n=1)<sup>4</sup>. All studies employed convenience sampling with participants recruited from clinical settings. One study also recruited via newspaper and radio advertising and snowball sampling<sup>7</sup>.

A total of 2158 cancer patients took part in the included studies along with 116 comparison or control participants from two studies<sup>13,17</sup>. Participants were aged between 19 and 89 years, with reported mean age of the samples ranging from 44 to 55 years. Many of the studies focused exclusively on female cancer patients (n=12), while the remaining studies reported 30-47% of their sample to be female<sup>1,5,17</sup>. Between 42 and 100% of participants were reported to be married or to have a partner. Where reported, the ethnicity of participants from North America was predominantly White Caucasian (64-97%), whilst studies carried out in Southeast Asia reported principally on samples of Thai, Chinese, and Malay patients. The level of education received by participants was variable across studies. Where reported as means, the number of years of education ranged from 8-16 years. Where reported, the proportion of participants having received tertiary level education was 28-100% for North American studies, 10-36% from studies in Hong Kong and Malaysia, and 7% for the study

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conducted in Spain. The percentage of participants reported to be in current employment ranged from 39% to 77%.

The cancer diagnoses of study participants included breast cancer (n=9)<sup>4,6,7,8,9,13,14,17,18</sup>, gynaecological cancer (n=2)<sup>10,11</sup>, brain tumour (n=1)<sup>1</sup>, head or neck cancer (n=1)<sup>5</sup>, haematological cancer (n=1)<sup>16</sup>, and colorectal cancer (n=1)<sup>6</sup>. Samples in all studies contained patients diagnosed with different stages of cancer: across studies 22-75% of patients were described as having stage I or stage II cancer whilst 8-77% had a stage III or IV diagnosis. Three studies reported some participants as having stage 0 breast cancer (7-24%)<sup>7,8,9</sup> where the abnormal cancer cells are classified as non-invasive (American Cancer Society, 2017). Where reported, all or most participants were experiencing a first diagnosis of cancer; one study included only patients experiencing their first cancer recurrence<sup>13</sup>. Participants were recruited from across the trajectory from pre- to post-treatment and treatments received by patients included surgery (including stem cell transplantation and cosmetic reconstruction), radiotherapy, chemotherapy, neoadjuvant therapy (including hormonal therapy), and experimental drugs.

### Measures

A selection of different self-report measures was used across studies to assess distress. Measures employed were the Hospital Anxiety and Depression Scale (n=3, HADS, Zigmond & Snaith, 1983), the POMS or POMS-SF (n=2, McNair, Lorr, & Droppleman, 1989), the State-Trait Anxiety Inventory (n=2, STAI, Spielberger, Sydeman, Owen, & Marsh, 1999), the 'psychological distress' subscale of the Psychosocial Adjustment to Illness Scale (n=2, PAIS, Shahid, Wilkinson, Marcu, & Shapiro, 2011), the Center for Epidemiological Studies-Depression (n=2, CES-D, Radloff, 1977), the Cancer Worry Scale (n=1, CWS, Custers et al., 2014), the Short Health Anxiety Inventory (n=1, SHAI, Salkovskis, Rimes, Warwick, & Clark, 2002), the Brief Symptom Inventory (n=1, BSI, Derogatis & Melisaratos, 1983), and

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the Beck Depression Inventory (n=1, BDI, Beck, Ward, Mendelson, Mock, & Erbaugh, 1961).

A smaller number of self-report measures was used to measure uncertainty. The majority of studies used the Mishel Uncertainty in Illness Scale (n=6, MUIS, Mishel & Epstein, 1990) or a modified condition- or context-specific version (n=3). These adaptations were the community form (MUIS-C, Mishel, 1999) and brain tumour form (MUIS-BT, Lin et al., 2012). Measures used in the remaining studies were the Intolerance of Uncertainty Scale (n= 2, IUS, Buhr & Dugas, 2002) or IUS short form (n=1, IUS-12, Carleton, Norton, & Asmundson, 2007), a single item about uncertainty from the Quality of Life Scale-Patient Version (n=1, QOL-PV, Padilla et al., 1983), the Uncertainty domain of the Decisional Conflict Scale, question format (n=1, DCS, O'Connor, 1993), and the Uncertainty sub-scale of the Cancer and Treatment Distress (CTDX) measure (n=1, Syrjala, Yi, & Langer, 2016).

### **Risk of Bias Assessment**

A full assessment of the risk of bias for each study is presented in Appendix 1-H (p. 1-77). All studies met AXIS criteria for reduced risk of bias in a number of areas including: presenting clear aims and objectives and selecting appropriate designs; offering a clear description of the target population; and assessing appropriate variables for study aims. Most studies also provided an adequate report of basic data in the results; only two studies were assessed as 'partial' on this item due to the description of sample characteristics lacking detail<sup>5,6</sup>. Reporting standards were met by most studies on items regarding internal consistency, with only three out of the eighteen studies having identified discrepancies in the reported figures<sup>1,2,7</sup>. The majority of studies also received a rating of 'yes' in relation to reporting of all analyses; where this was not the case the analyses had not been reported adequately in the methods sections in order to establish what should be reported in the results<sup>10,11,14,18</sup>.

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Mixed outcomes were found across studies in relation to a number of items. While ten studies reported on the use of reliable, previously published measures<sup>1,3,4,6,7,12,13,14,15,18</sup> the remaining studies received a rating of ‘partial’ for this item where variable measures had been newly developed or where variables were measured using unvalidated single-item questions<sup>2,5,8,9,10,11,16,17</sup>. For the most part, authors’ discussions and conclusions were comprehensive and justified by the results, although a minority of studies (n=4)<sup>1,6,10,12</sup> failed to offer a full overview of findings or consider confounding variables. A number of studies also failed to adequately acknowledge study limitations<sup>3,6,9,10,11,12,13</sup>. Only one study explicitly identified a potential conflict of interest (COI)<sup>1</sup> while twelve studies provided some information confirming there to be no conflictual funding sources or other COIs<sup>2,3,6,8,9,11,12,13,14,15,16,17</sup>. In the remaining studies no information was provided. Eight studies provided explicit information regarding processes for gaining ethical approval and informed consent<sup>4,5,6,8,9,14,15,16</sup>. A further five studies provided information regarding one of these processes<sup>3,7,11,17,18</sup>, while the remaining five studies did not report on either<sup>1,2,10,12,13</sup>.

There were several areas where risk of bias was found to affect most or all of the included studies. Firstly, risks of sampling bias were identified. The majority of the studies reported on a convenience sample recruited from a single site or otherwise narrow pool of potential participants<sup>1,2,3,4,5,6,7,9,10,11,12,14,15,17,18</sup>, such as hospitals from one metropolitan area. Exclusion criteria in ten studies<sup>1,2,3,4,6,8,15,16,17,18</sup> (such as geographical area, treatment type, functional ability, and previous psychiatric treatment) were also identified as reducing the overall representativeness of the sample. Secondly, reporting and methodological biases were identified in relation to study non-responders. Ten studies omitted any description from the methods of how participant non-response would be managed<sup>1,2,3,4,5,6,7,12,15,17</sup>. Eight studies did not state the rate of non-response<sup>1,3,5,7,10,12,15,17</sup> while three studies reported response rates of less than 80%<sup>8,3,16</sup>. Of those reporting on participant non-response, only two provided partial

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information on reasons for non-response<sup>8,10</sup>; no demographic data regarding non-responders were available. Thirdly, risks of bias in relation to study results and interpretation were identified. This included most studies providing no<sup>15</sup> or partial<sup>2,4,7,9,10,11,12,13,17,18</sup> explanation regarding determination of statistical significance or other effects. Additionally, only two studies provided a justification of sample size based on a power analysis<sup>6,14</sup>.

Ratings on the additional items from the AHRQ applied to only a small number of studies (n=4) incorporating either a control condition<sup>17</sup> or longitudinal design<sup>8,9,10</sup>. The one study employing a control condition was awarded a rating of ‘partial’ as samples were matched for age but had differences in other demographic variables including ethnicity, education, and marital status<sup>17</sup>. Of the longitudinal studies, one provided a clear rationale for follow-up duration<sup>9</sup>, reducing risk of bias, while the remaining two were rated as ‘partial’ where justification for follow-up was less robust<sup>8,10</sup>.

### Findings

#### **Relationship between uncertainty and distress.**

All of the included studies reported a statistically significant relationship between uncertainty or intolerance of uncertainty and distress. Correlation analysis was used in 10 studies to assess the strength of the relationship<sup>2,6,9,10,11,13,14,15,16,18</sup>. The findings from these studies demonstrated statistically significant positive correlations explaining between 16% and 62% of the variance between variables. Where distress was measured using an overall distress measure (POMS, PAIS, or BSI)<sup>2,6,10,11,13,16</sup>, 27-54% of the variance was found to be shared with uncertainty. When distress was measured using scales more specifically assessing anxiety or depression, shared variance with uncertainty was reported to be 16-42%<sup>9,14,18</sup> and 20-62%<sup>9,14,16,17</sup> respectively. Intolerance of uncertainty was demonstrated to share 64% variance with depression in one study<sup>17</sup> and 50% variance with health anxiety in another<sup>7</sup>. Two studies found only the ambiguity sub-scale of the MUIS to be statistically significantly

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associated with distress<sup>10,11</sup>. When interpreted in accordance with Cohen's (1988) guidance, the magnitudes of the reported correlation effect sizes were small in five studies<sup>9,11,14,15</sup>, medium in four studies<sup>10,13,15,18</sup>, and large in three studies<sup>7,16,17</sup>. It is acknowledged that, as per Cohen's guidance, these effect sizes can only offer a rough rule-of-thumb and must be interpreted with caution. All studies where a large effect size was found focused on pre-treatment samples, although other studies reporting smaller effects also involved patients at this point in their cancer journey.

A number of studies conducted further analyses to investigate the nature of the association between uncertainty and distress, including analyses testing a number of theoretical models aiming to explain the psychological experiences of cancer patients. Most of these analyses suggested uncertainty to be a statistically significant predictor of distress, including both depression and anxiety<sup>3,8,10,14,15</sup>. One study demonstrated that intolerance of uncertainty was also a significant predictor for depression<sup>4</sup>. A further study, however, provided evidence that increased distress was predictive of greater levels of uncertainty<sup>1</sup>. Non-significant effects were reported for the impact of intolerance of uncertainty on health anxiety<sup>7</sup> and uncertainty on depression in two of the studies<sup>9,17</sup>.

**Mediation effects.**

Several studies incorporated mediation analyses investigating the relationship of other related variables, particularly coping strategies, to both distress and uncertainty. Mishel et al.'s (1991)<sup>12</sup> regression analysis demonstrated the relationship between uncertainty and distress to be mediated by mastery, danger appraisal, and the emotion-focused coping strategy of wishful thinking. Emotion-focused coping was also found to be a mediating variable between intolerance of uncertainty and depression by Taha, Matheson, & Anisman (2012)<sup>17</sup>. Coping strategies more broadly were found to mediate the relationship between uncertainty and distress, assessed as mood state, by Sharif, Ahadzadeh, & Perdamen (2017)<sup>14</sup>.



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This study also demonstrated distress to mediate the relationship of uncertainty and coping strategies with quality of life. Findings from Cahill et al. (2014)<sup>1</sup> and Lin et al. (2013)<sup>3</sup> showed distress mediated the effect of uncertainty on symptom severity, while Detprapon et al. (2009)<sup>5</sup> and Mishel and Braden (1987)<sup>10</sup> found uncertainty to mediate the effect of symptom experience and physical function on distress.

Analyses of the mediating relationships of other variables were not statistically significant. These included the impact of uncertainty in the relationship between locus of control and anxiety and depression, and of daily hassle intensity in the relationship between intolerance of uncertainty and depression.

### **Effects of time.**

Three studies employed a longitudinal design to assess the relationship between distress and uncertainty at two time points across the cancer treatment trajectory<sup>8,10,18</sup>. Increases in the association between variables over time were seen in two studies. Results reported by Mishel and Braden (1987)<sup>10</sup> showed that during the diagnostic period for women with gynaecological cancer there was no statistically significant relationship between the two uncertainty and distress, rather distress was shown to be predicted by lower levels of social affirmation. However, when followed up during treatment, a statistically significant relationship between distress and uncertainty was observed. Similarly, Wong and Bramwell (1992)<sup>18</sup> reported a non-significant relationship between distress and uncertainty in women with breast cancer when assessed prior to hospital discharge following mastectomy when re-assessed post-discharge was found to reach the level of statistical significance. Conversely, Lam et al. (2012)<sup>8</sup> reported a decrease in the strength of the relationship between distress and uncertainty over time. When assessed in their sample of breast cancer patients, the relationship was found to be statistically significant prior to surgery but to have weakened to a level of non-significance one-month post-surgery.

### **Discussion**

The primary aim of this systematic literature review was to synthesise the current evidence pertaining to the relationship between uncertainty and distress for younger adults with cancer. Overall, the findings of the included studies suggest that the relationship between uncertainty and distress is noteworthy, as demonstrated by the small to large correlational effect sizes reported. In several studies, uncertainty and intolerance of uncertainty were shown to be predictive, offering support to Mishel's uncertainty in illness theory and the inferred impact of uncertainty upon distress via increased danger appraisal. However, the limitations identified within the included studies and inherent within the review design mean that these findings must be interpreted with caution.

The consistently reported findings of a statistically significant positive correlation between uncertainty and distress are comparable with the results presented by Jabloo et al. (2017) in their review of uncertainty amongst older adults with cancer. As in Jabloo et al.'s review, the relationship was seen to be significant for patients with various cancer diagnoses and stages of progression, at different stages in the treatment trajectory, suggesting the experience of both uncertainty and distress to perhaps unsurprisingly characterise the entire cancer experience. Supporting this are a large number of qualitative studies exploring patients' lived experiences of cancer where the interlinked themes of distress and uncertainty repeatedly emerge (Bailey, Wallace, & Mishel, 2007; Drageset, Lindstrøm, Giske, & Underlid, 2011; Halldórsdóttir & Hamrin, 1996; Hansen et al., 2012; Thomas 2008).

Despite the majority of findings suggesting a significant relationship between variables, some variation in findings was reported, suggesting that the relationship between uncertainty and distress cannot be assumed to be static or ubiquitous. Findings from Wong and Bramwell (1992) demonstrated the relationship between uncertainty and distress was not significant for breast cancer patients having undergone surgery whilst they remained in

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hospital, but was statistically significant post discharge. Conversely, Lam et al. (2012) found that the strength of the relationship decreased over time, being statistically significant prior to breast cancer operation and falling to non-significant levels one-month post-operation. These findings may be demonstrative of the rapid changeability of psychological variables for individuals with cancer. Times when the relationship is weaker between distress and uncertainty may reflect the role of other factors such as physician communication (Zachariae et al., 2003), social support (Kornblith et al., 2001; Pinar, Okdem, Buyukgonenc, & Ayhan, 2012), or physical symptoms (Liao et al., 2011).

Of those studies using predictive modelling techniques, the majority suggested uncertainty or intolerance of uncertainty to predict distress. These findings can be considered consistent with Mishel's uncertainty in illness theory (1988), according to which, uncertainty is potentially appraised as dangerous which may lead to increased distress. The findings in several studies indicating the relationship between uncertainty and distress to be mediated by emotion-focused coping strategies also lends support to the model whereby affect-control strategies are employed in response to danger appraisals and postulated to facilitate more effective adaptation to illness.

A minority of analyses did not find uncertainty or intolerance of uncertainty to have a statistically significant predictive effect on distress (Kryanou et al., 2014; Northouse, Dorris, & Charron-Moore, 1995). A further study demonstrated conflicting findings, with results showing distress to be a significant predictor of uncertainty (Cahill et al., 2014). These findings suggest that the relationship between distress and uncertainty is complex and is not necessarily linear or monodirectional. The variability in the nature of the relationship presented in these findings may also give an indication that there are other factors and variables impacting upon distress and uncertainty which may not have been considered within the analyses. The findings also omitted any analysis in relation to non-distressing

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uncertainty, i.e. where uncertainty may be framed as opportunity (Mishel, 1988) which could partially explain outcomes where uncertainty and distress were not significantly related (McCormack et al, 2011).

### **Limitations of the Included Studies**

Although the results demonstrated a compelling case for the importance of the relationship between uncertainty and distress in younger cancer patients, the findings must be interpreted in light of the quality of the research. A number of limitations were identified across the included studies, potentially increasing the risk of bias. The descriptive methodological designs of the included studies are limited by a lack of control for potential confounding variables or inclusion of control subjects (with the exclusion of one study), meaning that results cannot be interpreted definitively.

The quality assessment of studies using the AXIS tool highlighted several methodological limitations. Risk of bias was incurred in most studies through the use of convenience sampling. Representativeness of the samples was also potentially affected by the relatively high proportion of white Caucasian, highly educated participants in the North American studies. A number of studies focused solely on female cancer patients; however, the mixed gender studies contained a greater proportion of male participants. This may impact upon the interpretation of results as previous research has demonstrated that female cancer patients tend to exhibit greater levels of distress (Keller & Henrick, 1999; Linden et al., 2012). While the focus of this review was on younger adults with cancer, the mean age of all studies was over 44, likely representing the increased likelihood of developing cancer with increased age (Cancer Research UK, n.d.), meaning that results may not necessarily be fully generalisable to young adults with cancer given the evinced inverse relationship between age and distress in cancer (Mosher & Danoff-Burg, 2006). Several studies excluded patients with greater levels of functional ability who are likely to be those with increased levels distress

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(Banks et al., 2010). Measures used across studies were generally appropriate, although a minority of studies employed unvalidated or single-item measurement tools. The potential for bias inherent within self-report measurement must also be considered (Van de Mortel, 2008).

Additional potential biases were identified in relation to quality of reporting and methodology. The omission of power analyses from all but two studies means that there is a possibility that analyses may have under- or over-estimated findings. The lack of information in all studies regarding non-responders also means it is impossible to know whose data has not been included in the study.

Another consideration is the inclusion within the review of two studies authored by Mishel and the potential for a vested interest in the publication of results providing evidence for her proposed uncertainty in illness theory.

### **Limitations of the Systematic Literature Review**

It is important to acknowledge the constraints inherent in the methodological approach of this systematic literature review and their impact upon the interpretation of findings. Firstly, while a great deal of attention was given to developing a comprehensive search strategy, it cannot be guaranteed that all relevant research has been retrieved. The process of hand-searching the reference lists of included studies and key reviews led to the retrieval of three studies meeting the inclusion criteria which were not found in the initial database searches. While the process of handsearching aims to increase the robustness of the search strategy, the number of additional relevant papers found during this process suggests that it is possible that further relevant papers have been missed. It is possible that additional trialling of search terms or searching of additional multi-disciplinary databases may have resulted in additional relevant findings. Secondly, while a second reviewer assessed the risk of bias in a sub-sample of papers, due to practical constraints it was not possible for all

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included papers to be reviewed independently in this manner as would be ideal to reduce the risk of bias.

A further limitation of this review relates to the conceptualisation of distress. While the review aimed to take a broad definition of distress, incorporating experiences of depression and anxiety, in order to maximise the incorporation of relevant findings, there is ongoing debate and conflictual findings regarding conceptualisation of these aspects of experience and whether they are overlapping or distinct but related experiences (Drapeau, Marchand, & Beaulieu-Prévost, 2011; Ridner, 2004).

As psychological distress was broadly defined within this review, a range of different measures was employed across studies to assess relevant and subsumed constructs including depression and anxiety. So too were various measures of uncertainty and intolerance of uncertainty used. This necessarily raises questions regarding the validity and sensitivity of the different measures used to assess the variables of interest, especially given the disparity amongst findings in different studies. It is possible that lack of convergence between measurement tools arising from the measurement of related but distinct phenomena (e.g. aspects of depression or anxiety) may have influenced individual study results. The presence of this kind of divergence between constructs assessed by measures purporting to evaluate the same psychological phenomena is a persistent challenge (Ro & Lawrence, 2007). This may be partially attributable to the variety of semantic, epistemological, and conceptual perspectives that exist in relation to psychological concepts, and the resulting inevitable presence of fallibility in psychological measurement (Hathcoat, 2013).

Whilst the aim of the review was to investigate the relationship between distress and uncertainty in cancer as a broad, super-ordinate phenomenon, it is acknowledged that the experience of cancer is very individual and impacted by a wide range of factors. Interpretation of results may be impacted by the inclusion within the review of studies

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relating to multiple types of cancer, cancers of all stages of progression, and patients at different temporal points in the treatment journey. Additionally, the definition of ‘younger’ cancer survivors included participants of a wide range of ages, and it is possible that the experiences associated with cancer may be very different for those at the polarities of this range.

### **Research Recommendations**

Although the majority of the included findings suggest that distress and uncertainty are related, and that uncertainty predicts distress, the shared variance for which findings are able to account is mixed, suggesting that there are possibly multiple other factors contributing to and interacting with the experience of distress for cancer patients. While some studies did consider other variables, including symptom distress and coping, research which generates a clearer understanding of the relationship between uncertainty, distress, and related factors would be beneficial. Therefore, controlled studies and methodological approaches allowing confounding variables to be controlled would be advantageous. Studies comparing the nature of the relationship between uncertainty and distress in different cancer populations at different points in the treatment journey would also be helpful to establish patterns in relationship intensity which could meaningfully inform when clinical interventions may be most useful. Studies investigating any differences in the relationship for patients with different stages of cancer would also be beneficial as in all studies patients with differing stages of cancer were grouped together.

Additionally, issues raised through quality appraisal should be considered as important steps in improving the methodological rigour of future research. As a priority, power analyses and non-response data should be reported to allow for more accurate interpretation of findings. More longitudinal data would also be advantageous to increase understanding of the relationship between uncertainty and distress over time.

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### **Clinical Implications**

The indication from a number of studies that uncertainty and intolerance of uncertainty are predictive of distress highlights the potential for interventions which enable management of uncertainty as a means of reducing distress. A number of studies have been published evaluating the outcomes from uncertainty management interventions demonstrating positive outcomes including enhanced coping skills and self-efficacy (Germino et al., 2013). While these interventions may be beneficial for cancer survivors faced with uncertainty following completion of treatment, they have less utility for patients at diagnosis and undergoing treatment due to the necessary prioritisation of medical treatments and time constraints which may get in the way of formalised interventions at this time. Therefore, opportunities to reduce uncertainty and enhance tolerance of uncertainty and adaptive coping during routine medical contact may be more effective and pragmatic for individuals newly diagnosed and undergoing treatment. As findings from this review demonstrated a strong relationship between uncertainty and distress pre-treatment, this may be an important time at which support with tolerating and reducing uncertainty may have a substantial impact on reducing associated distress. Therefore, although communicating uncertainty may be an essential aspect of medical practitioners' duties, it is possible that the way in which this is communicated can serve to alleviate uncertainty associated-distress (Kruijver, Kerkstra, Bensing, & van de Wiel, 2000). Identified aspects of effective nurse to patient communication may support this, including empathy and ongoing training in communication skills. Additionally, interventive communication could be facilitated through use of the patient-centred communication model which highlights the management of uncertainty (including attention to coping strategies) as a key function of the communication (Epstein & Street, 2007; McCormack et al., 2011). The findings from Mishel et al. (1984) and Mishel and Braden (1987) also highlight that ambiguity as a specific sub-component of uncertainty



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has a particularly strong relationship with distress which could be an important area for intervention. This is consistent with evidence that uncertainty can increase ambiguity aversion which leads to elevated cancer worry (Han et al., 2011). As ambiguity is defined as “unclear or ever-changing bodily cues about the state of the illness that may be confused with other illness concerns” (Mishel, 1997), it is possible that greater focus on education and information relating to interpretation of bodily cues could help to reduce ambiguity and associated distress.

### **Conclusion**

Findings from the 15 included studies provided evidence that uncertainty and distress are significantly associated for patients with different types and grades of cancer and at different points in the treatment journey. The majority of results also suggested that uncertainty is predictive of distress, supporting Mishel’s uncertainty in illness model which posits that uncertainty may be appraised as threatening and which may raise distress. Emotion-focused coping strategies were shown in several studies to mediate between uncertainty or intolerance of uncertainty and distress. The relationship between variables, however, is not necessarily static or ubiquitous and may vary over time and in relation to other factors which were not elucidated within the research. Results must be interpreted cautiously in light of the identified methodological weaknesses across studies, including an absence of power analyses and recurrent sampling biases. Future research should focus upon addressing these identified limitations and providing a clearer picture of the impact of associated variables and cancer stage. Findings highlight the potential for effective communication as an intervention to support tolerance and reduction of uncertainty, particularly areas of ambiguity, which may in turn reduce the experience of distress for younger cancer patients.

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## Tables and Figures

**Table 1-A: PICO Framework**

PICO Item	Criteria for this review
Population	Younger adults (aged $\leq 55$ )  Living with cancer (any kind of cancer; any stage of cancer (I-IV), including curative and palliative patients; pre-, during-, or up to 5 years post-treatment)
Intervention	Not applicable (although intervention studies reporting data for control groups meeting inclusion criteria will be eligible for inclusion)
Comparison	Not applicable (although groups where a comparison condition is employed may be eligible for inclusion)
Outcomes	Measure of uncertainty; measure of psychological distress

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**Table 1-B: Overview of Study Characteristics**

Study	Country	Sample Demographics				Cancer Status				Measures		Analysis: Key Outcomes	
		N	Age range (mean)	% female	Type %	Stage %	Occurrence %	Treatment status %	Treatment type %	Uncertainty	Distress		
1 Cahill et al. (2014)	USA	186	19-80 (44)	47	WC= 86 A/P= 6 B= 5 NA= 2	BT = 100	I= 2 II= 20 III= 32 IV = 45	1 <sup>st</sup> = 60 2 <sup>nd</sup> = 31 3 <sup>rd</sup> or more = 37 9	Pre= 17 On= 46 Post/ no = 37	S= 100 <sup>a</sup>	MUIS-BT	POMS-SF	Path analysis: Statistically significant ( $p<0.001$ ) effect found for mood on uncertainty (unstandardized/standardized coefficient = 5.35/0.54). Mood state found to mediate the relationship between uncertainty and symptoms.  More frequent use of personal health records found to decrease uncertainty.
2 Lin et al. (2012)													Correlation: significant positive correlation ( $p<0.01$ ) between uncertainty and mood state as measured by the five negative mood subscales of the POMS-SF. Uncertainty was negatively correlated ( $p<0.01$ ) with the vigour sub-scale.
3 Lin et al. (2013)													Structural equation modelling: Uncertainty had a significant ( $p<0.05$ ) direct impact on all negative mood states (tension, anger, depression, fatigue & confusion).  Uncertainty had a significant ( $p<0.05$ ) indirect impact (via mood state) on symptom severity for all mood states except confusion.

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4	Spain	31	30-78 (53)	100	n/a	BC = 100	I= 10 II= 26 III= 52 IV = 13	1 <sup>st</sup> = 97 2 <sup>nd</sup> or more = 3	Post= 100	S+R+ C= 13 S+C+ H= 13 S+R+ C+H = 29 S+R= 16 R+C +Br+ H= 3 S+R+ H= 20 S+H= 3 S+R+ C+Br +H= 3	IUS	HADS  CWS	Multivariate analysis: No significant association between intolerance of uncertainty and distress or cancer worry.  Post-hoc univariate ANOVA: Significant effect found for intolerance of uncertainty on HADS-Depression ( $F=6.86, p=0.02$ ) and cancer worry ( $F=7.15, p=0.02$ ). Association between intolerance of uncertainty and HADS-Anxiety was non-significant.
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Costa-  
Requena et  
al.  
(2011)

## UNCERTAINTY AND DISTRESS IN CANCER

5 Detprapon et al. (2009)	Thailand	240	19-89 (55)	30	TB= 100	HN = 100	I& II= 43 III & IV = 57	n/a	Post= 100	S+R= 43	MUIS- C'	CES-D	<p>Linear Structural Relationship analysis: Modified model demonstrated a statistically significant direct effect of uncertainty on depression (0.82, <math>p&lt;0.001</math>). Uncertainty was seen in the model to mediate the relationships between symptom experience, and depression and quality of life.</p> <p>Buddhist practices had a non-significant inverse relationship with uncertainty and depression.</p>
6 Ehrenberg- er et al. (2002)	USA	40	23-76 (55)	100	WC= 93 B= 8	BC =75 CR =13 O= 13	I& II = 75 III & IV = 23	n/a	Pre= 100	CT= 68	MUIS- C	POMS	<p>Spearman's rank order correlation: statistically significant relationship found between uncertainty and distress (<math>r_s=0.5</math>, <math>p=0.001</math>).</p> <p>No significance difference in variables between women opting in and out of clinical trial. Evidence provided (in part) for the King's framework and relationship of uncertainty with emotional wellbeing and impact on decision making.</p>
7 Jones et al. (2014)	Canada	137	27-80 (49)	100	WC= 97 O= 2	BC = 100	0= 7, I= 29, II= 35, III= 22, IV =6	n/a	n/a	S= 100 R= 64 C= 66 O= 58	IUS-12	SHAI	<p>Pearson's correlations: statistically significant relationship between health anxiety and intolerance of uncertainty (<math>r=0.50</math>, <math>p&lt;0.001</math>).</p> <p>Multiple regression: intolerance of uncertainty was not a significant unique predictor of health anxiety, however other unique predictors identified were younger age, more advanced cancer stage, increased body vigilance, and cognitive anxiety sensitivity.</p>

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8 Kyranou et al. (2014)	USA	396	(55-SD 11.6)	100	WC=64 O=36	BC=100	0=18, I=38, II=36, III & IV =8	n/a	Pre to post=100	S=100 N=20 R=56 C=33	QOL-PV (uncertainty sub item)	STAI	<p>Hierarchical linear modelling: Uncertainty about the future was a significant predictor of pre-operative anxiety (coefficient= -.426, standard error.130, <math>p&lt;0.01</math>). Six months post-surgery this association was not significant.</p> <p>Pre-operative anxiety was also predicted by higher levels of depression, lower levels of life satisfaction, less sense of control, and difficulty coping. Higher anxiety across time following surgery was predicted by higher pre-operative anxiety, poorer physical health, lower sense of control, and increased feelings of isolation.</p>
9 Lam et al. (2012)	Hong Kong	471	29-86 (54)	100	Ch=100	BC=100	0=24, I=26, II=23, III & IV =10	1 <sup>st</sup> =100	Pre to post=100	S=100	DCS (uncertainty & effective decision sub-scale)	HADS	<p>Pearson's correlation: Pre surgery there was a significant positive relationship between uncertainty and anxiety (<math>r=0.16</math>, <math>p&lt;0.001</math>) and depression (<math>r=0.20</math>, <math>p&lt;0.001</math>). One month post-surgery both of these relationships were found to be non-significant.</p>
10 Mishel & Braden	USA	44	20-83 (53)	100	n/a	G=100	n/a	1 <sup>st</sup> =100	Pre to post=	S=28 O=	MUIS	PAIS- psychological	<p>Pearson's correlation: Significant positive correlation between psychological distress and ambiguity about illness (MUIS sub-</p>

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(1987)									100	22 S+O= 50		distress sub-scale	scale) during treatment ( $r=0.46, p<.001$ ). The relationship between psychological distress and other sub-scales of uncertainty were not reported to be significant.  Regression analysis: During treatment ambiguity about illness (MUIS sub-scale) significantly predicts psychological distress. Ambiguity about illness was found to mediate the relationship of social affirmation and control over physical function with psychological distress.
11 Mishel et al. (1984)	USA	54	20-89 (52)	100	n/a	G= 100	n/a	1 <sup>st</sup> = 100	Pre= 100	S= 52 R= 26 C= 13 O= 9	MUIS	PAIS- psycho- logical distress sub- scale	Pearson's correlation: Significant positive correlation between psychological distress and ambiguity about illness (MUIS sub-scale) ( $r=0.27, p<0.05$ ). Correlation between total MUIS score and psychological distress was non-significant ( $p>0.05$ ).  Hierarchical multiple regression: A strong relationship was found between uncertainty and pessimism; women with more uncertainty and pessimism had greater adjustment problems.
12 Mishel et al. (1991)	USA	100	20-81 (53)	100	n/a	G= 100	I= 46, II= 16, III= 26, IV =8	1 <sup>st</sup> = 100	In= 100	S= 91 R= 31 C= 25 O= 13	MUIS	POMS	Regression analysis: Testing of model found the relationship between uncertainty and psychological distress to be mediated by statistically significant ( $p<0.05$ ) relationships between mastery, danger appraisal, and wishful thinking (a sub-category of emotion-focused coping).  Mastery was found to mediate the



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13	USA	81	30-82	100	WC=	BC	n/a	2 <sup>nd</sup> =	In=	S=	MUIS	BSI	relationship between uncertainty and danger appraisal, accounting for 17% of the variance (2% variance explained by uncertainty). Danger appraisal was found to have a highly significant relationship with uncertainty ( $p<0.001$ ). The mediating effect of coping strategy of wishful thinking between danger appraisal and emotional distress was found to contribute 2% of the variance, while danger appraisal contributed 41% of the variance.
Northouse et al. (1995)		Plus 74 husbands	(54)		96	=		100	89	84			Pearson's correlation: Statistically significant relationship found between psychological distress and uncertainty ( $r=0.42, p<0.01$ ).
					B=	100			Post=				Multiple regression: Uncertainty found to have a non-significant contribution to regression equation of emotional distress. Symptom distress, personal support and hopelessness all significantly contributed to the model, (total variance $R_2=0.43$ ).
					4				11				Husbands' distress levels were found to significantly increase patients' distress, not vice versa.
14	Malaysia	118	(51	100	Ch=	BC	I=	n/a	n/a	S=	MUIS	HADS	Pearson's correlation: Significant relationship found between uncertainty and
Sharif	a		S.D.=		49	=	40,			100			

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(2017)	9.5)	M= 29 Ind= 10 O= 12	100 II= 42, III= 18	C/H/ R= 63	<p>anxiety (<math>r= 0.287, p&lt;0.01</math>) and uncertainty and depression (<math>r=0.321, p&lt;0.01</math>).</p> <p>Partial least squares-structural equation modelling: Direct effect found for uncertainty on anxiety (standardized path coefficient 0.24, <math>p&lt;0.05, t=2.490</math>) Direct effect found for uncertainty on depression (standardized path coefficient 0.25, <math>p&lt;0.05, t=2.548</math>).</p> <p>Analyses of the mediation effect of uncertainty between locus of control and psychological distress were not statistically significant (<math>p\leq 0.1</math>).</p> <p>Uncertainty did significantly mediate the effect of uncertainty on quality of life (standardized path coefficient=0.085, <math>R^2=24.18, p&lt;0.05</math>)</p>	
15 <i>Sharif et al.</i> (2017)	135	Ch= 52 M= 27 Ind= 9 O= 12	I= 39, II= 43, III= 19	In= 89	S= 100 C/H/ R= 64	<p>Pearson's correlation: Significant relationship found between uncertainty and anxiety (<math>r= 0.274, p&lt;0.01</math>) and uncertainty and depression (<math>r=0.319, p&lt;0.01</math>).</p> <p>Partial least squares-structural equation modelling: Direct effect found for uncertainty on depression and anxiety (standardized path coefficient 0.253, <math>p&lt;0.01, t=2.885</math>).</p> <p>BC patients experiencing greater uncertainty are more likely to use avoidant rather than emotional coping strategies which amplifies anxiety and depression and</p>

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													decreases quality of life.
16 Syrjala et al. (2016)	USA	176	(47 SD= 11.9)	41	WC= 93	Ha= 100	n/a	n/a	Pre= 100	HCT = 100	CTXD uncert- ainty sub- scale	CES-D POMS	Pearson's correlation: Statistically significant relationships found between uncertainty and mood state ( $r=0.54$ , $p<0.001$ ), and uncertainty and depression ( $r=0.62$ , $p<0.001$ ).
17 Taha et al. 2012	Canada	42 Plus 42 Co- ntrol	22-63 (44) 22-63 (43)	100	WC= 67 A= 14 L= 2 B= 2 O= 14	BC = 100	n/a	n/a	Post= 100	n/a	IUS	BDI	<p>Pearson's <math>r</math> correlation: Statistically significant relationships found between intolerance of uncertainty (IU) and depression (<math>r=.64</math>, <math>p&lt;0.01</math>).</p> <p>Hierarchical regression analysis: Daily hassle intensity mediates the relationship between IU and depressive symptoms for controls but not BC survivors. Emotion-focused coping mediated the relationship between IU and depressive symptoms for patients (<math>F(4, 37)=10.94</math>, <math>p&lt;0.001</math>, <math>R_2=.54</math>)</p> <p>Additional findings: Depression levels and experience of daily hassles for patients was similar to controls', patients had lower IU than controls. Women with greater IU were more likely to use emotion-focused coping and have depressive symptoms. IU and depressive symptoms decrease over time since treatment.</p>
18 Wong & Bramwell (1992)	Canada	25	33-76 (55)	100	n/a	BC = 100	n/a	n/a	Post= 100	S= 100	MUIS	STAI	Pearson's $r$ correlations: Pre-discharge following surgery the relationship between uncertainty and anxiety was not significant ( $r= 0.09$ , $p=0.34$ ). One to two weeks post-hospital discharge the relationship was found to be significant ( $r= 0.42$ , $p=0.02$ )

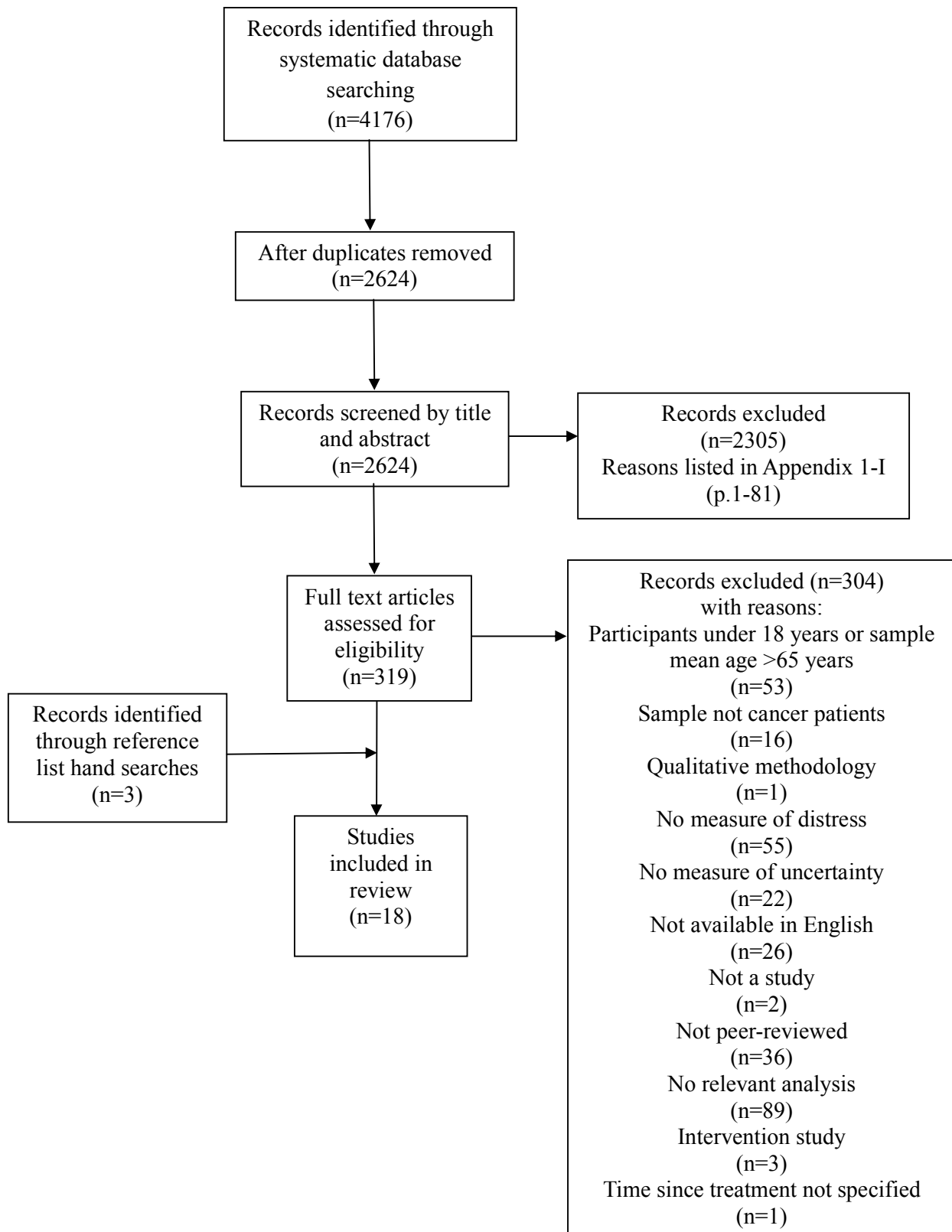
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T-tests (time 1- 1-2 days pre-discharge, time 2-1-2 weeks post-discharge): Time 1 to time 2- no significant change in anxiety or uncertainty.

*Note.* Abbreviations in alphabetical order: A- Asian; A/P- Asian/Pacific Islander; ANOVA- analysis of variance; B- Black; BC- breast cancer; BDI- Beck depression inventory; Br- brachytherapy; BSI- brief symptom inventory; BT- brain tumour; C- chemotherapy; CES-D- centre for epidemiological studies- depression scale; Ch- Chinese; CR- colorectal; CT- clinical trial; CTXD- cancer and treatment distress measure; CWS- cancer worry scale; DCS- decisional conflict scale; G- gynaecological; H- hormonal treatment; Ha- haematological; HADS- hospital anxiety and depression scale; HCT- hematopoietic cell transplantation; HN- head and neck; Ind- Indian; IUS- intolerance of uncertainty scale; IUS-12- intolerance of uncertainty scale- short form; L- Latin/South American; M- Malay; MUIS- BT- Mishel uncertainty in illness scale- brain tumour form; MUIS-C- Mishel uncertainty in illness scale- community form; N- neoadjuvant therapy; NA- Native American/Alaskan; O- other; PAIS- psychological adjustment to illness scale; POMS- profile of mood states; POMS-SF- profile of mood states- short form; QOL- PV- quality of life scale- patient version; R= radiotherapy; S- surgery; SD- standard deviation; SHAI- short health anxiety inventory; STAI- state-trait anxiety inventory; TB- Thai Buddhist.

Postscript(s): a- 28% biopsy, 34% partial resection, 38% gross total resection

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**Figure 1-A: Screening and Selection Process**

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## Appendices

## Appendix 1-A: Search Term Trial Results

Database	Search terms	Cancer terms	Uncertainty terms	Distress terms	Total combined with AND	Filters applied
Psychinfo	Final search strategy	78329	31171	1320771	667	440
	Strategy with additional cancer terms	79451	"	"	678	448
Medline	Final search strategy	3422994	87506	3360102	2073	n/a
	Strategy with additional cancer terms	3551583	"	"	2097	n/a
CINAHL	Final search strategy	572455	19329	682156	1012	n/a
	Strategy with additional cancer terms	590164	"	"	1029	n/a
Web of science	Final search strategy	3709786	444964	5364510	2555	661
	Strategy with additional cancer terms	4091136	"	"	2585	665

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## Appendix 1-B: Full Search Strategy

Database	Concept 1: Cancer	Concept 2: Uncertainty	Concept 3: Distress	Concept 4: Younger Adults
PsycINFO	<p><b>Thesaurus term (DE)</b> “Neoplasms”</p> <p>OR</p> <p><b>Free text in Abstract</b> cancer or neoplasm* or onco* or tumour or malign*</p> <p>OR</p> <p><b>Free text in Title</b> cancer or neoplasm* or onco* or tumour or malign*</p>	<p><b>Thesaurus term (DE)</b> “Uncertainty”</p> <p>OR</p> <p><b>Free text in Abstract</b> Uncertainty</p> <p>OR</p> <p><b>Free text in Title</b> Uncertainty</p>	<p><b>Thesaurus term (DE)</b> “Emotional states” or “stress” or “well being” or “mental health”</p> <p>OR</p> <p><b>Free text in Abstract</b> distress or anx* or worry* or depress* or mood or affect* or wellbeing or well-being or well being or emotion* or mental health or stress</p> <p>OR</p> <p><b>Free text in Title</b> distress or anx* or worry* or depress* or mood or affect* or wellbeing or well-being or well being or emotion* or mental health or stress</p>	<p><b>Limit</b> by applying Age limiter 'Adulthood (18 years and older)'</p> <p>(Manually screened by author)</p>
MEDLINE complete	<p><b>MeSH heading (MH)</b> “neoplasms”</p> <p>OR</p> <p><b>Free text in Abstract</b> cancer or neoplasm* or onco* or tumour or malign*</p> <p>OR</p> <p><b>Free text in Title</b></p>	<p><b>Mesh Heading (MH)</b> “Uncertainty”</p> <p>OR</p> <p><b>Free text in Abstract</b> Uncertainty</p> <p>OR</p> <p><b>Free text in Title</b></p>	<p><b>Mesh Heading (MH)</b> “Anxiety” or “anxiety disorders” or “depression” or “depressive disorder” or “affect” or “emotions” or “mental health” or “stress, psychological”</p> <p>OR</p> <p><b>Free text in Abstract</b> distress or anx* or worry* or depress* or mood or affect* or wellbeing or well-being or well being or emotion* or mental health or stress</p> <p>OR</p> <p><b>Free text in Title</b> distress or anx* or worry* or</p>	

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	cancer or neoplasm* or onco* or tumour or malign*		<b>Title</b> Uncertainty		depress* or mood or affect* or wellbeing or well-being or well being or emotion* or mental health or stress	
CINAHL	<b>MeSH Heading (MH)</b> "Neoplasms"  OR <b>Free text in Abstract</b> cancer or neoplasm* or onco* or tumour or malign*	AND	<b>Mesh Heading (MH)</b> "Uncertainty" or "mishel uncertainty in illness theory" or "mishel uncertainty in illness scale"	AND	<b>Mesh Heading (MH)</b> "symptom distress" or "anxiety" or "anxiety disorders" or "generalized anxiety disorder" or "depression" or "depression, reactive" or "psychological well-being" or "psychological aspects of illness" or "mental health"	Limit- all adult
	OR <b>Free text in Title</b> cancer or neoplasm* or onco* or tumour or malign*		OR <b>Free text in Abstract</b> Uncertainty		OR <b>Free text in Abstract</b> distress or anx* or worr* or depress* or mood or affect* or wellbeing or well-being or well being or emotion* or mental health or stress	
			OR <b>Free text in Title</b> Uncertainty		<b>Free text in Title</b> distress or anx* or worr* or depress* or mood or affect* or wellbeing or well-being or well being or emotion* or mental health or stress	
Web of Science <sup>1</sup>	<b>TOPIC:</b> cancer or neoplasm* or onco* or tumour or malign*	AND	<b>TITLE:</b> Uncertainty	AND	<b>TOPIC:</b> distress or anx* or worr* or depress* or mood or affect* or wellbeing or well-being or well being or emotion* or mental health or stress	(Manually screened by author)
	OR <b>TITLE:</b> cancer or neoplasm* or onco*		OR <b>TOPIC:</b> Uncertainty		OR <b>TITLE:</b> distress or anx* or worr* or depress* or mood	

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\_\_\_\_\_ or tumour or malign\* \_\_\_\_\_

\_\_\_\_\_ or affect\* or wellbeing or well-being or well  
being or emotion\* or mental health or stress \_\_\_\_\_

<sup>1</sup> Additional Web of Science Limiters Applied: psychology, psychology multidisciplinary, psychology clinical, social sciences interdisciplinary, psychiatry, psychology social, psychology developmental, social work, sociology, social sciences biomedical, nursing

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**Appendix 1-C: Data Extraction Form (Based on that of Booth et al. [2016])**

Reference	
Setting	
Sample (n)	
Sampling /Recruitment	
Sample Characteristics	
Study date/duration	
Methods of data collection	
Research tools/measures	
Intervention description	
Control	
Results	
Strengths	
Limitations	
Author Conclusions	
Comments	

## UNCERTAINTY AND DISTRESS IN CANCER

**Appendix 1-D: Second Reviewer Quality Appraisal Ratings**

Section	#	Question (yes/no/partial/don't know/not applicable [n/a])	Ehrenberg			
			er et al. 2002	Lin et al. 2012	Mishel et al. 1991	Syrjala et al. 2016
Introduction	1	Were the aims/objectives of the study clear?	yes	yes	yes	yes
Methods	2	Was the study design appropriate for the stated aim(s)?	yes	yes	yes	yes
	3	Was the sample size justified?	yes	partial	no	partial
	4	Was the target/reference population clearly described?	yes	yes	yes	yes
	5	Was the sample frame taken from an appropriate population base so that it closely represented the target/reference population under investigation?	partial	partial	partial	yes
	6	Was the selection process likely to select subjects/participants that were representative of the target/reference population under investigation?	partial	partial	yes	partial

## UNCERTAINTY AND DISTRESS IN CANCER

7	Were measures taken to address and categorise non-responders?	don't know	no	don't know	partial
8	Were the risk factor and outcome variables measured appropriate to the aims of the study? (validity)	yes	yes	yes	yes
9	Were the risk factor and outcome variables measured correctly using instruments that had been trialled, piloted, or published previously? (reliability)	yes	partial	yes	partial
10	Is it clear what was used to determine statistical significance and/or precision estimates? (e.g. p-values, confidence intervals)	yes	partial	partial	yes
11	Were the methods (including statistical methods) sufficiently described to enable them to be repeated?	yes	yes	yes	yes†

## UNCERTAINTY AND DISTRESS IN CANCER

Additional AHRQ	A	Selection minimizes baseline differences in prognostic factors? (For controlled studies only)	n/a	n/a	n/a	n/a	
		<p>Factors to consider:</p> <ul style="list-style-type: none"> <li>• Was selection of the comparison group appropriate? <ul style="list-style-type: none"> <li>o Consider whether these two sources are likely to differ on factors related to the outcome (besides cancer status).</li> </ul> </li> <li>• Did the study investigators do other things to ensure that exposed/unexposed groups were comparable, e.g., by using stratification, matching, or propensity scores?</li> </ul>					
		B	Adequate follow-up period (longitudinal studies only)?	n/a	n/a	n/a	n/a
		<p>Factors to consider:</p> <ul style="list-style-type: none"> <li>• A justification of the follow-up period length is preferable.</li> </ul>					
Results	12	Were the basic data adequately described?	partial	yes	yes	yes	
	13	Does the response rate raise concerns about non-response bias?	no	no	don't know	partial	

## UNCERTAINTY AND DISTRESS IN CANCER

	14	If appropriate, was information about non-responders described?	no	no	no	no
	15	Were the results internally consistent?	yes	no	yes	yes
	16	Were the results presented for all the analyses described in the methods?	yes	yes	yes	yes
Discussion	17	Were the authors' discussions and conclusions justified by the results?	partial	yes	partial	yes
	18	Were the limitations of the study discussed?	partial	yes	partial	yes
	19	Were there any funding sources or conflicts of interest that may affect the authors' interpretation of the results?	don't know	no	don't know	don't know
	20	Was ethical approval or consent of participants attained?	yes	don't know	don't know	yes

---

†- On reviewing Syrjala et al. (2016), discrepant ratings were given on item 11 by the first and second reviewer. A partial rating was given by the first reviewer and a yes rating was given by the second reviewer. Based on discussion and reappraisal of the paper, the reviewers agreed upon a rating of 'yes' for this criterion as adequate information was provided about the study methodology for the study to be replicated. This was the only discrepancy identified between the ratings of the independent reviewers.

**Appendix 1-E: Meta-Analysis**

A meta-analysis can be used to synthesise the findings of multiple studies to provide a weighted average of the combined study effect sizes (Borenstein, Hedges, Higgins, & Rothstein, 2009). While many criticisms of meta-analytic techniques have been made, asserting that an entire research field cannot be distilled meaningfully into one number (Bailar, 1997), the technique can provide a convenient way to summarise large amounts of data.

Due to the different statistical techniques used across the studies included in this review, a meta-analysis combining all of the findings was not possible. As such, a meta-analysis was conducted only upon findings of the correlational relationship between uncertainty and distress to establish the combined effect size of the reported correlation coefficients. Pearson's  $r$  was extracted from seven of the included studies. Where studies reported distinct correlations for both depression and uncertainty and anxiety and uncertainty, these effects were combined to form an overall effect for the relationship between psychological distress and uncertainty prior to inclusion of data in the meta-analysis. The study by Syrjala et al. (2016) reported on the relationship between an uncertainty measure and both the POMS and CES-D. The effect size from the analysis including the POMS was selected as this is widely used as an overall measure of distress, rather than just the depressive symptoms captured by the CES-D. The two reported effect sizes from different time points in Wong et al.'s paper were combined prior to meta-analysis to give an overall effect for the sample. Of the two papers authored by Sharif (2017) and Sharif et al. (2017) which were based upon the same study, the analysis with the larger sample was chosen for inclusion.

Analysis was carried out using 'MedCalc' online software. The software calculates meta-analyses using both a fixed effects and random effects model (MedCalc, n.d.):

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MedCalc uses the Hedges-Olkin (1985) method for calculating the weighted summary Correlation coefficient under the fixed effects model, using a Fisher Z transformation of the correlation coefficients. Next the heterogeneity statistic is incorporated to calculate the summary Correlation coefficient under the random effects model (DerSimonian and Laird, 1986).

For the purposes of this meta-analysis, the random-effects model is likely to be the more appropriate approach due to the level of heterogeneity in study variables such as cancer type, stage, and treatment (Borenstein et al., 2009).

The extracted data and results of the meta-analysis are presented in figure 1-E-1. A forest plot of the included effects and meta-analysis is presented as a forest plot in figure 1-E-2. The random effects meta-analysis suggested a combined effect of  $r=0.35$  (95% CI 0.21-0.48), indicating a highly statistically significant relationship between uncertainty and distress in younger adults with cancer ( $p<.001$ ). Interpreted in light of guidance from Cohen (1988), the magnitude of the effect size is within the medium range.

Variable for studies	Study						
Variable for number of cases	N						
Variable for correlation coefficients	Correlation_coefficient						
Study	Sample size	Correlation coefficient	95% CI	z	P	Weight (%)	
						Fixed	Random
Lam et al. (2012)	471	0.180	0.0911 to 0.266			48.50	19.49
Mishel & Braden (1987)	44	0.460	0.189 to 0.666			4.25	11.36
Mishel (1984)	54	0.270	0.00241 to 0.502			5.28	12.48
Northouse et al. (1985)	81	0.420	0.222 to 0.585			8.08	14.50
Sharif et al. (2017)	135	0.297	0.135 to 0.444			13.68	16.59
Syrjala et al. (2017)	176	0.540	0.426 to 0.637			17.93	17.45
Wong & Bramwell (1992)	25	0.263	-0.147 to 0.596			2.28	8.14
Total (fixed effects)	986	0.306	0.248 to 0.362	9.833	<0.001	100.00	100.00
Total (random effects)	986	0.354	0.214 to 0.479	4.749	<0.001	100.00	100.00
Test for heterogeneity							
Q	25.6093						
DF	6						
Significance level	P = 0.0003						
I <sup>2</sup> (inconsistency)	76.57%						
95% CI for I <sup>2</sup>	50.86 to 88.83						

Figure 1-E-1: Meta-analysis results



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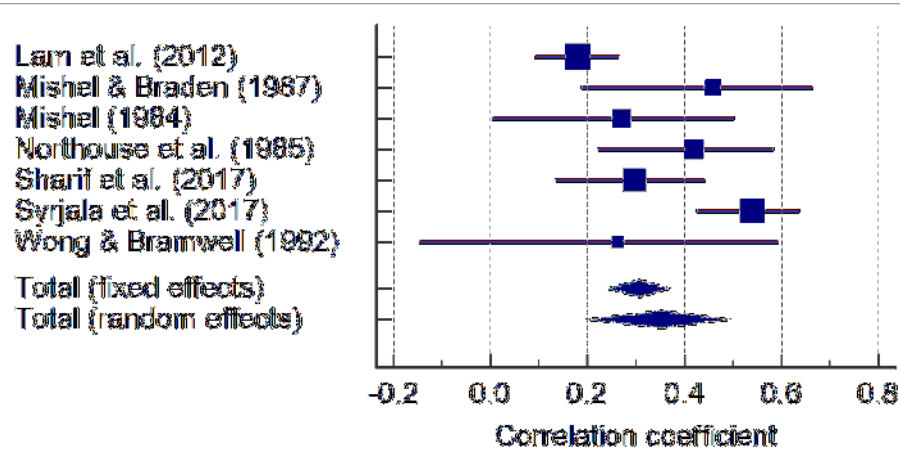


Figure 1-E-2: Forest plot of the meta-analysis of the relationship between uncertainty and psychological distress in younger adults with cancer

The meta-analysis adds to the findings presented in the main body of the systematic review that there is a clear and significant relationship between uncertainty and psychological distress for younger adults with cancers. As highlighted in the review discussion, this may be an important factor when considering communication and psychological interventions for this particular population. However, other factors that contribute to the remaining variance between these two variables merit further investigation. Of course, the limitations associated with the systematic review as a whole, which are highlighted in the discussion section, must be kept in mind when interpreting the outcomes of the meta-analysis.

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## Appendix 1-F: AXIS Quality Appraisal Tool

<i>Aims</i>				
2	Was the study design appropriate for the stated aim(s)?			
3	Was the sample size justified?			
4	Was the target/reference population clearly defined? (Is it clear who the research was about?)			
5	Was the sample frame taken from an appropriate population base so that it closely represented the target/reference population under investigation?			
6	Was the selection process likely to select subjects/participants that were representative of the target/reference population under investigation?			
7	Were measures undertaken to address and categorise non-responders?			
8	Were the risk factor and outcome variables measured appropriate to the aims of the study?			
9	Were the risk factor and outcome variables measured correctly using instruments/measurements that had been trialled, piloted or published previously?			
10	Is it clear what was used to determine statistical significance and/or precision estimates? (e.g. p-values, confidence intervals)			
11	Were the methods (including statistical methods) sufficiently described to enable them to be repeated?			
<i>Results</i>				
12	Were the basic data adequately described?			
13	Does the response rate raise concerns about non-response bias?			
14	If appropriate, was information about non-responders described?			
15	Were the results internally consistent?			
16	Were the results presented for all the analysis described in the methods?			
<i>Discussion</i>				
17	Were the authors' discussions and conclusions justified by the results?			
18	Were the limitations of the study discussed?			
<i>Other</i>				

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**Appendix 1-G: Additional Study Characteristics**

Study	Setting/ Recruitment	Demographic Characteristics			Cancer Status	
		Marital Status	Employment status	Education	Recurrence status	Time since/diagnosis/treatment
1 Cahill et al. (2014)	Via sample of parent study-recruited from single Brain and Spine Clinic	75% married 10% divorced 10% widowed/separated 15% single	n/a	18% high school 53% college 29% postgraduate	60% first occurrence; 31 % first recurrence; 9% repeated recurrence	n/a
2 <i>Lin et al. (2012)</i>	Outpatient hospital	10% single 65% married/partnered 26% divorced/separated/widowed	n/a	55%primary 39% high school 7% university	n=1 recurrence	26% 3-6 months 61% 6-12 months 13% >12 months
3 <i>Lin et al. (2013)</i>	Outpatient hospitals	70% married	n/a	Range=0-21 years Mean: 8 years	n/a	n/a

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4 Costa-Requena et al. (2011)	4 cancer care facilities	58% married 18% widowed 13% single 13% other	55% unemployed 38% ft 8% pt	Range=7-17 years Mean=13.5 years	n/a	n/a
5 Detprap-on et al. (2009)	Recruited via cancer organisations and support groups, posters in GPs and radio/news paper adverts, snowball sampling	75% married/common law partner 24% other (e.g. single, divorced, widowed)	unemployed 39% ft 48% pt 13%	49% some university or higher 51% college certificate or less	n/a	Less than 5 years
6 Ehrenberger et al. (2002)	Cancer centres, public hospitals, community practices	42% married/partner 24% single	48% employed	Mean= 16 years (standard deviation 2.7 years)	n/a	n/a
7 Jones et al. (2014)	Recruitment via 2 breast cancer	14% single 67% married/cohabiting 20% divorced/separated/widowed	34%ft 7% pt 20% retired 31% housewife	6% no formal education 30% primary 55% secondary	0%	n/a

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	centres		7% unemployed before diagnosis 1% unemployed since diagnosis	10% tertiary		
8 Kyranou et al. (2014)	Single brain and spine clinic	75% married; 10% divorced, widowed, separated; 15% single	52% employed 13% employed on sick leave 10% retired 17% unemployed due to diagnosis 7% unemployed prior to diagnosis/student	18% high school 53% college 29% postgraduate	60% first occurrence 31 % first recurrence 9% repeated recurrence	n/a
9 Lam et al. (2012)	Recruited via sample from larger study validating the MUIs-BT	75% married; 10% divorced, widowed, separated; 15% single	n/a	high school 18%, college 53%, postgraduate 29%	60% first occurrence; 31 % first recurrence; 9% repeated recurrence	n/a
10 Mishel & Braden (1987)	Via gynecological oncology service	56% married	n/a	32% college educated	0%	n/a
11 Mishel et al.	Recruited via cancer clinic	63% married 11% single seven 13% widowed	n/a	59% high school 28% college	0%	n/a

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(1984)		13% divorced/separated				
12 Mishel et al. (1991)	national referral treatment centre	15 single 49 married 16 widowed 14 divorced, 6 separated	n/a	Range=5-20 years Mean=13 years, Standard deviation=2.6	0%	1 month to 1 year
13 Northouse et al. (1995)	Letters sent to eligible participants via regional medical oncology offices	100% married/spouse	39% employed, 29% retired, 33% homemakers	Mean=13 years (range 3-18 years)	All first recurrence	1 month-3 years post-recurrence (mean=13 months)
14 Sharif (2017)	Private hospital	75% married 15% single 9% divorced/widowed	n/a	8% primary 25% secondary 28% diploma/professional certificate 38% university	n/a	Mean= 3 years
15 Sharif et al. (2017)	Private hospital	14% single 75% married 6% divorced 4% widowed	45% ft 13% pt 25% unemployed 13% retired	8% primary 27% secondary 27% diploma/professional certificate 36% university	n/a	26% 0-1 year 18% 1-2 yr 14% 2-3 yrs 16% 3-4 yrs 22% 4 yrs+

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16	Eight transplant centres	93% married/partner 7% single/divorced	n/a	69% more than high school	n/a	n/a
17	Cancer support centres and online	17% single 71% married/partner 12% separated/divorced	17% pt 60% ft 10% retired 12% unemployed	17%, high school or less 83% tertiary	n/a	n/a
18	Two acute-care hospitals	68% married 20% single 8% divorced 4% separated	40% employed	n/a	n/a	n/a

*Note.* Studies in italics/grouped by single braces indicate where multiple studies were based on data from the same sample. Abbreviations: n/a= not available; pt=part time; ft=full time.

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Appendix 1-H: Risk of Bias Assessment

Section	Question	Cahill et al., 2014	Costa-Requena et al., 2011	Detraponet al., 2009	Ehrenberger et al., 2002	Jones et al., 2014	Kyranou et al., 2014	Lam et al., 2015	Lin et al., 2012	Lin et al., 2013	Mishel & Braden, 1987	Mishelet al., 1984	Mishel et al., 1991	Northouse et al., 1995	Sharif, 2017	Sharif et al., 2017	Syrjala et al., 2016	Taha et al., 2012	Wong & Bramwell, 1992
Introduction	1) Were the aims/objectives of the study clear?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Methods	2) Was the study design appropriate for the stated aim(s)?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
	3) Was the sample size justified?	N	N	N	Y	N	N	N	Y	P	N	N	N	N	Y	N	Y	N	N
	4) Was the target/reference population clearly described?	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
	5) Was the sample frame taken from an appropriate population base so that it closely represented the target/reference population under investigation?	P	P	P	P	P	Y	P	P	P	P	P	P	Y	P	P	Y	P	P
	6) Was the selection process likely to select subjects/ participants that were representative of the target/reference population under investigation?	P	P	Y	P	Y	P	Y	P	P	Y	Y	Y	Y	Y	P	P	P	P



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7) Were measures taken to address and categorise non-responders?	D K	N	D K	D K	D K	P	P	N	N	P	P	D	P	P	D	P	D	P
8) Were the risk factor and outcome variables measured appropriate to the aims of the study? (validity)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
9) Were the risk factor and outcome variables measured correctly using instruments that had been trialled, piloted, or published previously? (reliability)	Y	Y	P	Y	Y	P	P	P	Y	P	P	Y	Y	Y	Y	P	P	Y
10) Is it clear what was used to determine statistical significance and/or precision estimates? (e.g. p-values, confidence intervals)	Y	P	Y	Y	P	Y	P	P	Y	P	P	P	P	Y	P	Y	P	P
11) Were the methods sufficiently described to enable them to be repeated?	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	P	Y	Y	Y	N	Y	Y	P

†

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Additional AHRQ Items	<p>A) Selection minimizes baseline differences in prognostic factors? (For controlled studies only)                  Factors to consider:                  • Was selection of the comparison group appropriate?                  o Consider whether these two sources are likely to differ on factors related to the outcome (besides cancer status).</p> <p>• Did the study investigators do other things to ensure that exposed/unexposed groups were comparable, e.g., by using stratification, matching, or propensity scores?</p>	<p>n/ n/ n/ n/ n/ n/ n/ n/ n/ n/ n/ n/ n/ n/ n/ P n/                  a a a a a a a a a a a a a a a a a</p>
	<p>B) Adequate follow-up period (longitudinal studies only)?                  Factors to consider:                  • A justification of the follow-up period length is preferable.</p>	<p>n/ n/ n/ n/ n/ P Y n/ n/ P n/ n/ n/ n/ n/ n/ n/ n/ n/                  a a a a a a a a a a a a a a a a a a</p>
Results	<p>12) Were the basic data adequately described?</p> <p>13) Does the response rate raise concerns about non-response bias?</p> <p>14) If appropriate, was information about non-responders described?</p>	<p>Y Y P P Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y</p> <p>D Y D Y D Y N N D D N D D N D P D P                  K K K K K K K K K K K K K K K</p> <p>N N N N N P N N N N N N N N N N N N N</p>

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	15) Were the results internally consistent?	P	Y	Y	Y	P	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	
	16) Were the results presented for all the analyses described in the methods?	Y	Y	Y	Y	Y	Y	Y	Y	Y	D	D	Y	Y	Y	D	Y	Y	D
Discussion	17) Were the authors' discussions and conclusions justified by the results?	P	Y	Y	P	Y	Y	Y	Y	Y	P	Y	P	Y	Y	Y	Y	Y	Y
	18) Were the limitations of the study discussed?	Y	Y	Y	P	Y	Y	P	Y	P	N	N	P	N	Y	Y	Y	Y	Y
Other	19) Were there any funding sources or conflicts of interest that may affect the authors' interpretation of the results?	Y	D	D	D	D	D	N	N	N	D	D	D	D	N	N	D	D	D
	20) Was ethical approval or consent of participants attained?	D	Y	Y	Y	P	Y	Y	D	Y	D	P	D	D	Y	Y	Y	P	P
		K							K		K		K	K					

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*Note.* † Amended to Y following discussion with second reviewer (see Appendix 1-D [p.1-64] for rationale). Abbreviations: Y= yes, N= no, P= partial, DK= don't know, n/a= not applicable.

## UNCERTAINTY AND DISTRESS IN CANCER

**Appendix 1-I: Reasons for Exclusion at Title and Abstract Screen**

Reason for exclusion	Number of studies excluded at title screening (n=2305)
Participants under 18 years or sample mean age >65 years	66
Sample not cancer patients	605
Qualitative methodology	373
No measure of distress	837
No measure of uncertainty	87
Not available in English	1
Not a study	332
Not peer-reviewed	3
No relevant analysis	1

**Appendix 1-J: Target Journal Author Guidelines***European Journal of Cancer Care* Author Guidelines

- 1. SUBMISSION**
- 2. AIMS AND SCOPE**
- 3. MANUSCRIPT CATEGORIES AND REQUIREMENTS**
- 4. PREPARING THE SUBMISSION**
- 5. EDITORIAL POLICIES AND ETHICAL CONSIDERATIONS**
- 6. AUTHOR LICENSING**
- 7. PUBLICATION PROCESS AFTER ACCEPTANCE**
- 8. POST PUBLICATION**
- 9. EDITORIAL OFFICE CONTACT DETAILS**

**1. SUBMISSION**

Authors should kindly note that submission implies that the content has not been published or submitted for publication elsewhere except as a brief abstract in the proceedings of a scientific meeting or symposium.

**Once the submission materials have been prepared in accordance with the Author Guidelines, manuscripts should be submitted online at <http://mc.manuscriptcentral.com/ecc>**

The submission system will prompt authors to use an ORCID iD (a unique author identifier) to help distinguish their work from that of other researchers. [Click here](#) to find out more.

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*The European Journal of Cancer Care* will consider for review articles previously available as preprints. Authors may also post the **submitted version** of a manuscript to a preprint server at any time. Authors are requested to update any pre-publication versions with a link to the final published article.

## UNCERTAINTY AND DISTRESS IN CANCER

### 2. AIMS AND SCOPE

The *European Journal of Cancer Care* aims to encourage comprehensive, multiprofessional cancer care across Europe and internationally. It publishes original research reports, literature reviews, commentaries, guest editorials, letters to the Editor and special features on current issues affecting the care of cancer patients. The Editor welcomes contributions which result from team working or collaboration between different health and social care providers, service users, patient groups and the voluntary sector in the areas of:

- Primary, secondary and tertiary care for cancer patients
- Multidisciplinary and service-user involvement in cancer care
- Rehabilitation, supportive, palliative and end of life care for cancer patients
- Policy, service development and healthcare evaluation in cancer care
- Psychosocial interventions for patients and family members
- International perspectives on cancer care

The journal provides a forum for multiprofessional and service-user dialogue, and the reporting of original research or rigorous reviews within the field of cancer care both in Europe and internationally. The journal welcomes original research, reviews and correspondence from individuals whose first language is not English, but places great weight in its published papers on accuracy, fluency and clarity of expression as befits any journal published for an international and multiprofessional audience.

### 3. MANUSCRIPT CATEGORIES AND REQUIREMENTS

#### Original Papers

Original articles, which report on new research findings or conceptual analyses that make a significant contribution to knowledge will be considered for publication.

WORD LIMIT: 4000 word limit, excluding references, figures, and tables).

ABSTRACT: A structured abstract is required (200 words maximum) under the following sub-headings: Objective; Methods; Results and Conclusion. The abstract should describe the purpose, study population, methodology, setting and details of the variables under study. It should also highlight the main results and conclusions of the study.

MAIN TEXT: Should be structured under the following sub-headings: introduction, methods, results, and discussion.

RESEARCH REPORTING CHECKLIST: may be required - see section 5 Editorial Policies and Ethical Considerations.

#### Review Papers

WORD LIMIT: 5000

ABSTRACT: A structured abstract is required (200 words maximum) under the following sub-headings: Introduction, Methods, Results, Conclusion.

MAIN TEXT: Reviews must contain a clear exposition of the background, search strategy, databases, keywords and any selection/evaluation criteria used in the review where appropriate. It should also highlight the main results and conclusions of the study.

RESEARCH REPORTING CHECKLIST: Please see [section 5](#) Research Reporting Guidelines.

#### Letters to the Editor

WORD LIMIT: 600

ABSTRACT: N/A

MAIN TEXT: Letters should be succinct and must relate to an article that has been published in the Journal. The Editor reserves the right to shorten letters if necessary, but will be sent to the

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authors for approval.  
RESEARCH REPORTING CHECKLIST: N/A

### **Commentaries**

WORD LIMIT: 1500  
ABSTRACT: N/A  
MAIN TEXT: evidence-based opinion pieces involving areas of broad interest.  
RESEARCH REPORTING CHECKLIST: N/A

### **Registered Reports**

*European Journal of Cancer Care* welcomes Registered Reports. This is a new article type designed to increase the transparency and reproducibility of hypothesis-driven science. Registered Reports differ from the conventional research article as part of the review process is conducted before authors collect and analyse data. The cornerstone of the Registered Reports format is that a significant part of the manuscript will be assessed prior to data collection, with the highest quality submissions accepted in advance. Please view the full Registered Reports author guidelines [here](#) to help prepare your submission.

## **4. PREPARING THE SUBMISSION**

### **Cover Letters**

Cover letters are not mandatory; however, they may be supplied at the author's discretion.

### **Parts of the Manuscript**

The manuscript should be submitted in separate files: title page; main text file; figures.

### **Title page**

The title page should contain:

- i. A short informative title containing the major key words. The title should not contain abbreviations (see Wiley's [best practice SEO tips](#));
- ii. A short running title of less than 40 characters;
- iii. The full names of the authors and email address and telephone number of corresponding author;
- iv. The author's institutional affiliations where the work was conducted, with a footnote for the author's present address if different from where the work was conducted;
- v. Acknowledgments.
- vi. Conflict of Interest statement for all authors;
- vii. Funding statements

### **Authorship**

Please refer to the journal's authorship policy the [Editorial Policies and Ethical Considerations](#) section for details on eligibility for author listing.

### **Acknowledgments**

Contributions from anyone who does not meet the criteria for authorship should be listed, with permission from the contributor, in an Acknowledgments section. Financial and material support should also be mentioned. Thanks to anonymous reviewers are not appropriate.

## UNCERTAINTY AND DISTRESS IN CANCER

### **Conflict of Interest Statement**

Authors will be asked to provide a conflict of interest statement during the submission process. For details on what to include in this section, see the section 'Conflict of Interest' in the **Editorial Policies and Ethical Considerations** section below. Submitting authors should ensure they liaise with all co-authors to confirm agreement with the final statement.

### **Main Text File**

As papers are double-blind peer reviewed the main text file should not include any information that might identify the authors.

The main text file should be presented in the following order:

- i. Title, abstract and key words;
- ii. Main text;
- iii. References;
- iv. Tables (each table complete with title and footnotes);
- v. Figure legends;
- vi. Appendices (if relevant).

Figures and supporting information should be supplied as separate files.

### **Title**

Should be clear, descriptive, and avoid the use of metaphor, elaborate language or respondent quotations which are less likely to be discovered by the electronic algorithms of modern search engines. Titles should include words pertaining to population or sample, the method of inquiry, any tools or measures used and its key findings as appropriate. These words should be reiterated at least once in the abstract.

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Section 2: Research Paper

Patients' Experiences of Coping Longer-Term with Cancer of Unknown Primary:

An Interpretative Phenomenological Analysis

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Written in preparation for submission to the European Journal of Cancer Care (author guidelines presented in Appendix 2-F, p.2-57)



## COPING LONGER-TERM WITH CUP

**Abstract**

Objective: Cancer of unknown primary (CUP) has been relatively overlooked by previous research investigating the psychological experiences of cancer patient populations. The condition is associated with elevated uncertainty which may exacerbate difficulties encountered in other cancers. This study aimed to explore the coping experiences of people living longer-term (>6 months) with CUP.

Methods: Semi-structured interviews were conducted with 10 participants. Interpretative phenomenological analysis was used to identify superordinate and subordinate themes from patients' accounts.

Results: Superordinate themes were: (1) "Fuss and Bother": The Upheaval of Everyday Life', with subordinate themes of 'Appointment threats', and 'Symptoms and side-effects'; (2) "It's the Unknowing": The Enduring Uncertainty of CUP', with subordinate themes of "What the bloody hell's that?!'", 'An uncertain future', and 'Hope'; and (3) "Just Get on With It": Managing and Moving Forwards', with subordinate themes of 'Maintaining normality', 'Acceptance', and 'Support'.

Conclusion: Findings demonstrated that the experiences of people living longer-term with CUP parallel those of other cancer patient populations, however, patients with CUP face particular challenges with perceived loss of control, burdensome medical regimes, and unrelenting uncertainty which may make coping harder. Findings were synthesised with existing literature and recommendations for clinical practice and future research were highlighted.

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### **Introduction**

Cancer of unknown primary (CUP) is a diagnosis given where a secondary cancer has been identified in the absence of an identifiable primary site (Fizazi et al., 2015; Varadhachary & Raber, 2014). The diagnosis can only be made once standardized investigations have failed to discover the primary cancer (Airoldi, 2012). Possible reasons that the primary cancer cannot be identified include: it being too small to register on scans or being obscured; the body's immune system eradicating it; or it passing from the body (The Christie NHS Foundation Trust, n.d.). Where all possible investigations have not yet taken place or cannot take place, the secondary cancer is referred to as a malignancy of undefined origin, differentiating this group of patients from those with 'confirmed' CUP (National Institute for Health and Care Excellence, NICE, 2010).

Approximately 9000 people in the UK are diagnosed with CUP annually (Cancer Research UK, 2017). The condition is usually associated with limited life expectancy (Hemminki, Bevier, Hemminki, & Sundquist, 2012). While a minority of patients (15-20%) belong to clinical subsets with more favourable prognoses, 80-85% of CUP patients belong to unfavourable subsets with a median survival time from diagnosis of six months (Airoldi, 2012; Fizazi et al 2015). However, a sub-group of these patients are able to be stabilised with treatment beyond this time, with approximately 20% surviving one year or more and 13% surviving three years or more from diagnosis (Cancer Research UK, 2017).

### **Psychological Aspects of Cancer**

Research has shown that individuals with cancer experience elevated distress (Carlson et al., 2004; Zabora, Brintzenhofe Szoc, Curbow, Hooker, & Piantadosi, 2001). Distress in relation to cancer has been defined by The National Comprehensive Cancer Network (NCCN, 2010) as "a multifactorial unpleasant emotional experience of a psychological (cognitive, behavioural, emotional), social, and/or spiritual nature that may interfere with the

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ability to cope effectively with cancer, its physical symptoms and its treatments.” Within this definition, distress is conceptualised as difficulties with mood, anxiety, and adjustment ranging from mild reactions to clinically diagnosable psychiatric disorders, and existential and spiritual crises. A meta-analysis by Singer, Das-Munshi and Brähler (2009) found that one in three people with cancer meet criteria for diagnosis of a psychiatric disorder, compared with between one in four and one in six people in the general population (Mind, 2017; Singer et al., 2009). NICE guidelines (2004) recommend that all cancer patients receive psychological assessment at key points in the treatment journey and have access to appropriate psychological support.

### **Psychological Aspects of CUP**

Few studies have been undertaken with CUP patients. Results from a study comparing patients with CUP to patients with cancers of known primary sites have shown individuals with CUP experience greater levels of depression, anxiety, and somatization (Hyphantis et al., 2013). Compared with patients with other cancers, CUP patients have less understanding of their condition and are more likely to want written information (Wagland et al., 2017). Previous studies have suggested that elevated illness uncertainty associated with CUP amplifies difficulties encountered across other cancers (La Pushin, 2009; Richardson et al., 2015). Uncertainty in CUP has been linked to: numerous investigative tests (Symons, James & Brooks, 2009); indefinite prognosis and lack of clarity in treatment plans (Ryan, Lawlor & Walshe, 2013); and lack of continuity in care (Richardson et al., 2015). Therefore, increased uncertainty and its impact in CUP may make coping particularly challenging (Hyphantis et al., 2013). A small number of published qualitative studies (Boyland & Davis, 2008; Isida, et al., 2016; Richardson et al.) support this, however, these studies have included predominantly individuals in the early stages following diagnosis which has been shown to be a time of high uncertainty across cancer patient populations (Worster & Holmes, 2008)

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and for many people with CUP life expectancy may be limited. No research has been conducted which investigates the experiences of individuals living longer beyond CUP diagnosis.

### **Coping**

Coping has been conceptualised in numerous ways. Lazarus and Folkman's (1984) definition of coping as "constantly changing cognitive and behavioural efforts to manage external and/or internal demands that are appraised as taxing or exceeding the resources of the person" has been widely accepted and applied. Based on this, Folkman and Lazarus (1980; 1985; Lazarus & Folkman, 1984) proposed, in line with their transactional model of stress and coping (TMSC), that coping can be separated into two categories: emotion-focused coping which relates to attempts to alter emotions through strategies such as re-appraisal; and problem-focused coping which pertains to attempts to change external factors via strategies such as problem-solving (Roesch et al., 2005). A further dimension to coping is direction of focus. Strategies directed towards a threat are described as 'approach coping' (e.g. problem-solving) and strategies directed away from a threat are labelled as 'avoidance coping' (e.g. distraction) (Moos & Schaefer, 1993). Corresponding conceptualisations of these phenomena in the literature include repression and sensitization (Byrne, 1964) and monitoring and blunting (Miller, 1987).

### **Coping with Cancer**

Previous research has demonstrated that various coping strategies are used by people with cancer (Nipp et al., 2016). Both emotion-focused and problem-focused approach coping have been linked to improved psychological and physical wellbeing (Roesch et al., 2005). Avoidance coping, conversely, has been associated with elevated distress and poorer physical functioning (Roesch et al.). However, it has been suggested that avoidance coping may

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facilitate short-term management of illness-related stress (Vos & Haes, 2007) and allow those with terminal illness to make the most of their time (van Laarhoven, 2012).

Uncertainty amongst cancer patients has been demonstrated to be negatively correlated with coping (Germino et al., 1998). Difficulty coping with uncertainty has been identified amongst patients with advanced cancers (Kimbell, Murray, Macpherson & Boyd, 2016). According to Mishel's uncertainty in illness theory (UIT, 1988), appraisal of uncertainty as 'danger' or 'opportunity' leads to different styles of coping. The use of emotion-focused coping strategies in response to 'danger' appraisals, has been found to mediate between fear of uncertainty and distress during and after cancer treatment (Taha, Matheson & Anisman, 2012).

### **Study Rationale**

The experience of uncertainty has been identified as a challenge to coping across different cancer patient populations. This is a particular issue for individuals with CUP which is associated with greater uncertainty than other cancers. Given the negative correlational relationship between uncertainty and implementation of coping strategies, this may make it harder for this patient group to effectively cope. Therefore, research investigating how individuals with CUP cope is warranted.

Existing qualitative research has focused predominantly on CUP patients soon after diagnosis, possibly due to often-limited life expectancy. However, a subgroup of CUP patients is medically stable at six months (the median life expectancy in this population) and beyond diagnosis. This group of patients have had a prolonged period of coping with the uncertainties of CUP and potential related distress; however, no research has focused on this population who are living 'longer-term' with CUP. Research addressing this gap in the literature is necessary to inform clinical practice around how this population can be supported.

## COPING LONGER-TERM WITH CUP

### **Aim**

The aim of the study was to explore the experiences of individuals coping longer-term with CUP. It was hoped that this knowledge would indicate how individuals perceived their capacity to cope, what factors influenced this, and what coping strategies were used.

### **Research questions.**

What are the coping experiences of people who are living longer-term with CUP?

- How do these patients perceive their ability to cope?
- What influences perceptions of coping?
- What are patients' experiences of coping over time?

### **Method**

The study protocol was registered with The National Cancer Research Institute.

Where applicable, recommendations on the standards for reporting qualitative research (O'Brien, Harris, Beckman, Reed, & Cook, 2014) were followed to enhance transparency and inform interpretation of findings. Ethical approval was granted by the Health Research Authority (HRA). The ethics application and associated documents are presented in Section Four.

### **Approach**

The approach was informed by the research questions and the underlying ontological and epistemological assumptions made therein. A relativist ontological position and interpretative epistemological paradigm guided the research process. The aims of the study and research questions assume that we can come to understand the reality of living longer-term with CUP through individuals' lived experiences. Therefore, interpretative phenomenological analysis was selected due to the approach's centralised focus upon the meaning derived from individuals' experiences of a particular phenomenon. IPA is characterised as an inductive, idiographic approach embedded within the interpretivist

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tradition (Tuffour, 2017). Distinct from other modes of qualitative analysis, IPA prioritises the ‘fine-grained’, detailed analysis of each individual account, the language used to convey the individual’s subjective reality, and the ‘psychological entailments’ therein (Murray & Wilde, 2020). Particular attention is given to the way in common themes “play out for individuals” (Smith, 2011, p.10). The analytic steps outlined by Smith and Osborn (2008) were followed to enhance consistency and replicability (Noble & Smith 2015). The explicit recognition of the researcher’s role in the interpretation of data is seen to be a strength of IPA. Thus, while the researcher may not always be consciously aware of biases, the approach emphasises reflexivity and openness in relation to the potential for researcher bias to influence results (Malim, Birch, & Wadeley, 1992).

### **Sample**

A purposive sampling strategy was used to identify eligible participants. Ten participants were recruited from four NHS Trusts in the North West of England. A sample of this size is recommended by Smith, Flowers, and Larkin (2009) for professional doctorate research and publication. A further two eligible patients were identified by clinical staff but did not consent to be contacted by the researcher. All patients that agreed to be contacted by the researcher consented to participate. These 12 CUP patients represented all eligible candidates for the study within the six recruiting NHS Trusts during the recruitment window (two Trusts did not have any patients meeting inclusion criteria). The response rate for the study is therefore 83.3%.

### **Inclusion and exclusion criteria.**

Participants were eligible for inclusion if: they had been diagnosed with CUP for six months or longer; they were deemed to be clinically stable by their medical team; they were aged 18 or over; and they were able to provide informed consent. Participants were excluded if: they were acutely unwell; they did not speak English; they were under 18 years of age; or

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they lacked capacity to provide consent to participate. Smith and Osborn (2008) posit that the sample for IPA should be homogeneous. Therefore, the inclusion and exclusion criteria aimed to ensure participants had comparable experiences.

### **Sample characteristics.**

Sample characteristics are presented in Table 2-A (p.2-41). The sample had a mean age of 72.3 years (median= 75 years), ranging from 58 to 77 years. An equal number of males and females were recruited, and all participants identified as white British. Time from CUP diagnosis ranged from six months to five years and seven months with a mean of 23.9 months (median=16 months). All participants had a histologically confirmed diagnosis of CUP and none of them were from favourable risk subsets of CUP. Four participants had nodal disease only while the other six patients had visceral metastases. Understandably, there was a longer time from diagnosis in patients without visceral metastases. All participants reported receiving some treatment (e.g. surgery, radiotherapy, and/or chemotherapy) since diagnosis.

TABLE 2-A HERE

### **Procedure**

Research materials were developed in consultation with a service user group from a participating NHS Trust, as recommended by the HRA (2018). Two changes to the consent form were made based on service-users' feedback. Firstly, the window of time given for participants to withdraw their data from the study following participation was extended from one week to two to allow more time for consideration. Secondly, the word 'anonymously' was replaced with 'without my details' to promote ease of understanding. The service user group was comprised of cancer patients, however, none of the members had a diagnosis of CUP.



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### **Data collection.**

Potential participants were identified by members of their medical team and informed consent was sought prior to data collection. Participants were given the choice of meeting in their own homes or at their local hospital site. Data was collected from July to September 2019 via audio-recorded semi-structured interviews. Interviews lasted between 27 and 101 minutes (mean=49 minutes). Questions for the interview schedule (Appendix 2-A, p.2-43) were informed by the research questions and guidance from Smith and Osborn (2008). Semi-structured interviews are deemed the 'exemplary' method for IPA and are widely used in phenomenological research (Brinkmann, 2014; Smith and Osborn, 2008).

### **Analysis**

The analytic strategy followed the recommendations of Smith and Osborn (2008). This involved each interview being transcribed verbatim then read independently several times to generate initial themes which were noted in the margins. Related initial themes were then organised into clusters. The clusters of themes from the first case were used to orient the analysis of subsequent transcripts. This process was repeated for each transcript, with convergences and divergences attended to. Themes from across the transcripts were synthesised and organised hierarchically to produce 'superordinate' and associated 'subordinate' themes. Initial annotation and coding were done manually. Microsoft Excel was used to organise exemplar quotations by theme. Examples of each stage of the theme development process are presented in Appendix 2-B (p.2-44).

To maintain an awareness of researcher biases, a reflective journal was kept throughout the research process, excerpts from which are documented in Appendix 2-C (p.2-51). Content from the journal was discussed in monthly research supervision. A reflexive statement acknowledging these biases has been included within Section Three.

### Results

Three superordinate themes were identified: (1) “‘Fuss and Bother’: The Upheaval of Everyday Life’, with subordinate themes of ‘Appointment threats’, and ‘Symptoms and side-effects’; (2) “‘It’s the Unknowing’: The Enduring Uncertainty of CUP’, with subordinate themes of “‘What the bloody hell’s that?!”, ‘An uncertain future’, and ‘Hope’; and (3) “‘Just Get on With It’: Managing and Moving Forwards’, with subordinate themes of ‘Maintaining normality’, ‘Acceptance’, and ‘Support’. Themes are presented diagrammatically in Figure 2-A (p.2-42). A table in Appendix 2-D (p.2-53) indicates which themes were present in which participants’ accounts.

FIGURE 2-A HERE

#### **“Fuss and Bother”: The Upheaval of Everyday Life**

The description of CUP as a disruptive presence in participants’ lives was present to varying degrees across the sample. Participants shared a narrative that the practical and mental time and attention demanded by CUP (for example, for attending appointments or ruminating upon concerns) led to difficulty engaging with valued activities. This was framed in the accounts as a significant threat to participants’ subjective sense of coping, as captured in this extract from Sarah:

All my normal activities just stopped [...] Fourteen months of...not easy examinations and all very upsetting knowing that [...] there’s nothing that can be done [...] I don’t know that I have actually coped. I haven’t had time to cope. I’ve just been busy [laughs] you know? Look at the calendar, what’s next? [...] How do we fit that in? Is it possible to go away? No! [...] I don’t feel I’ve dealt with it, [laughs] haven’t made...any decision...I’ve just gone along with everything...I’ve been told “you’ve got an appointment”, a PET scan here, or a CAT scan, or MRI scan...it’s gone on and on.

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Sarah's sense of not having coped seems underpinned by feelings of passivity and powerlessness in relation to CUP itself and associated medical procedures. Her impression that she had not been coping reflects an underlying assumption that coping is an active process, involving the deliberate employment of strategies. Sarah's account suggests that the unremitting nature of her medical care, which feels outside of her control, has drained her of the internal resources to activate a conscious coping response.

### **Appointment threats.**

Appointments were perceived to entail multiple threats including burden on time, anxiety, and loss of control. Graham's comment, "I'm sick of going to the doctor's, I seemed to be living there at one time," demonstrates his frustration caused by the frequency of appointments and interruption they cause to his life.

The threatening nature of appointments for many participants also related to anticipatory anxiety:

I think the worst times for you, every three months you have your scan and then the week when you're going for your results, your head starts going [...] Mentally sometimes it screws you up a bit [...] It's like, I don't know...an axe hanging over your head every three months (David).

David's comments indicate the increase in anxiety associated with appointments relates to the potential for 'bad news' and increased awareness of his own mortality.

Despite the identified threats associated with appointments, all participants reported compliance with their medical regimes. This may reflect a perspective amongst patients that appointments are obligatory, and not something they have active choice over, leading to the subjective loss of control. Moreover, continued willingness to attend appointments despite identified threats may suggest that the threat of not attending, and potential repercussions of having less information about their CUP status, is perceived as more threatening. Thus,

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patients choose the least aversive option, with the information provided in consultations, despite threatening aspects, seen as more tolerable than not knowing.

### **Symptoms and side-effects.**

Where participants were experiencing CUP-related symptoms or side-effects from prior treatment, these were described as aversive and disruptive of day-to-day activities. The below extract from Emily offers an example of this:

I don't think I'm going to be 100% ever again. I would like to feel that I could feel a little bit better than I am. I'm normally quite an energetic person [...] and I find I can't even peel potatoes [...] I can't even go and walk the dog...I've been so athletic all my life, so this is a great big sort of come down.

As Emily describes the functional limitations she faces, these are interpreted in relation to their impact upon valued aspects of her identity. This suggests that not only has activity, and its adaptive coping function, been impacted by CUP, but consequently Emily's sense of herself more globally. Her description of a 'come down' may also reflect feelings of grief associated with experiencing multiple, cumulative losses.

### **“It's the Unknowing”: The Enduring Uncertainty of CUP**

The uncertainty associated with CUP was recognised by participants as non-conducive to coping. As summarised by Sarah; “anybody can cope with anything if they know what's going on and why they're doing it.” For patients with CUP, these ‘what’ and ‘why’ conditions of knowledge for coping are unobtainable, leading to a collective sense of CUP being confusing, unpredictable, and thus inherently threatening. Ruth shared her experience: “Well you see, I don't understand really, because I was told it might never appear [...].I examine myself [laughs], and I can't see anything[...] It is very perplexing, and I still find it difficult to believe.” Ruth's bewilderment, as for other participants, stems from her

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perceived lack of understanding of CUP and an absence of evidence which inhibit her ability to process her experiences.

### **“What the bloody hell’s that?!”**

Numerous factors were found to influence participants’ sense of CUP being unusual or strange. Central to this in several accounts was the fact that prior to diagnosis participants had not heard of CUP. Emily’s comment exemplifies this: “this was a medical title I’d not heard of before, and I had assumed something could be done up to this point.” For Emily, as with others, a lack of prior awareness of CUP seemed to exacerbate uncertainty due to an absence of transferrable expectations.

Several participants remarked on their understanding of CUP’s course as different to the usual trajectory of other cancers: “I’ve had two cancers but I’ve just followed a normal trail of [...] treatments and...and expected to get better and I have done [...] This is... really weird,...it’s not at all what one expects” (Sarah). Sarah’s experience suggests that living with CUP for her has been qualitatively different to her other experiences of cancer. Other participants, who had not previously had another form of cancer, also remarked on their sense that living with CUP was different to living with other cancers due to its unknowability.

### **An uncertain future.**

Participants described the uncertainty associated with how CUP might progress to be one of the most challenging aspects of their experience, as conveyed by Paula:

Well, it is a big mystery really isn’t it! [laughs] [...] I think a good grasp of it now but it’s just the thoughts that it can be popping up anywhere [...] it’s difficult to live with sometimes.

Paula’s account demonstrates that despite having come to understand the pathological mechanisms of CUP, a sense of threat in relation to the unpredictable course of the disease

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persists. This fear of cancer ‘popping up’ in other sites was prevalent across participant accounts and was linked to anxieties about the possibility of increased physical symptoms.

A proportion of participants also reported that these fears had led to hyper-vigilance towards potential signs of illness progression and interpretation of possibly benign or unrelated experiences as highly threatening. Stephen shared a recent example of this: “the only thing that I think of at the moment is this hiccup business, you know, and, wonder whether there’s something happening here that’s...shouldn’t be.”

### **Hope.**

Several participants described their interpretation of CUP’s uncertainties as opportunity to hope for an extended period of wellness or recovery. Chris expressed his hopes for further investigations: “It would be nice actually if they did another biopsy, and this is what frustrates me ...because if [...] they look, they might say ‘ooh it’s not there, the cancer’s gone!’” In some instances, these expressions of hope were in the context of a period of relatively symptom-free stability. For others these interpretations existed in a context of progressive metastases, indicating possibly a false hope facilitated by denial, particularly if hopes were in relation to a cure being identified. In both scenarios, however, these hopeful interpretations seemed to serve to reduce distress.

### **“Just Get on With It”: Managing and Moving Forwards**

A pervasive theme across participants’ accounts was that being able to carry on as much as possible with ordinary life was the most significant factor in feeling able to cope. While the ability and confidence to do this varied in relation to the context of appointments and symptoms, participants shared a perspective that ‘getting on’ with life served as a proxy measure for effective coping. An extract from David demonstrates this:

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Just get on with it, don't you? What option have I got? I haven't got an option really, have I? I mean I could sit there and be miserable as sin, and that's not going to help me is it? You know, you've got to pick yourself up

In this comment, David seems to suggest a polarised conceptualisation of 'getting on' as coping versus negative emotions and inactivity which represent inability to cope. To 'not cope' is not seen as a viable choice. Conscious efforts are made to avoid inactivity and difficult emotions which could influence coping perceptions.

### **Maintaining normality.**

Central to the conceptualisation of 'getting on', participants conveyed that maintaining a subjective continuation of their pre-CUP normality was highly valued:

I just carry on, don't I? And that's it. I love my garden, I've always said that gardening is good therapy [...] people mustn't let it get hold of them, right? Or let it take control of their life, basically. With some people it does, they can lock themselves away, they can do that, and lock themselves away up here [gestures to head] as well, you know? Just carry on, try to carry on as per normal, and always do the things you love doing (Peter).

Peter's description suggests that continuing to engage with everyday aspects of life enable a sense of control and protects against introspective withdrawal which is perceived as maladaptive.

For a number of participants, ability to maintain normality was bolstered by an absence of physical symptoms or perceptions of themselves as 'ill.' This is exemplified in Stephen's comment: "I never felt unwell." For participants experiencing more physical symptoms, a process of adaptation was described. Sarah, for example, reported focusing on "everyday activities that don't require a lot of energy," to facilitate a continued sense of normalcy.

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The construction of a subjective continued normality also served the function of allowing participants to maintain a coherent sense of identity and remain connected to valued aspects of themselves, as demonstrated in a comment from Jean, “I’ve always been an active person and that so I just, you know, get on with it”. This extract demonstrates that personality constructs such as being ‘active’ may be perceived as fixed, despite possible challenges or threats posed by CUP, and this may enhance perceived coping capacity and activation of coping skills.

Another important aspect of maintaining pre-CUP normality for participants was the potential for their usual activities to offer distraction:

I play guitar as well so that helps [...] It’s the distraction. I mean, if you’re thinking about something else... alright we are capable of thinking about two things at once, but I’m a bit mono like that [laughs]. I would say once I’ve got my sights set on something, I research it and look at it and think about it and nothing else comes in (Graham).

Graham description highlights the potential for valued activities to offer an alternative attentional focus, preventing pre-occupation with CUP which could activate a threat-response and appraisals of being less able to cope.

### **Acceptance.**

Most participants voiced that having had a period of six months or longer since diagnosis had enabled them to foster a sense of acceptance in relation to CUP after the initial shock of diagnosis, as articulated by Peter:

I try and accept things, you know what I mean, I don’t dwell on anything like that, I’ve kind of accepted it and did what we could do about it, to better it. They told me it was terminal and well basically there’s no cure for it, but they can keep it [...] harnessed a little bit.



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This statement from Peter reflects that acceptance is effortful, something that Peter is striving towards, with a view that being able to accept the realities of CUP will be adaptive and beneficial. There is also an element of conflict between ‘true’ acceptance and the desire to push away aversive thoughts seen as ‘dwelling.’

A number of participants shared a view that accepting CUP had become easier with time:

It took a couple of years to get myself back up [...] At first it was... always the first thought was “oh, will I be ok next week?” And now I can just put it to the back of my head and... forget about it [...] time heals, and yeah, I certainly feel that I’ve overcome it (Jean).

Several participants also expressed a belief that their age helped them to accept CUP.

Accordingly, participants expressed a sense of gratitude: “I’m 76, it’s ok, I’ve made it, I’ve got here... I can be comfortable, so I’m very lucky” (Sarah). Additionally, participants reported that having come to accept CUP had also enabled them to adjust their priorities to ‘make the most’ of their lives: “Little trivial things that are normal life that worry you are not really important, are they? You know, when you think what could happen to me. Yeah, so it puts a different perspective on things” (David).

### **Support.**

External support was identified as a coping resource by the majority of participants.

Paula shared the important impact of supportive personal relationships for her: “I get good support as I say from my family... and friends you know, they boost you on, you know.”

Participants reported varying levels of engagement with professional support. For some participants, the knowledge that they could approach their specialist nurse or providers like Macmillan if required, was felt to be reassuring enough for their current needs: “I know they’re there” (Jean). Other participants had accessed additional support from their specialist

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nurses: “she’s made everything easy,” (Sarah) or the third sector or local hospices: “[The hospice] have really, really been very, very helpful” (Emily).

### **Discussion**

The themes from the study elucidate experiences of coping amongst people living longer-term with CUP and the mechanisms of coping-related processes. The findings are discussed within the context of relevant literature and coping theory.

#### **“Fuss and Bother”: The Upheaval of Everyday Life**

Experiences appraised as life-disruptive “fuss and bother” have been previously highlighted within the broader cancer patient population. Of the multiple threats associated with appointments, the burden upon patients’ time was perceived as a significant barrier to engagement with valued activity and employment of behavioural coping strategies. This finding is supported by research by Lövgren, Tishelman, and Hamberg (2010) who suggested there is a discordance between ‘clock time’ in the healthcare system and ‘embodied time’ of cancer patients with limited life expectancy. This was proposed to produce a misalignment of priorities between clinicians and patients regarding how patients’ time should be spent. Findings such as these have been emphasised by the ‘Last 1000 Days’ NHS Improvement initiative which highlights the value of patient time for those in the final 1000 days of their lives, as many CUP patients are likely to be (Dolan & Holt, 2017; NHS Improvement, 2016). This is of particular relevance for patients with CUP due to the significant amount of time already required for diagnostic procedures (Boyland & Davis, 2008).

Anxiety in relation to routine appointments was described as a challenge to coping. This finding is supported by a study by Sandeman and Wells (2011) which identified anticipatory anxiety prior to appointments to be a recurring challenge for lung cancer patients. As with the sample of this study, however, anxiety did not prevent attendance. Accordingly, this was suggested by Sandeman and Wells to be due to the potential for

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reassurance from medical consultations to relieve more general cancer-related anxieties. As experiences in CUP have been previously suggested to be amplified in comparison with the broader cancer population (Richardson et al., 2015), it is possible that anticipatory anxiety before appointments is exacerbated for CUP patients due to the perceived volatility of their condition.

Perceived loss of control was a further characteristic of the “fuss and bother” of CUP, with some patients describing a passive role in their medical care and a sense of CUP-related events as uncontrollable. In other cancer patient populations, reduced perceived control has been linked with diminished adjustment to illness and greater levels of anxiety and depression (Naus, Price & Peter, 2005).

The appraisal of threat and disruption to daily life associated with physical symptoms was considerable for a proportion of participants. This is consistent with prior findings that physical symptoms persist for many individuals after completion of cancer treatment (Harrington, Hansen, Moskowitz, Todd, & Feuerstein, 2010) and have a substantial impact upon quality of life, psychological wellbeing, and functioning (Polanski, Jankowska-Polanska, Rosinczuk, Chabowski, & Szymanska-Chabowska, 2016). So too have physical symptoms been documented as a threat to identity (Mathieson & Stam, 1995).

### **“It’s the Unknowing”: The Enduring Uncertainty of CUP**

The finding that uncertainty remained prevalent amongst participants supports existing findings on the psychological aspects of CUP (Boyland & Davis, 2008; Richardson et al., 2015). The results of this study, however, provide evidence that this experience persists over time, however the appraised level of threat associated with this for many was felt to decrease over time as individuals felt more able to accept the uncertainties of their condition.

The uncertainty associated with not having heard of CUP and as such not knowing what to expect of the illness was described as a source of anxiety. Uncertainty as a

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consequence of limited information is a common theme for patients with other cancers (Shaha, Cox, Talman, & Kelly, 2008), however, is likely to be amplified for patients with CUP (Richardson et al., 2015). The experience of ongoing uncertainty was also linked to fears about the future, a prevalent concern for the wider cancer patient population.

Findings indicated that the uncertainty associated with CUP and related threat appraisals may be linked to increased vigilance to physical symptoms. While a degree of body vigilance is considered adaptive for initiating help-seeking behaviour during illness (Winstanley, Renzi, Smith, Wardle, & Whitaker, 2016), research has demonstrated an increased prevalence of health anxiety and related hyper-vigilance and misinterpretation of bodily experiences amongst cancer survivors (Jones, Hadjistavropoulos, & Gullickson, 2014). It is possible that this experience is particularly pertinent to patients with CUP given an absence of information about the location of the primary cancer, perhaps leading to a greater propensity for misinterpretation of benign symptoms.

The perceived opportunity for hope in response to uncertainty identified by several participants is consistent with Mishel's (1988) UIT. McClement and Cochinov (2008) have proposed that perceiving hope in uncertainty may be viewed as an active coping strategy. Findings suggested that hope for desired outcomes can enable participants to cope even where these hopes seem to be unlikely, suggesting that for participants with more advanced illness hope may be facilitated by a process of denial. Differing perspectives exist regarding the adaptiveness of denial in illness (Vos & Haes, 2007), however, evidence suggests, in line with the study findings and the propositions of Horowitz (1983), that it may offer a protective function in the face of distressing information, reducing perceived threat and enabling coping.

### **“Just Get on With It”: Managing and Moving Forwards**

The theme of ““Just Get on With It”: Managing and Moving Forwards’ captured processes which enable coping. As documented in previous research with patients with

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advanced cancer, participants relied predominantly upon strategies to influence and manage their emotional responses to their CUP-related experiences, rather than problem-focused strategies (Thomsen, Rydahl-Hansen, & Wagner 2010).

All participants described the perceived maintenance of their pre-CUP normality, or attempts to live as closely to this as possible, as a significant aspect of coping. Continued participation in valued activities was central to this, providing opportunity to sustain a coherent sense of self and distraction from threatening stimuli and appraisals. Unsurprisingly, maintenance of activity and confidence to do so have been widely recognised as important aspects of coping with cancer (Thomsen et al. 2010). While much of the existing literature suggests that avoidance coping leads to negative outcomes for cancer patients (Roesch et al., 2005), the findings of this study indicate that cognitive avoidance via distraction is an adaptive, self-preserving strategy. Therefore, ‘blunting’ (Miller, 1987) strategies may have beneficial effects for individuals with CUP, as demonstrated in other patients with terminal cancer (Block, 2006).

The findings suggested that people living longer-term with CUP increasingly accept their condition and associated challenges over time. This experience, however, was neither universal nor static, with many participants describing conflictual positions of accepting some aspects of their reality and whilst rejecting or denying others. This suggests that acceptance for those living longer-term with CUP is an ongoing dynamic process rather than an acquired state. Definitions of illness acceptance commonly include references to ‘making peace’ with the realities of one’s situation and “willingness to be present with one's illness-related thoughts, feelings, and bodily sensations without judging or making unnecessary attempts to control them” (Secinti, Tometich, Johns, & Mosher, 2019, p.28). Acceptance has been framed as an adaptive cognitive coping strategy linked to lower distress and positive growth (Bussell and Naus, 2010). The potential link between acceptance and positive growth is

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suggested in the findings of this study where participants reported new perspectives and priorities since diagnosis. The reflection from participants that older age makes accepting the realities of CUP easier is consistent with prior findings linking older age and acceptance of cancer (Politi, Enright, & Weihs, 2007).

Finally, participants widely attributed their ability to cope to external support, both from personal relationships and healthcare professionals. This is consistent with the systematic review by Thomsen et al. (2010) which indicated that social support provides a “sense of safety or inner strength” (p.3412). The importance of social support as a coping resource is also theorised by Schaefer and Moos (1998).

### **Theoretical Implications**

The findings are compatible with both Lazarus and Folkman’s TMSC (1984) and Mishel’s UIT (1988). A diagrammatic model and accompanying explanation are presented in Appendix 2-E (p.2-54), synthesising the research outcomes with these two theoretical frameworks to elucidate the mechanisms of the coping process for people living longer-term with CUP.

While the findings correspond in many ways with the propositions of UIT and TMSC, these models are unable to account in totality for the experiences of participants. Sarah’s comment, “I don’t know that I have actually coped. I haven’t had time to cope” captures the possibility that for some people living with CUP, coping may not be a significantly relevant or salient aspect of their experience. There are several possible explanations for this. Firstly, neither model was developed with CUP patients or even cancer patients more generally. Rather, both models have developed through wide application across both acute and chronic presentations of illness, the breadth of which entail such a range of differing experiences that to distil the coping process to a single theoretical model will inevitably be flawed and miss aspects of individuals’ nuanced realities. Secondly, lay applications of the term ‘coping’ often

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mistakenly frame coping as an outcome, rather than a process as per Lazarus and Folkman's proposals. There can therefore be confusion caused by perceptions that coping is the act of mastering stressful situations, rather than managing or enduring to varying degrees throughout them. Corr and Doka (2001) discuss that for this reason referring to 'adaptive strategies' rather than coping may be helpful, although this terminology is also fraught with room for misinterpretation and false emphasis upon the obtainment of an adjusted/adapted/coping state of being. Thirdly, it may be that the emphasis upon coping or adjustment in illness, which have been a prevalent paradigm on dying within psychological and social work studies, overlooks other aspects of the end of life experience which may hold relevance for people with CUP. Nakashima (2003) has argued that the emphasis upon these concepts is the product of western socially constructed attitudes to death and dying as a struggle that must be mastered. This narrow view omits experiences such as emotional healing and spiritual growth that people may experience at the end of life.

### **Answering the Research Questions**

#### **What are the coping experiences of people who are living longer-term with CUP?**

The findings of this study signify that coping for people living longer-term with CUP is a dynamic and multifactorial process. The identified themes and relationships between them correspond with existing coping theory (Lazarus & Folkman, 1984; Mishel, 1988), highlighting the centrality of the appraisal process in patient's ability to manage and respond to stress associated with CUP. As outlined above, the experiences of coping for patients with CUP seems to be similar in many ways to those of comparable cancer patient populations. However, the research highlights several areas where it is possible that patients living longer-term with CUP may face particular challenges to coping. These include: the acute sense of threat associated with loss of control and perceived passivity in relation to medical regimes; and a high volume of medical appointments; as well as the sustained uncertainty associated

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with having a previously unheard-of illness, and therefore limited established knowledge and expectation, which follows an unpredictable trajectory.

### *How do these patients perceive their ability to cope?*

Most participants expressed a consensus that at the point of participation they did feel able to cope. This experience was not, however, static or universal, with participants describing times where they were more pre-occupied and distressed by CUP. Patients who identified with being less able to cope expressed their sense of CUP-related stress leaving them with insufficient resources (both internal and external) to initiate an active coping response.

### *What influences perceptions of coping?*

Reduced perceived coping capacity was found to occur as a result of threat-appraisals regarding fluctuating “fuss and bother” associated with physical symptoms and appointments, as well as ongoing uncertainty. Identified coping strategies were acceptance, avoidance and distraction, hope, and support from others.

### *What are patients’ experiences of coping over time?*

The findings of the study demonstrate that generally the sense of threat associated with CUP reduces over time, although this fluctuates in relation to current CUP-related life-disruptive phenomena. Patients used a mixture of coping styles, using avoidant strategies to manage distressing stimuli, but feeling increasingly able to accept the realities of their circumstances over time.

## **Clinical Implications and Recommendations**

The research findings highlight several points relevant to clinical practice in CUP services. Firstly, clinicians should be mindful of the factors that CUP patients perceive as most threatening to minimise patients’ negative experiences associated with these. In line with the ‘last 1000 days’ initiative (Dolan & Holt, 2017; NHS Improvement, 2016), patient



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time should be prioritised to decrease the perceived disruption caused by frequent appointments where possible. This may be achieved by considering patients' opinions about how their time is best spent, reducing appointment frequency where possible, and minimising patient travel. Greater availability of phone or skype consultation for routine reviews where physical examinations or discussions regarding results of investigations are not required may be one way to facilitate this. Also, investigations should be guided by symptoms, as frequent scans and other investigations are unlikely to impact on patients' outcomes (Fizazi et al., 2015). Individualized approaches to frequency of consultations should be preferred.

Secondly, given the increased potential for CUP patients to experience a subjective loss of control in relation to their medical input, discussion of patient preferences and collaborative decision making is paramount. Thirdly, focusing on optimal symptom management with appropriate access to palliative care services is essential for this patient group, for many of whom physical symptoms have a significant impact upon daily functioning. Fourthly, while uncertainty is an inherent aspect of CUP, provision of adequate information to patients may be important to alleviate this where possible. Especially important may be providing space for patient questions and information giving in routine appointments and signposting to relevant resources such as the CUP foundation and Macmillan's 'Understanding Cancer of Unknown Primary' booklet (2014) which may help patients to gain an understanding of CUP and realise that they are not alone with this 'unusual' condition. Of course, based on the findings that patients cope via a mixture of approach and avoidant strategies, it is crucial that clinicians explore with patients what support or information they feel they need and can manage with at any time as this is likely to fluctuate throughout the patient journey.

Information in relation to expected physical symptoms may be particularly important given the potential for CUP patients to be particularly sensitised to symptom experiences and possible misinterpretation of these. Finally, given the importance of support for coping,

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health care professionals should be particularly aware of patients who have a less robust network of social and family support, who may require additional professional support to enable coping responses.

Psychological interventions aimed at supporting patients with CUP to cope with their illness experiences should focus upon strategies of both avoidance and acceptance, and achieving a balance between these processes in the context of current illness-related threats. While in many ways, the psychological needs of the CUP patients may be similar those of other patients with advanced cancers, results indicate that CUP patients view their condition as 'unusual'. As such, group psychological and supportive interventions aimed at all cancer patients may be less appropriate for CUP patients given the potential for them to feel 'different' to other participants. Clinical psychologists working in oncology settings may have a particular role in providing training and consultation to medical staff working with CUP patients to enable all professionals working in CUP services to better understand the coping challenges faced by CUP patients and how patients can be best supported.

### **Recommendations for Future Research**

Findings have highlighted areas where further research would be valuable. Support from others was highlighted as a significant factor in enabling coping. Future studies should explore the experiences of professionals and carers supporting individuals with CUP and how they cope with the uncertainties faced by those they care for. The potential for misinterpretation of physical symptoms amongst CUP patients was also identified. Research exploring this further or assessing the prevalence of health anxiety in patients with CUP versus other cancers may help to increase understanding of this phenomenon, although it is recognised that the heterogeneous and unpredictable patterns of metastases in CUP may present a challenge to this. While results demonstrate that patients living longer-term with

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CUP feel more able to cope than immediately post-diagnosis, longitudinal research would elucidate patients' experiences over time.

### **Limitations**

The findings of this study are subject to several limitations. Firstly, IPA methodology requires the recruitment of a homogeneous sample; while every effort was made to meet this criterion, the included participants diverged on several factors which may have influenced findings. The extent of metastases differed across the sample and it is possible that the experiences of those with less extensive disease and better response to treatment versus those with a more extensive and symptomatic disease may be quite different and lead to different experiences of coping. Likewise, the site of metastases may influence these experiences, with involvement of the vital organs possibly being perceived as more threatening than secondaries in areas of the body (e.g. lymph nodes) which are less likely to impact survival (Zabora et al., 2001). Another factor which may have caused participants to have had differing experiences was treatment type and recency (Admiraal, Reyners, & Hoekstra & Weebers, 2013). Heterogeneity also presented in relation to time from diagnosis. It is possible that those who had longer to adjust to their diagnosis may have reported greater perceived coping and acceptance. Additionally, the age range of the sample spanned almost 20 years across what may be categorised as middle- and older-age. It has been previously established that experience of cancer is different for individuals in these different life stages (Cimprich, Ronis, & Martinez & Ramos, 2002).

Secondly, as all participants were White British and from the north west of England, findings may not reflect the experiences of people from other localities or ethnic backgrounds. As the age range of the sample was 58-77 years, findings may not account for the experiences of younger or older CUP patients.

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Thirdly, the employment of a convenience sampling relied upon participants opting-in to the study. While the study had a relatively high response rate (83%), a minority of eligible patients did not opt-in. It is possible that those experiencing greatest difficulty with coping may have been less likely to volunteer.

Finally, while efforts were made to incorporate patient perspectives within the design of the research through consultation, it is acknowledged that the scope of this to lead to meaningful outcomes may have been limited by the absence of any patients with CUP within the consulting group and the stage of the research at which this occurred. Opportunity to consult directly with CUP patients at an early stage of the research process could have led to greater potential for CUP survivors to orient the research questions to aspects of their experience that they view as most important.

### **Conclusion**

This study explored the experiences of coping of people living longer-term with CUP. Coping was shown to be a dynamic and multifactorial process, with perceived stress and coping capacity seen to fluctuate in response to contextual phenomena. The results demonstrated that despite being six months or more after diagnosis and clinically stable, CUP continued to play a disruptive role in participants lives and to be associated with uncertainty. Both of these experiences were appraised as significant stressors, with the potential to elevate distress. Despite this, participants reported feeling increasingly able to cope over time since diagnosis, which was enabled through employment of emotion-focused strategies of avoidance, acceptance, hope, and external support systems. These findings correspond with Lazarus and Folkman's TMSC (1984) and Mishel's UIT (1988). In many ways, the experiences of this population are similar to those of other cancer populations, however, patients with CUP may face particular challenges as a result of the uncertainty entailed in their condition. Supportive care which takes these factors into account is essential to enable

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patients living longer-term with CUP to cope with the multiple stressors associated with the condition.

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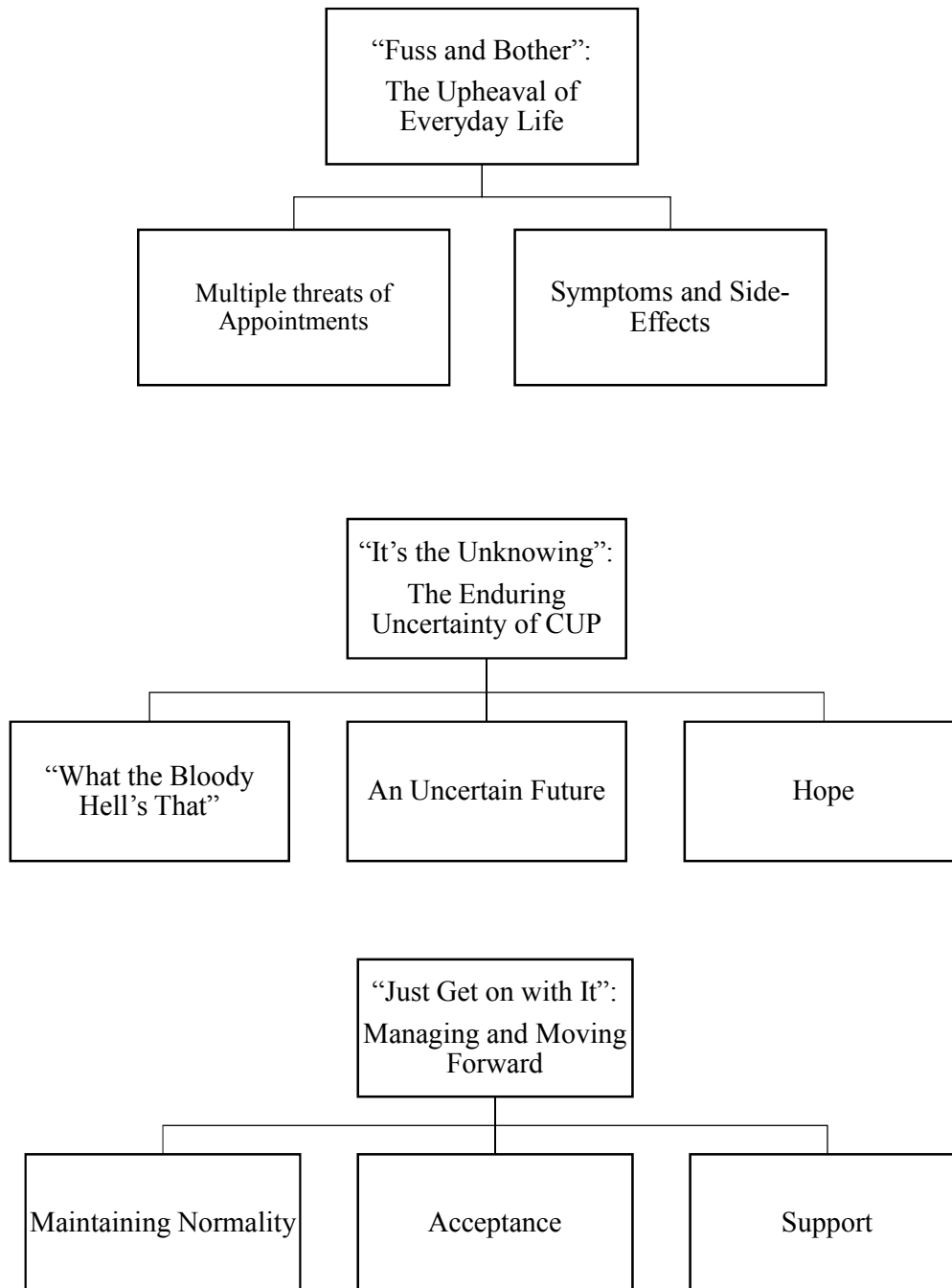
## Tables and Figures

Table 2-A: Sample Characteristics

Age	Gender	Ethnicity	Months since diagnosis	Site(s) of secondary cancer
77	Female	White British	38	Abdominal wall
72	Female	White British	67	Lymph nodes
58	Male	White British	6	Pelvis
76	Female	White British	9	Kidneys, lymph nodes, thoracic cavity
74	Male	White British	7	Liver
67	Male	White British	38	Lymph nodes
77	Male	White British	14	Oesophagus
70	Male	White British	18	Lymph nodes
76	Female	White British	15	Ovaries, liver
76	Female	White British	44	Lymph nodes



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**Figure 2-A: Superordinate and Subordinate Themes**

## Appendices

### Appendix 2-A: Interview Schedule

Interview schedule (Version 0.1, created 11/07/2018)

- **Could you tell me about what things have been like for you since your diagnosis of CUP?**

*Prompts: response to diagnosis, now*

- **What is your understanding of the diagnosis?**

*Prompts: Anything not understood/unclear; had you heard of CUP before?*

- **On a day-to-day basis, how do you deal with having CUP?**

- **Since your diagnosis has there been times when you have felt more or less able to cope?**

- **Has there been any things which have helped you to cope?**

*Prompts: personal qualities and strengths, actions, external resources*

- **Have any things made coping more challenging?**

- **Are there any things that you think would help you feel more able to manage?**

- **Has the way you've dealt with CUP been similar or different to how you have dealt with any other difficult things in your life?**

- **Do you think that knowing the primary site of your cancer would make things different in any ways?**

*Prompts: would anything be easier/more difficult*

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**Appendix 2-B: Theme Development**

**Examples of manual transcript analysis.**

Comments	Transcript (Sarah, p. 9)	Emerging themes
<p>Impact of treatment on appearance/sense of self. More 'relaxed' over time. Time wasted/life and goals on hold.</p>	<p>P: Erm, and my hair's grown back more or less, it's a bit spikey but it...so I feel...I feel more relaxed about myself and I...but I've achieved nil [laughs]</p> <p>I: Hmm</p>	<p>Symptoms and side-effects</p> <p>Easier with time</p> <p>Upheaval of daily life</p>
<p>Multiple investigations-frustration, loss of time, futility.</p>	<p>P: Fourteen months of...of not...not easy examinations and all very upsetting knowing that it...it...whatever they look at is not going...there's nothing that can be done</p> <p>I: Hmm</p>	<p>Burden on time</p> <p>Multiple tests and investigations</p>
<p>Fatigue. Concern about loved ones.</p>	<p>P: Erm, it's very draining indeed. And I've had to worry about my husband, you know, this is not easy for him, we're not used to his...we've never had anything...I...I have...I've had two cancers but I've just followed a normal trail of</p> <p>I: Hmm</p>	<p>Concern for family</p>
<p>CUP seen as 'different', compared to other cancers, unpredictable.</p>	<p>P: Treatments and...and expected to get better and I have done. This is...is...is really weird, it...it's not at all what one expects...would expect. I actually made a comment here there seems to be a parallel with surviving an old age because in [laughs] old age you don't know what's gonna hit you next. We have so many friends who have sudden illnesses</p> <p>I: Hmm</p>	<p>Uncertainty: CUP as 'different'</p> <p>Uncertain trajectory</p>
<p>Comparison to ageing process- similar unpredictability? Or part of normal ageing to experience 'sudden illness'? Injustice/lack of control.</p>	<p>P: That, erm...but they all seem to be very recognisable [laughs] with...with erm...erm treatments that can help and support them</p>	<p>Loss of control in CUP</p>

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Comments	Transcript (David, p.3)	Emerging themes
<p>Keeping busy distracted as a way of coping.</p> <p>Fear of time to think? Could make illness worse/increase distress?</p>	<p>P: And then I've got grandkids, and I have my own caravan but we got another one for the kids to use with the grandkids, but I have to tow it wherever it's going, dump it, and come back, you know, then go and pick it up, so I'm always busy. It's the only way to do it, I mean if you sit down and start worrying about it, you're going to go quick aren't you! [Laughs]</p> <p>I: Hmm</p> <p>P: But, I mean, this last result I only had last Thursday, I think my last ones were, I think. Yeah, when she asked me about seeing you</p> <p>I: Yeah so it was quite recent</p>	<p>Distraction Avoidance</p>
<p>Perception of self as an unusual case within an unusual illness- positively framed, feeling fortunate. Doctors not having the answers. Hope or denial? Creation of a narrative to make sense of things.</p>	<p>P: And they said to me, normally with a cancer of unidentified primary, from what I can gather off what she said was, the...the primary appears quite quickly, after you've been diagnosed as cancer with unidentified primary. And in my case I've gone nearly two years now, so she said that's good in itself, but she said "we don't quite understand the biology of it all" themselves, so...and I just think "well if they can't find it I haven't got it, have I?" Scan's not showing anything, so, you've just got to look on the bright side, don't you? [laughs]</p> <p>I: Hmm</p>	<p>Uncertainty- lack of information Hope Optimism</p>
<p>CUP as strange Increased anxiety- fear of 'bad news' versus desire to 'know' and clarity of treatment plan</p>	<p>P: I'll worry about it when I go and they tell me they've found something. Strange really, it's just odd. I mean, I must admit once or twice I've been and, like I say, a couple of nights before your mind starts "are they going to find something?" and I sometimes think, "I wish they'd find something" then at least I'd go and they'd say "right, we're going to do this, this, and this and they're going to get rid of it"</p>	<p>CUP as unusual Appointment anxiety Desire to 'know'</p>

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Comments	Transcript (Joanne, p.8)	Emerging themes
<p>Avoidance of questions/additional information. ? Acceptance of the unknown aspects of the illness- no point in asking. CUP as 'strange'.</p>	<p>P: Yes, so...I never ask questions about it. I never say, "when you say cancer of unknown primary, where could it be", sort of thing, or "where does it tend to be?". Obviously, because it's <i>unknown</i> they don't know. But...no. So...strange</p> <p>I: Yeah, and that not really asking many questions- is that just because you've not really wanted to know or?</p>	<p>Avoidance of salient information Acceptance of the unknown CUP as unusual</p>
<p>Making own narrative to make sense based on available information- Hopeful interpretation of the unknown status of the primary</p>	<p>P: No, it's just because I look at it that I've had the chemo and it's cleared the other up...it must have cleared the other up, you know, the unknown one, because when I have CT scans and that they just say it's all clear. But, I suppose it wouldn't be cancer of unknown primary if they could [laughs]</p> <p>I: yeah, if it were as simple as that</p>	<p>Hope/optimism Making sense</p>
<p>Difficult to comprehend/make sense of the unknown</p>	<p>P: Yeah, yeah. But it...it does interest me that it's called a cancer of unknown primary, and yet it's probably still in your body, or it's not. It's a difficult one, that one, to explain really</p> <p>I: Yeah, certainly, and again looking at the booklet there, it says something on it about coping with uncertainty doesn't it, which I think is there for any kind of cancer but can be more so with Cup sometimes</p>	<p>Uncertainty Confusion</p>
<p>Hope that the treatment has 'cured' the primary-based in reality? Or denial?</p>	<p>P: Yeah, as I say, even now with that, that it's uncertain, I've still got in my mind that the chemo has cleared up the other one so it's obviously gone through my body and wherever it was...I did have a little thing removed off my face here, a little...and that, you know...whether that could have been it? But they gave me the all clear off it afterwards</p>	<p>Hope/optimism Making sense Denial</p>
<p>No desire to know more- 'good enough' understanding</p>	<p>I: Yeah. But it sounds like that's a good enough explanation to give you a bit of certainty about it</p> <p>P: Yeah, yeah, yeah, that's about the only...you know....yep</p>	<p>Acceptance of remaining uncertainty</p>

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**Examples of clustered ‘emerging themes’ to form superordinate or subordinate themes.**

<b>Emerging themes</b>	<b>Superordinate/subordinate cluster</b>
Adaptation	Maintaining Normality
Avoidance	
Keeping busy	
Distraction	
Carrying on as normal	
Denial	
Cognitive avoidance	
Behavioural avoidance	
Avoidance of information	
Avoidance of reminders	
Ill but not <i>ill</i>	
Gratitude	Acceptance
Feeling fortunate	
Part of normal ageing	
Making the most of remaining time	
Getting used to it	
Easier with time	
Accepting uncertainty	
Making sense	
Coming to terms	
Understanding CUP	

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**Examples of supporting quotations for superordinate/subordinate themes (grouped using Microsoft Excel).**

Superordinate theme	Subordinate theme	Contributing emerging theme	Example quotation 1	Example quotation 1
“It’s the Unknowing”: The Enduring Uncertainty of CUP			P4p9 I’ve had two cancers but I’ve just followed a normal trail of [...] Treatments and...and expected to get better and I have done [...] This is...is...is really weird, it...it’s not at all what one expects...would expect	P5p14: there’s one question...how...it keeps coming into my mind all the time...if it’s secondary, it’s coming from somewhere, right? It must be cancer of somewhere else in the body. Now, how can’t we tell in this day and age where it’s coming from? This is the big question in my head.
	“What the bloody hell’s that?!”		P1p11: It’s not advertised like all the other cancers, you hear on the news, but not CUP- You don’t see any posters up in the surgery, there’s nothing, you know, but there’s plenty of posters or on the screen about cancer but nothing about CUP, but I suppose it would have opened my eyes a bit	P6p5: Well I just say “look, they found cancer cells, they don’t know where they’ve originated from. They’ve taken them cancer cells out and I’m still here, and there’s no more shown up, so” and that’s the easiest way I can explain it [...] if you don’t understand it, people aren’t going to understand it are they?
		Never heard of it		P1p9: No never, so, erm, that was a completely new to me
		Other’s lack of understanding	P4p27 They argue with me, “no, no such thing” [laughs] it’s one of the reasons why I didn’t want to go back to the art groups because I...I don’t want to talk about it to anybody [...] Erm, they won’t believe	P8p10: the lads I think sometimes, unless they’ve seen my appointments, they think ‘you’re pulling my leg’, you know,

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An uncertain future	P4p13 So it's just lack of information about how I'm...how I'm developing	P2p5: Well, it is a big mystery really isn't it! [laughs] You know, I can't pinpoint anything I think I've got a... I've got I think a good grasp of it now but it's just the thoughts that it can be popping up anywhere sort of thing that's just, it's difficult to live with sometimes
Fear of decline	P4p13 pain worries me, I haven't got any at the moment but I don't know how I would react. [...] I don't like feeling helpless, I don't want to feel helpless, I don't want to feel dependant	P2p13: Yeah it's very difficult. I know I've got two tumours and I know they were growing and I know that this last lot of chemo has shrunk them down but they're still there and in the past 3 months they could have gone up in leaps and bounds for all I know, or they could be sitting there still just not progressing, hopefully [laughs]
Interpretation of physical symptoms	P8p9: I've been alright since. I got a lump last Christmas that appeared and I thought "oh God, here we go [...]" So I went and had my scan, and I said while I'm there, "I've got another lump", she said "oh yeah, that's definitely s lump", and then my results came back, I was expecting 'this is going to be it', and she said, "no, it's clear"	P10p4: I just had another scan. I hadn't...my tum hadn't been right or something...I do have a pretty sort of solid tum "but look at it this way, if there's anything wrong, they can do something about it, and if everything's ok, you can go away and you'll be ok" and as it turned out it was ok. There is a little cyst or something but nothing too, you know, nothing untoward. she just said everything was clear, clear, clear.
Hope	P1p16: I like to think that I am a fighter, you know, just hope that it ...I put it off and you know	P6p10: take everything when it comes, and cross that bridge when it does come. And hope there's not a big toll on it.
Opportunity for longer life/cure	P4p52 another thing is if...if I've got rid of the primary, why can't I get rid of the secondaries? My husband has stayed	P5p12: what's at the back of my mind is this drug that I'm on did hold it, did shrink it, so whether it's got next time...that it's there the same or not, we know it



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with that idea

can do it

[...] if it is coming back, basically, you know raising its ugly head again, we know that treatment does work [...] And there's a possibility that I go back on it.

Denial

P3p35: But it would be nice actually if they did another biopsy, and this is what frustrates me, they keep saying...because if it is another one and they look, they might say "ooh it's not there, the cancer's gone!"

P5p21: I do not think of an end. It never comes in my head about an end. To me there is no end.

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**Appendix 2-C: Reflective Journal Excerpts**10/06/2019- Pre-data collection

First two interviews scheduled for Friday. Calls made to participants to arranged- surprised when one lady sounded quite sprightly on the phone. I think I have been expecting that participants will mainly be really struggling- maybe this won't be the case. Limited knowledge about what 'clinical stability' from the medical perspective actually means- (speak to [REDACTED] [REDACTED] [field supervisors] about this).

Assumptions going in to interview process- that patients will be quite frail/visibly unwell- probably based on my ideas of what a 'typical' patient with advanced cancer or during treatment might look like. This is strange really as patients on placement don't necessarily look this way- influence of stereo-types from media/family. Not having met anybody with CUP before- feels a bit mysterious so think I'm expecting the worst- based probably on the literature but also attitudes of Medics in CUP network. Likewise, expecting participants will probably find talking about their experiences quite difficult/distressing.

12/07/2019- Reflections After Interview 4

Participant 4- most distressed so far, seemed that life had been placed of pause for CUP. Felt incredibly sad for this lovely lady who clearly has so many ambitions and goals that she currently doesn't feel able to pursue. I think that after the first three this has come as a bit of a surprise, although probably more what I expected initially. Focus upon suicide as a 'way out' - some really hard conversations- could really sympathise with her position that it probably would be a 'kinder' end- has left me thinking and feeling frustrated about UK laws around assisted suicide for those that do end up with little quality of life and lots of pain etc. Had to contact Anna re. risk concerns, actions carried out to pass concerns on to specialist

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nurse. Feel conflicted about this- necessity of carrying out professional obligations vs the sense that by reducing 'risk' it may also reduce this lady's access to the thing that is providing her with a safety net/ability to continue knowing she can remain in control of her own destiny.

### 27/08/2019- Reflections after Interview 8

Interview carried out with male participant in own home- genuinely surprised at how well this man seems to be managing with his situation- very personable/humorous, laughed easily about the uncertainties faced, seemed to have come to a place of accepting how things are. helped by? – no symptoms, secondary cancer treated, long period of wellness since treatment, lots of interests and distractions.

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**Appendix 2-D: Occurrences of Themes by Participant**

Superordinate theme	Subordinate Theme	Participants
“Fuss and Bother”: The Upheaval of Everyday Life		Sarah, Peter, Ruth, Graham, Joanne
	Multiple threats of appointments	Chris, Sarah, Graham, Stephen, David, Ruth, Joanne
	Symptoms and side-effects	Emily, Paula, Chris, Sarah, Peter, Graham, Ruth, Joanne
“It’s the Unknowing”: The Enduring Uncertainty of CUP		All
	“What the bloody hell’s that!?”	Emily, Sarah, Graham, Stephen
	An uncertain future	Emily, Paula, Chris, Sarah, Stephen, David, Ruth, Joanne
“Just Get on With It”: Managing and Moving Forwards	Hope	Emily, Chris, Sarah, Peter
		Emily, Paula, Chris, Graham, Stephen, David
	Maintaining normality	All
	Acceptance	Emily, Chris, Sarah, Peter, Graham, Stephen, David, Ruth, Joanne
	Support	Emily, Paula, Chris, Sarah, Peter, Graham, David, Ruth, Joanne

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## Appendix 2-E: Theoretical Synthesis

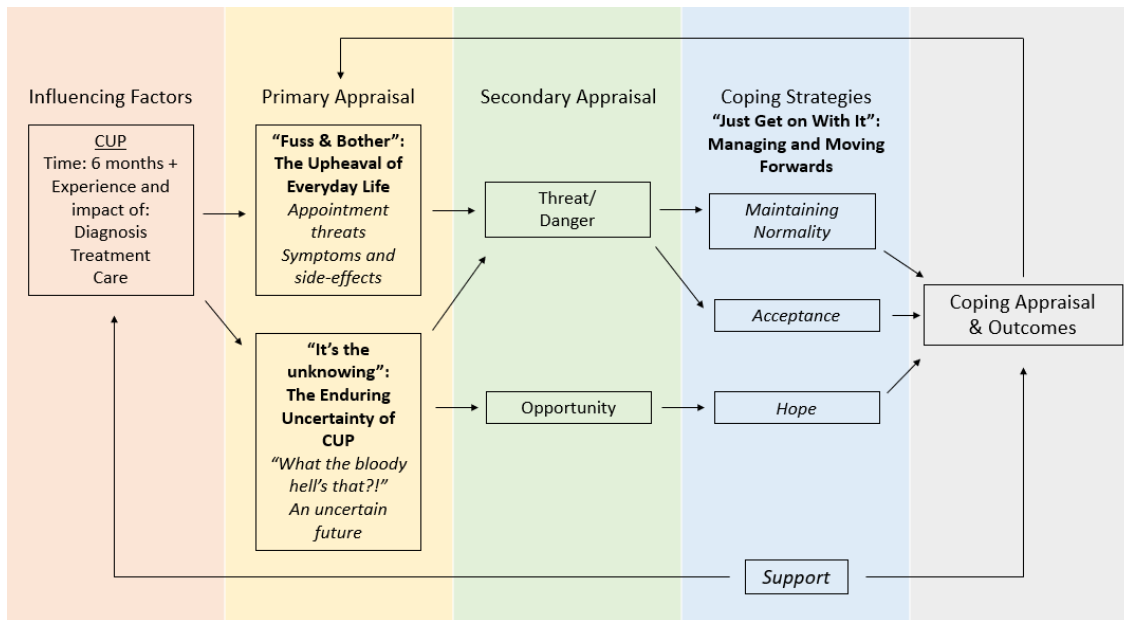


Figure 2-E-1. Model of Coping Longer-Term with CUP Based Upon Study Findings and Existing Coping Theory

According to Lazarus and Folkman's TMSC, the stressor exists within the context of personal and situational 'influencing factors.' For patients living longer-term with CUP, situational factors including time since diagnosis and experiences of diagnosis, treatment, and care are likely to have contributed towards patients' illness experiences. Findings demonstrated that support is a significant personal factor with potential to influence the sense patients make of their illness in context.

Lazarus and Folkman theorised that these experiences are subject to two stages of appraisal. Findings showed that CUP experiences were initially appraised as both highly disruptive of patients' everyday lives and entailing a high degree of uncertainty. These interpretations, in line with the model, were subject to secondary appraisal of the meaning these subjective experiences have to the individual. Perceived "fuss and bother" and uncertainty were appraised predominantly as threatening or dangerous. However, consistent

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with Mishel's UIT (1988), uncertainty was also appraised by some participants at the secondary stage as opportunity for more favourable outcomes.

Secondary appraisals within the TMSC serve to prompt the employment of emotion-focused and problem-focused coping strategies. Consistent with Thomsen et al.'s (2010) review findings, participants relied predominantly upon emotion-focused strategies to reduce negative emotional responses. Strategies were compiled under the theme of "Just get on with it": Managing and Moving Forwards', within which patients described their behavioural and cognitive attempts to maintain their pre-CUP sense of self and distract themselves via avoidant strategies. These findings also fit with Moos and Schaefer's (1993) concepts of approach and avoidance coping, with acceptance used when participants felt able to orient attention towards CUP and distraction used to orient away and protect from the negative emotional experiences associated with CUP. The concept of hope was also found to be a significant emotion-focused coping strategy. This was suggested to be protective regardless of accuracy. Findings suggested that participants drew upon different strategies at different times and moved back and forth between approach and avoidance coping to manage with the fluctuating threat associated with CUP. Data suggested that as time had passed, patients progressively moved towards strategies of acceptance.

In the final stage of Lazarus and Folkman's TMSC, coping itself is appraised, along with the outcomes of coping efforts forming a 'transactional' loop feeding back into primary stress appraisals. Accordingly, participants for the most-part expressed a sense of being able to employ coping strategies and therefore cope effectively, reducing CUP-associated distress. Where patients reported feeling less able to employ active coping strategies, particularly behavioural responses, coping was perceived as less effective, potentially creating negative appraisals which serve to increase the sense of perceived threat in the re-appraisal process. Furthermore, participants described support from personal relationships and the healthcare

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system as facilitative of increased coping capacity and outcomes, as such this relationship is represented in figure 2-E-1 as a complementary adaptation to the original model.

**Appendix 2-F: Target journal author guidelines****1.1** *European Journal of Cancer Care* Author Guidelines

1. SUBMISSION
2. AIMS AND SCOPE
3. MANUSCRIPT CATEGORIES AND REQUIREMENTS
4. PREPARING THE SUBMISSION
5. EDITORIAL POLICIES AND ETHICAL CONSIDERATIONS
6. AUTHOR LICENSING
7. PUBLICATION PROCESS AFTER ACCEPTANCE
8. POST PUBLICATION
9. EDITORIAL OFFICE CONTACT DETAILS

**1. SUBMISSION**

Authors should kindly note that submission implies that the content has not been published or submitted for publication elsewhere except as a brief abstract in the proceedings of a scientific meeting or symposium.

**Once the submission materials have been prepared in accordance with the Author Guidelines, manuscripts should be submitted online at <http://mc.manuscriptcentral.com/ecc>**

The submission system will prompt authors to use an ORCID iD (a unique author identifier) to help distinguish their work from that of other researchers. [Click here](#) to find out more.

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For help with submissions, please contact: [ECCedoffice@wiley.com](mailto:ECCedoffice@wiley.com)

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*The European Journal of Cancer Care* will consider for review articles previously available as preprints. Authors may also post the [submitted version](#) of a manuscript to a preprint server at any time. Authors are requested to update any pre-publication versions with a link to the final published article.



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### 2. AIMS AND SCOPE

The *European Journal of Cancer Care* aims to encourage comprehensive, multiprofessional cancer care across Europe and internationally. It publishes original research reports, literature reviews, commentaries, guest editorials, letters to the Editor and special features on current issues affecting the care of cancer patients. The Editor welcomes contributions which result from team working or collaboration between different health and social care providers, service users, patient groups and the voluntary sector in the areas of:

- Primary, secondary and tertiary care for cancer patients
- Multidisciplinary and service-user involvement in cancer care
- Rehabilitation, supportive, palliative and end of life care for cancer patients
- Policy, service development and healthcare evaluation in cancer care
- Psychosocial interventions for patients and family members
- International perspectives on cancer care

The journal provides a forum for multiprofessional and service-user dialogue, and the reporting of original research or rigorous reviews within the field of cancer care both in Europe and internationally. The journal welcomes original research, reviews and correspondence from individuals whose first language is not English, but places great weight in its published papers on accuracy, fluency and clarity of expression as befits any journal published for an international and multiprofessional audience.

### 3. MANUSCRIPT CATEGORIES AND REQUIREMENTS

#### Original Papers

Original articles, which report on new research findings or conceptual analyses that make a significant contribution to knowledge will be considered for publication.

WORD LIMIT: 4000 word limit, excluding references, figures, and tables).

ABSTRACT: A structured abstract is required (200 words maximum) under the following sub-headings: Objective; Methods; Results and Conclusion. The abstract should describe the purpose, study population, methodology, setting and details of the variables under study. It should also highlight the main results and conclusions of the study.

MAIN TEXT: Should be structured under the following sub-headings: introduction, methods, results, and discussion.

RESEARCH REPORTING CHECKLIST: may be required - see section 5 Editorial Policies and Ethical Considerations.

#### Review Papers

WORD LIMIT: 5000

ABSTRACT: A structured abstract is required (200 words maximum) under the following sub-headings: Introduction, Methods, Results, Conclusion.

MAIN TEXT: Reviews must contain a clear exposition of the background, search strategy, databases, keywords and any selection/evaluation criteria used in the review where appropriate. It should also highlight the main results and conclusions of the study.

RESEARCH REPORTING CHECKLIST: Please see [section 5](#) Research Reporting Guidelines.

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ABSTRACT: N/A

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authors for approval.  
RESEARCH REPORTING CHECKLIST: N/A

### **Commentaries**

WORD LIMIT: 1500  
ABSTRACT: N/A  
MAIN TEXT: evidence-based opinion pieces involving areas of broad interest.  
RESEARCH REPORTING CHECKLIST: N/A

### **Registered Reports**

*European Journal of Cancer Care* welcomes Registered Reports. This is a new article type designed to increase the transparency and reproducibility of hypothesis-driven science. Registered Reports differ from the conventional research article as part of the review process is conducted before authors collect and analyse data. The cornerstone of the Registered Reports format is that a significant part of the manuscript will be assessed prior to data collection, with the highest quality submissions accepted in advance. Please view the full Registered Reports author guidelines [here](#) to help prepare your submission.

## **4. PREPARING THE SUBMISSION**

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Cover letters are not mandatory; however, they may be supplied at the author's discretion.

### **Parts of the Manuscript**

The manuscript should be submitted in separate files: title page; main text file; figures.

### **Title page**

The title page should contain:

- i. A short informative title containing the major key words. The title should not contain abbreviations (see Wiley's [best practice SEO tips](#));
- ii. A short running title of less than 40 characters;
- iii. The full names of the authors and email address and telephone number of corresponding author;
- iv. The author's institutional affiliations where the work was conducted, with a footnote for the author's present address if different from where the work was conducted;
- v. Acknowledgments.
- vi. Conflict of Interest statement for all authors;
- vii. Funding statements

### **Authorship**

Please refer to the journal's authorship policy the [Editorial Policies and Ethical Considerations](#) section for details on eligibility for author listing.

### **Acknowledgments**

Contributions from anyone who does not meet the criteria for authorship should be listed, with permission from the contributor, in an Acknowledgments section. Financial and material support should also be mentioned. Thanks to anonymous reviewers are not appropriate.

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### ***Conflict of Interest Statement***

Authors will be asked to provide a conflict of interest statement during the submission process. For details on what to include in this section, see the section 'Conflict of Interest' in the [Editorial Policies and Ethical Considerations](#) section below. Submitting authors should ensure they liaise with all co-authors to confirm agreement with the final statement.

### **Main Text File**

As papers are double-blind peer reviewed the main text file should not include any information that might identify the authors.

The main text file should be presented in the following order:

- i. Title, abstract and key words;
- ii. Main text;
- iii. References;
- iv. Tables (each table complete with title and footnotes);
- v. Figure legends;
- vi. Appendices (if relevant).

Figures and supporting information should be supplied as separate files.

### ***Title***

Should be clear, descriptive, and avoid the use of metaphor, elaborate language or respondent quotations which are less likely to be discovered by the electronic algorithms of modern search engines. Titles should include words pertaining to population or sample, the method of inquiry, any tools or measures used and its key findings as appropriate. These words should be reiterated at least once in the abstract.

### ***Keywords***

Please provide six keywords. When selecting keywords, Authors should consider how readers will search for their articles. These words should be reiterated at least once in the abstract and or title. Keywords should be taken from those recommended by the US National Library of Medicine's Medical Subject Headings (MeSH) browser list at [www.nlm.nih.gov/mesh](http://www.nlm.nih.gov/mesh).

### ***Main Text General Style Points***

- **Anonymity:** As papers are double-blind peer reviewed, the main text file should not include any information that might identify the authors.
- **Spelling:** The journal uses British UK spelling; however, authors may submit using either UK or US spelling, as this is converted to UK spelling by the production team.
- **Footnotes:** to the text are not allowed and any such material should be incorporated into the text as parenthetical matter.
- **Abbreviations:** In general, terms should not be abbreviated unless they are used repeatedly and the abbreviation is helpful to the reader. Initially, use the word in full, followed by the abbreviation in parentheses. Thereafter use the abbreviation only.
- **Units of measurement:** Measurements should be given in SI or SI-derived units. Visit the Bureau International des Poids et Mesures (BIPM) website at [www.bipm.fr](http://www.bipm.fr) for more information about SI units.
- **Numbers:** numbers under 10 are spelt out, except for: measurements with a unit (8mmol/l); age (6 weeks old), or lists with other numbers (11 dogs, 9 cats, 4 gerbils).

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- **Trade Names:** Chemical substances should be referred to by the generic name only. Trade names should not be used. Drugs should be referred to by their generic names. If proprietary drugs have been used in the study, refer to these by their generic name, mentioning the proprietary name and the name and location of the manufacturer in parentheses.

### References

References should be prepared according to the *Publication Manual of the American Psychological Association* (6th edition). This means in text citations should follow the author-date method whereby the author's last name and the year of publication for the source should appear in the text, for example, (Jones, 1998). The complete reference list should appear alphabetically by name at the end of the paper.

A sample of the most common entries in reference lists appears below. For more information about APA referencing style, please refer to the [APA FAQ](#). Note that for journal articles, issue numbers are not included unless each issue in the volume begins with page one, and a DOI should be provided for all references where available.

#### Journal article

Beers, S. R. , & De Bellis, M. D. (2002). Neuropsychological function in children with maltreatment-related posttraumatic stress disorder. *The American Journal of Psychiatry*, 159, 483–486. doi:10.1176/appi.ajp.159.3.483

#### Book

Bradley-Johnson, S. (1994). *Psychoeducational assessment of students who are visually impaired or blind: Infancy through high school* (2nd ed.). Austin, TX: Pro-ed.

#### Internet Document

Norton, R. (2006, November 4). How to train a cat to operate a light switch [Video file]. Retrieved from <http://www.youtube.com/watch?v=Vja83KLQXZs>

### Tables

Tables should be self-contained and complement, not duplicate, information contained in the text. They should be supplied as editable files, not pasted as images. Legends should be concise but comprehensive – the table, legend, and footnotes must be understandable without reference to the text. All abbreviations must be defined in footnotes. Footnote symbols: †, ‡, §, ¶, should be used (in that order) and \*, \*\*, \*\*\* should be reserved for P-values. Statistical measures such as SD or SEM should be identified in the headings.

### Figure Legends

Legends should be concise but comprehensive – the figure and its legend must be understandable without reference to the text. Include definitions of any symbols used and define/explain all abbreviations and units of measurement.

### Figures

Although authors are encouraged to send the highest-quality figures possible, for peer-review purposes, a wide variety of formats, sizes, and resolutions are accepted. [Click here](#) for the basic figure requirements for figures submitted with manuscripts for initial peer review, as well as the

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more detailed post-acceptance figure requirements.

Figures may be reproduced in colour online free of charge. Please note, however, that it is preferable that line figures (e.g. graphs and charts) are supplied in black and white so that they are legible if printed by a reader in black and white.

### **Additional Files**

#### ***Appendices***

Appendices will be published after the references. For submission they should be supplied as separate files but referred to in the text.

#### ***Supporting Information***

Supporting information is information that is not essential to the article, but provides greater depth and background. It is hosted online and appears without editing or typesetting. It may include tables, figures, videos, datasets, etc.

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The acceptance criteria for all papers are the quality and originality of the research and its significance to journal readership. Except where otherwise stated, manuscripts are double-blind peer reviewed. Papers will only be sent to review if the Editor-in-Chief determines that the paper meets the appropriate quality and relevance requirements.

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*European Journal of Cancer Care* encourages authors to share the data and other artefacts supporting the results in the paper by archiving it in an appropriate public repository. Authors should include a data accessibility statement, including a link to the repository they have used, in order that this statement can be published alongside their paper.” If data cannot be shared for reasons such as ethical, privacy, or confidentiality matters, please inform the Editors in your cover letter on submission.

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In recognition of the significance of data as an output of research effort, Wiley has endorsed [the FORCE11 Data Citation Principles](#) and is implementing a mandatory data citation policy. Journal policies should require data to be cited in the same way as article, book, and web citations and authors are required to include data citations as part of their reference list. Data citation is appropriate for data held within institutional, subject focused, or more general data repositories. It is not intended to take the place of community standards such as in-line citation of GenBank accession codes.

When citing or making claims based on data, authors must refer to the data at the relevant place in the manuscript text and in addition provide a formal citation in the reference list. We recommend the format proposed by the [Joint Declaration of Data Citation Principles](#):

*Authors; Year; Dataset title; Data repository or archive; Version (if any); Persistent identifier (e.g. DOI)*

### Human Studies and Subjects

For manuscripts reporting medical studies that involve human participants, a statement identifying the ethics committee that approved the study and confirmation that the study conforms to recognized standards is required, for example: [Declaration of Helsinki](#); [US Federal Policy for the Protection of Human Subjects](#); or [European Medicines Agency Guidelines for Good Clinical Practice](#). It should also state clearly in the text that all persons gave their informed consent prior to their inclusion in the study.

Patient anonymity should be preserved. Photographs need to be cropped sufficiently to prevent human subjects being recognized (or an eye bar should be used). Images and information from individual participants will only be published where the authors have obtained the individual's free prior informed consent. Authors do not need to provide a copy of the consent form to the publisher; however, in signing the author license to publish, authors are required to confirm that consent has been obtained. Wiley has a [standard patient consent form](#) available for use.

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Accurate and complete reporting enables readers to fully appraise research, replicate it, and use it. Authors are encouraged to adhere to the following research reporting standards.

- [CONSORT](#) checklist for reports of randomised trials and cluster randomised trials
- [TREND](#) checklist for non-randomised controlled trials
- [PRISMA](#) checklist for systematic reviews and meta-analyses
- [STROBE](#) checklist for observational research
- [SRQR](#) or [CASP](#) checklist for qualitative studies
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## CRITICAL APPRAISAL

This paper is intended to provide a critical appraisal of the research study entitled ‘Patients’ experiences of coping longer-term with cancer of unknown primary’(CUP). The paper commences with an overview of the findings of both the literature review and research paper incorporated in the thesis. The remainder of the paper is split into three sections focusing upon: epistemological and ontological assumptions and apparent dissonance between sections one and two of the thesis; reflections upon the position of the researcher and importance of researcher reflexivity; and reflections upon the research process and the study’s strengths, limitations, and implications for future research.

### **Overview of the Research Findings**

The systematic review synthesised the results of 15 quantitative studies examining the relationship between uncertainty and psychological distress amongst younger adults with cancer. Findings indicated uncertainty and psychological distress are significantly associated for patients at differing time points in the cancer journey and with differing types and grades of cancer. Analyses of causality in the relationship tended to suggest that uncertainty is causal of distress which lends support to Mishel’s uncertainty in illness theory (1988). Findings indicated the potential for communication to act as an intervention for reducing uncertainty in order to minimise experiences of psychological distress amongst younger adults with cancer.

The research paper aimed to understand the coping experiences of people living longer-term with CUP. Interpretative phenomenological analysis was used to generate themes from interview data from 10 participants. Three superordinate themes were generated from the data. “‘Fuss and Bother’: The Upheaval of Everyday Life’ captured the disruptive nature of CUP in patients’ lives and impact on ability to engage with valued activity. This was seen to adversely affect patients’ through negative appraisals, leading to increased anxiety, perceived loss of control, and challenged concepts of identity. “‘It’s the Unknowing’: The Enduring Uncertainty of CUP’ brought together patients’ ongoing experiences of uncertainty,

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highlighting that while uncertainty associated with an absence of transferrable expectations and anxieties about the future were perceived as highly threatening, some participants appraised uncertainty as opportunity and were able to generate hope in response to unknown aspects of CUP. “‘Just Get on With It’: Managing and Moving Forwards’ subsumed the various strategies used by participants to cope with CUP-related threats, including emotion-focused strategies of maintaining normality through cognitive and behavioural avoidance, moving increasingly towards adaptive acceptance of the realities of CUP, and drawing on the external support of others to bolster internal resources for coping. Findings demonstrated that while the experiences of patients living longer-term with CUP are in many ways similar to those of other populations living with cancer, this population may face particular challenges, including high levels of threat associated with perceived passivity and loss of control in the face of intensive medical regimes, and living with the relentless uncertainties of having an illness perceived as unusual, unpredictable, and volatile. Despite these challenges, the majority of patients reported generally feeling able to cope, and that this had become easier over time since diagnosis. Findings indicate that this patient population would benefit from more collaborative decision making processes in relation to their medical care and how their time is used, opportunity to gather more information about their condition to reduce uncertainties where possible, and that those experiencing high levels of psychological distress may benefit from interventions to enhance skills of avoidance and acceptance.

Together, the systematic review and research paper offer an insight into the experiences of distress and uncertainty faced by cancer patients and the ways that these might be coped with. Jointly, findings demonstrate the potential for uncertainty to generate distress and reduce subjective coping. The findings contribute to the well-established psycho-oncology evidence base, by providing insights into the experiences of younger cancer

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survivors and CUP patients, two cancer-patient groups that have been previously overlooked respectively in systematic reviews and empirical research.

### **Ontological and Epistemological Assumptions of the Thesis**

The ontological assumptions by which research is underpinned inform the epistemological position taken, and subsequently the methodological approach (Mack, 2010). The two over-arching positions in ontological theory are realism and relativism (Willig, 2008). Realist positions assume there to be an objective reality made up of structures and objects with observable cause and effect relationships. Relativist positions, on the other hand, posit that reality is not objectively knowable and instead is constructed by the individual based upon personal interpretations (Mertens, 2010; Willig).

These opposing understandings of the essential nature of reality have informed differing epistemological theories of and approaches to how knowledge might be attained. Epistemological assumptions based upon realist ideas assume that a singular reality can be known or 'seen'. This stance underlies empiricist and positivist paradigms, most often associated with quantitative research methods which seeks to use 'objective' measurement to reveal universal 'truths' (Darlaston-Jones, 2007). Relativist ideas, on the other hand, have informed the development of epistemological paradigms such as social constructionism and interpretivism which are broadly allied with qualitative research methodologies, concerned with individual, subjective perceptions and the construction of meaning in context. Resultingly, qualitative and quantitative research methods can be understood to stem from conflictual theoretical ancestries and are frequently framed as incompatible (Howe, 1992).

For this reason, during the conception phase of this thesis, I grappled uneasily with the theoretical implications of conducting a quantitative literature review and a qualitative research paper. While I was assured by conversations with my research supervisors that such an undertaking was not unusual, I had reservations about the meaning and implications of

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mixing paradigms in this way and the potential for incongruence with my own ontological and epistemological views.

Personally, I have come to take a relativist view which is consistent with critical realism. Critical realist theory suggests that “no one can step out of their conceptual world and see if reality ‘really exists’ or what it ‘essentially is,’ free of conceptual prejudging” (Danermark, Ekstrom, Jakobsen, & Karlsson, 2002, p. 18). This, I believe, has implications for both qualitative and quantitative research, however, is an issue that is rarely acknowledged explicitly in quantitative studies which are usually presented within a positivist frame, as though presenting universal truths. However, with a critical realist lens in place, I believe that both qualitative and quantitative research can offer much to our shared understanding of psychological issues. Thus, my own views also align somewhat with pragmatist ideas, further understanding of which has helped me through the thesis process to reconcile the apparent incompatibility between the systematic review and research paper.

Pragmatism, similarly to constructionism, rejects positivist conceptions that scientific enquiry and a single scientific method can lead to the uncovering of ‘truths’ (Mertens, 2010). As the paradigm has evolved, the focus has been upon a common sense approach to research (Mertens), and pragmatic ideas have come to be associated with mixed methods research (Tashakkori & Teddlie, 2003). In transcending concerns about metaphysical concepts of ‘truth’ and ‘reality’ which have conventionally created a barrier between research methodologies, pragmatism expounds a dual understanding that “there is a single ‘real world’ and that all individuals have their own unique interpretations of that world” (Mertens, p.36), consistent with critical realist ideas. Based on this, both qualitative and quantitative research methods are compatible with pragmatism which emphasises that the method should be dictated primarily by the research aims (Patton, 2002).

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### **The Researcher Position**

Consistent with critical realist and pragmatist perspectives, Foster (2009) highlights the false dichotomy often used to position the researcher as an 'insider' or 'outsider' in relation to their subject of inquiry. While traditional positivist theory suggest that the researcher is separate to the research subject and able to hold an unbiased 'outsider' lens over an objective reality, Foster argues that "all research is, at least in part, a product of human thought and meaning-making, including that of the researcher" (p. 18). Therefore, consistent with pragmatic and critical realist ideas that the 'real' world cannot be seen without the individual interpretation of research participants, so too do the researcher's interpretations influence the research. According to Foster's thesis, we must acknowledge the role of inescapable researcher bias in the conception and design of research, regardless of the methodological approach, which often places them as an 'insider' in the research process. Forster outlines four conditions under which the researcher becomes an 'insider':

1. experienced that which is being researched (Farnsworth, 1996),
2. experienced that which is being researched and has a personal relationship with many of the participants (Sherry, 2002)
3. been part of the community being researched (Bolak, 1995), or
4. worked with the population under study (Bland 1987; Coglán 2000, cited in Sherry).

Based upon the interpretation of the above criteria, it may be argued that all researchers in the field of psychology are part of the human population which they study, and even if they have not experienced the particular phenomenon of enquiry, are likely to have developed preconceptions as a result of co-existing in a society with others that have. By virtue of their researcher role, they will normally also meet criterion four.



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### **Research credibility and rigour.**

Due to the inextricable role of the researcher as an ‘insider’ and creator of meaning in IPA and other qualitative research methods, qualitative research has traditionally come under criticism for lacking scientific rigour (Rolfe, 2006). Noble and Smith (2015) have argued, however, that reduced rigour in qualitative research does not relate to methodology, but rather to a lack of consensus regarding the quality standards that qualitative research should be assessed against. They argue that concepts of reliability and validity used to assess quality in quantitative research are not transferrable to qualitative enquiry, and as such, posit that the emphasis should instead be placed upon the ‘trustworthiness’ of findings. This, they suggest, may be achieved via strategies which enhance the ‘truth value’, ‘consistency’, ‘neutrality’, and ‘applicability’ of the research.

The ‘truth value’, according to Noble and Smith, is met through the acknowledgement that multiple realities exist and transparent researcher reflexivity. In order to meet this criterion, a reflective journal was kept throughout the research process. Excerpts from this journal are presented in Appendix 3-A (p.3-17). According to Vicary, Young, and Hicks (2017), “The use of a journal is an established tool for the recording of learning and prompts the process of interpretation and bracketing as a reflective mechanism” (p.563). The process of keeping reflective notes, especially prior to and immediately after interviews, allowed me to notice assumptions contemporarily. Potential biases highlighted in journal content and more generally were also discussed in ‘debriefing’ discussions carried out in monthly research supervision sessions. Based upon the output generated via these reflexive mechanisms, a section highlighting my own experiences and ways in which these may have influenced the research process and interpretation of data has also been included below.

‘Consistency’ and ‘neutrality’ relate to the transparency of researcher decision making and openness about the impact of researcher’s own philosophical position. To comply with

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these criteria, and enhance 'auditability', decision making and rationales were captured in the reflective journal and also discussed in research supervision. The use of Standards for Reporting Qualitative Research was also seen to support this, by ensuring that each aspect of the research was reported and justified in the body of the research paper. Additionally, the analysis and generation of themes was carried out in consultation with my field and research supervisors who jointly have a significant level of experience of qualitative research and working in settings with cancer patients.

'Applicability' is framed as a qualitative research-appropriate alternative to the concept of generalisability, focusing upon whether findings can be applied to other 'contexts, settings, or groups'. This is seen to have been achieved through rich description of the research setting(s) and sample. This has been achieved through thorough description of the study setting(s), inclusion and exclusion criteria, and sample characteristics.

### **Researcher reflexivity.**

The focus on the 'double hermeneutic' process in IPA explicitly acknowledges the researcher's role in interpreting meaning from data based on their own, often unconsciously held, knowledge, experience, and beliefs. As outlined above, this reflexivity is viewed as a fundamental tenet of 'quality' and 'trustworthiness' in qualitative research. The impact of my own experiences of and understandings of cancer, and position as an 'insider', will undoubtedly have influenced the findings of the empirical paper. Additionally, they have probably coloured the entirety of both components of the thesis, in terms of the way that cancer and associated experiences have been described and framed. As such, to increase transparency and 'credibility' it feels important to consider the experiences I am aware have shaped my conceptualisation of cancer.

Given the prevalence of cancer, there are very few people who have not been affected by its unexpected appearance in their lives or the lives of their loved ones. To this I am no

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exception. I have lost two grandparents to cancer and have witnessed many of those I care about lose family and friends, both young and old, as a consequence of malignant disease. I have also seen people survive cancer and go on with their lives. My mum, whose cancer was caught early by an impromptu screening appointment I will always be grateful for, is one of those fortunate enough to be here. From these experiences and the narratives formed around cancer's presence in the lives of myself and my loved ones, I came to develop a sense of cancer as a frightening, destructive force which indiscriminately enters and shatters lives.

Whilst writing this thesis I have been on a trainee placement in a clinical health psychology service, working directly with cancer patients. In this role, I had borne witness to the high levels of distress a cancer diagnosis can bring and the devastating impact it can have on individuals' emotional wellbeing, relationships, social roles, and belief systems. I was struck by the strength, humility, humour, and determination of the people I worked with. So too was I touched by their sense of loss, injustice, and sorrow in the face of the threats posed by cancer.

As I commenced data collection, I became aware of a contrast between those I was working clinically with and those I was interviewing for research purposes. Several of the CUP patients I was fortunate enough to speak with expressed positive experiences despite CUP's presence. While this was not universal, and participants also reported distress, loss, and struggle, I was struck by how well some participants reported to be managing and feeling in their circumstances. This caused me to reflect upon the assumptions I had been unconsciously carrying in relation to cancer being a pervasively negative and life-shattering experience. I considered my professional experiences with cancer patients, recognising with renewed awareness that individuals referred to clinical psychology are likely to be those patients experiencing the highest, clinically significant levels of distress, and while these

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experiences can affect a significant proportion of cancer patients, there are many more patients who do not come into contact with psychological services.

My assumptions may have been further coloured by my knowledge, or lack thereof, of CUP. Prior to embarking on this research project, much like many of the participants, I had not heard of CUP. I was shocked upon learning more about the condition to discover how little modern medicine seemed to be able to offer to this patient population. Based upon the existing literature I had read about high levels of uncertainty and distress amongst people newly diagnosed with CUP, along with my existing assumptions around cancer more generally, when embarking on the research I believe I had fully expected study participants to be experiencing a high level of psychological distress and functional limitation and therefore difficulty with coping. I was therefore pleasantly surprised to hear just how well some of the study participants reported feeling both physically and psychologically and was struck on multiple occasions by the remarkable resilience and stoicism shown by the people I was fortunate enough to meet.

### **Reflections on the Thesis Process**

The following section offers an overview of the challenges and limitations associated with the thesis process as well as strengths and implications for future research.

#### **Limitations and challenges.**

##### ***Practical challenges.***

Pragmatic challenges in relation to time constraints and recruitment arose during the research process which had a considerable impact upon the time-scales of the project and hand in date. In the early stages of the empirical research process, I was fortunate to have opportunity to discuss potential topics and ideas with clinical oncology staff working across recruitment sites and learn from their perspectives. A recurring theme of these discussions was that individuals meeting the study's inclusion and exclusion criteria were a clinical

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minority and relatively rare. I recall at one network meeting that one oncologist present made it quite clear that he believed recruiting the target sample number would not be possible. With the reassurance of my supervision team, including an extremely experienced and enthusiastic consultant in clinical oncology, I opted to embark on the research regardless of these warnings. Acutely aware from the offset that recruitment may be challenging, early discussions with my field supervisor focused on ways to optimise recruitment opportunities. With this aim in mind, I attended the north-west CUP education day and had opportunity to present my research proposal to staff from across numerous NHS Trusts with the aim of recruiting staff contacts in CUP services that my supervision team did not already have links with via the local network. Through this process I was able to include three more recruitment sites (although unfortunately it transpired that one of these Trusts was not currently open to external research due to capacity issues). I have no doubt that taking this extra time during the set-up of the study was essential to the eventual success of the study. Three of the total ten participants came from the additional three sites, as such reaching the target sample number would not have been feasible without them. Nor would it have been feasible without developing relationships with contacts in each of the recruiting sites who I was totally dependent upon to identify and initially seek consent from. Of course, going through separate R&D processes for six Trusts was an additional and unforeseen task which demanded a significant amount of time.

The process of conducting the research was in many ways dependent upon the structure of the DClinPsy programme. One challenge of this was a relatively short time-frame to complete the thesis research. A significant delay occurred at the ethics application stage, firstly due to supervisor absence whilst putting the application together, and secondly as a consequence of the ethics process itself. While the Health Research Authority (HRA) have made recent system changes to make the process of gaining ethical approval for research in

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NHS settings more streamlined and less lengthy (HRA, 2017), it remains a notoriously time-consuming process (Whitburn, Singh, & Sooriakumaran, 2017). With hindsight, it would have been necessary to commence this process much earlier in order to gain relevant approvals, conduct recruitment and data collection, and complete the analysis and write-up of the project within the original estimated time frames.

Reflecting upon these process issues, it is possible that both of the challenges with recruitment and timescales for ethical approval may have been overcome through a different recruitment strategy. Recruitment nationally via relevant organisations (e.g. The CUP Foundation) or social media (there are three CUP-specific Facebook pages offering information and support) may have allowed access to a much wider pool of potential participants. Due to the potential for this mode of recruitment to access patients all over the country, it would likely have been necessary for interviews to be carried out either over the telephone or via internet-based video communication software such as 'Skype'. Voice over Internet Protocol (VoIP) technologies are increasingly employed as a method of data collection in qualitative research which have a high level of acceptability and convenience (Lo Iacono, Symonds, & Brown, 2016). This approach would also have negated the need for HRA ethical approval, with approval instead being sought via Lancaster University's Faculty of Health and Medicine Research Ethics Committee, a process which anecdotally and in my personal experience is considerably quicker. I believe, however, that there would also have been some drawbacks to this approach. One possible drawback would have been an absence of links with patients' clinical nurse specialists to direct any concerns or highlight any needs for additional support to. I also believe that the opportunity for building rapport and providing a 'safe' space to discuss very difficult subject matter is better facilitated in face-to-face discussion than it could be over the telephone or VoIP technology due to greater potential for non-verbal cues to be missed (Irvine, Drew, & Sainsbury, 2012).

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### *Ethical challenges.*

One of the major findings of the research paper was about the importance of patient time and minimising the time-burden of CUP-related appointments in order to allow patients to better engage with valued activities in their daily lives. Of course, this has made me reflect upon the request placed upon participants to give up their precious time to attend an interview and focus explicitly upon the more distressing aspects of their experiences. While participants opted-in to the study voluntarily, I have wondered about the ethical implications of this within the context of patient compliance and whether patients may have felt obliged to participate due to the research being raised by the medical professionals responsible for their care.

Also on the theme of participant time, I became aware during the research process of potential challenges associated with the option of having a summary of the study findings posted out after completion of the research. Given the uncertain trajectory of CUP and the possibly limited life expectancy faced by some participants, comments arose on several occasions from participants about the possibility that they may no longer be alive at the point at which summaries are posted. At no time in these discussions did participants seem overtly distressed, and from some these comments seemed to be made jokingly, however it made me consider the impact of this relatively standard research procedure. While it is common practice for participants to be offered feedback upon the outcomes of research they have been part of, I had not prior to data collection really considered the practice within the sample context. The focus upon the future and possible mortality raised could have been particularly challenging and is certainly a learning point that I will take forward.

### **Strengths.**

The research focused upon the lived experience of people living 'longer-term' with CUP. No prior research has focused upon this patient population, and as such a significant

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strength of the research is the opportunity for the voices of these patients to be heard and consequently for their needs to be better understood by the services that provide their healthcare.

The involvement of stakeholders, including both service-user representatives and medical staff working in CUP services, in the early stages of research design was also seen to be a strength of the research as this provided opportunity to ensure that the research would be both acceptable to participants and valuable to the services that work with people with CUP.

### **Implications for future research.**

The research findings indicate a number of areas where further research is needed. As in other cancer populations, social support is an important coping resource for people with CUP. Research investigating the experiences of those providing care and support to individuals with CUP as yet has not been undertaken. It is possible that these individuals may face similar struggles with coping as a result of the uncertainty associated with the condition as patients themselves. Findings also highlighted the potential for misinterpretation of physical symptoms amongst CUP patients and research investigating these experiences further may be very useful as it may be that individuals with CUP are more likely to experience health anxiety than other cancer patients. While findings provided insights into the way that participants' appraisals and sense of coping have changed over time, longitudinal research investigating these experiences over time would be beneficial to better understand patterns in psychological experiences associated with CUP over time.



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**Appendices****Appendix 3-A- Reflective Journal Excerpts**10/06/2019- Pre-data collection

First two interviews scheduled for Friday. Calls made to participants to arranged- surprised when one lady sounded quite sprightly on the phone. I think I have been expecting that participants will mainly be really struggling- maybe this won't be the case. Limited knowledge about what 'clinical stability' from the medical perspective actually means- (speak to [REDACTED] [REDACTED] [field supervisors] about this).

Assumptions going in to interview process- that patients will be quite frail/visibly unwell- probably based on my ideas of what a 'typical' patient with advanced cancer or during treatment might look like. This is strange really as patients on placement don't necessarily look this way- influence of stereo-types from media/family. Not having met anybody with CUP before- feels a bit mysterious so think I'm expecting the worst- based probably on the literature but also attitudes of Medics in CUP network. Likewise, expecting participants will probably find talking about their experiences quite difficult/distressing.

12/07/2019- Reflections After Interview 4

Participant 4- most distressed so far, seemed that life had been placed of pause for CUP. Felt incredibly sad for this lovely lady who clearly has so many ambitions and goals that she currently doesn't feel able to pursue. I think that after the first three this has come as a bit of a surprise, although probably more what I expected initially. Focus upon suicide as a 'way out'- some really hard conversations- could really sympathise with her position that it probably would be a 'kinder' end- has left me thinking and feeling frustrated about UK laws around assisted suicide for those that do end up with little quality of life and lots of pain etc.

## CRITICAL APPRAISAL

Had to contact Anna re. risk concerns, actions carried out to pass concerns on to specialist nurse. Feel conflicted about this- necessity of carrying out professional obligations vs the sense that by reducing 'risk' it may also reduce this lady's access to the thing that is providing her with a safety net/ability to continue knowing she can remain in control of her own destiny.

### 27/08/2019- Reflections after Interview 8

Interview carried out with male participant in own home- genuinely surprised at how well this man seems to be managing with his situation- very personable/humorous, laughed easily about the uncertainties faced, seemed to have come to a place of accepting how things are. helped by? – no symptoms, secondary cancer treated, long period of wellness since treatment, lots of interests and distractions.

Section 4: Ethics Form

Hayley Slater

Doctorate in Clinical Psychology

Division of Health Research, Lancaster University

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## ETHICS FORM

**Research Protocol**

This protocol does not have regard for the HRA guidance and order of content

**Study Title****Full Title of the Study**

Patients' experiences of coping longer-term with cancer of unknown primary

**Short Study Title**

Coping longer-term with CUP

**Version Number and Date**

0.1 (28/07/2018)

**Reference Numbers**

IRAS Number	251064
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**Study Summary**

Study Title	Patients' experiences of coping longer-term with cancer of unknown primary
Study Design	Qualitative- Interpretative Phenomenological Analysis. Data gathered via one in depth interview with each participant.
Study Participants	Patient's living with a diagnosis of cancer of unknown primary (CUP) who are clinically stable 6 months following their diagnosis
Planned Size of Sample (if applicable)	10-12
Planned Study Period	December 2018-August 2019
Research Question/Aim(s)	<p>What are the coping experiences of people who are living longer term with CUP?</p> <ul style="list-style-type: none"> <li>• Do these patients feel able to cope? What factors increase or decrease perceived coping capacity?</li> <li>• Has their sense of 'coping' changed throughout their illness?</li> <li>• Do patients feel that coping longer term with CUP is qualitatively different than coping with a cancer of known primary site?</li> </ul>

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**Applicant Details**

Role	Details	Responsibilities
Chief Investigator	<p>Hayley Slater, Trainee Clinical Psychologist, Lancaster University</p> <p>Tel: [REDACTED]</p> <p>Email: <a href="mailto:h.slater1@lancaster.ac.uk">h.slater1@lancaster.ac.uk</a></p>	<p>Primarily responsible for all aspects of the research project. Completion of the research project will form part of Hayley's thesis which will be submitted in partial fulfilment of a doctorate in clinical psychology (DClinPsy) at Lancaster University.</p>

**Details of other individuals/organisations involved in the research**

Role	Details	Responsibilities
Academic Supervisor(s)	<p>Dr Anna Daiches, Clinical Director, Lancaster University</p> <p>Tel: 01524 594406</p> <p>Email: <a href="mailto:a.daiches@lancaster.ac.uk">a.daiches@lancaster.ac.uk</a></p> <p>Dr Anna Duxbury, Clinical Tutor, Lancaster University</p> <p>Tel: 01524 592 974</p> <p>Email: <a href="mailto:a.duxbury@lancaster.ac.uk">a.duxbury@lancaster.ac.uk</a></p>	<p>Responsible for providing expertise and advice in relation to the research process, methodology, and provision of draft reads.</p>
Field Supervisor(s)	<p>[REDACTED]</p> <p>Tel: [REDACTED]</p> <p>Email: [REDACTED]</p> <p>[REDACTED]</p> <p>Tel: [REDACTED]</p>	<p>Responsible for providing expertise and advice in relation to clinical area.</p>

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	Email [REDACTED]	
Research consultant	Dr Craig Murray, Senior Lecturer, Lancaster University  Tel: 01524 592754  Email: c.murray@lancaster.ac.uk	Offering methodological expertise on the application of IPA
Sponsor	Becky Gordon, Research Ethics Officer, B14 Furness College, Lancaster University, LA1 4YT  Tel: 01524 592981  Email: ethics@lancaster.ac.uk	Provision of sponsorship and associated legal cover via Lancaster University
Internal Supervisor at [REDACTED]	[REDACTED] [REDACTED] [REDACTED] [REDACTED]  Tel: [REDACTED]  Email: [REDACTED]	Responsible for acting as internal supervisor for involvement of any patients recruited via [REDACTED]. [REDACTED] Responsibilities to include facilitation of recruitment and overseeing the internal risk assessment process as required by the Trust Research and Development department.

### Introduction

#### Background

Previous research has shown that individuals living with a diagnosis of cancer are likely to experience elevated emotional distress (Carlson et al., 2004; Zabora et al., 1997; Zabora et al., 2001). This distress in relation to cancer has been defined by The National Comprehensive Cancer Network (NCCN, 2013) as “a multifactorial unpleasant emotional experience of a psychological (cognitive, behavioural, emotional), social, and/or spiritual nature that may interfere with the ability to cope effectively with cancer, its physical symptoms and its treatments.” Within this definition, distress is conceptualised as difficulties with mood, anxiety, and adjustment across a continuum ranging from ‘normal’ reactions such as feelings of fear and sadness, to more disabling experiences including anxiety, depression,



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and existential and spiritual crises (NCCN, 2013). The evidenced increase in distress has been linked to an increased prevalence of mental health difficulties amongst cancer patients. A meta-analysis of eight studies by Singer, Das-Munshi and Brähler (2010) found that around one in three people with cancer meet criteria for diagnosis of a mental health difficulty, indicating a greater prevalence than in the general population.

Quality of life (QoL) has also been shown to be negatively impacted by a diagnosis of cancer. While inversely associated with distress, QoL includes a broader range of phenomena “including physical, social, cognitive, spiritual, emotional, and role functioning, as well as psychological difficulties and physical symptoms such as pain, nausea and vomiting, and fatigue” (Carlson & Bultz, 2003). Research findings have shown that following diagnosis of cancer, QoL is impaired in a number of areas, particularly fatigue, sleep disturbance, and financial concerns (Götze, Ernst, Brähler, Romer, & von Klitzing, 2015). Due to the negative implications of living with cancer described above, a large volume of research has been undertaken investigating how people cope with the life-altering changes and emotional distress associated with a cancer diagnosis.

Coping has been conceptualised in numerous ways within psychology. Lazarus and Folkman’s (1984) definition of coping as “constantly changing cognitive and behavioural efforts to manage external and/or internal demands that are appraised as taxing or exceeding the resources of the person” has been widely accepted and applied. Based on this definition, Folkman & Lazarus (1980; 1985; Lazarus & Folkman, 1984) proposed that coping can be separated into the two distinct categories. Emotion-focused coping relates to attempts to manage or alter internal conflicts and emotions through strategies such as re-appraisal. Problem-focused coping pertains to attempts to change external factors or reduce conflict between the individual and the environment via strategies such as support seeking (Roesch, 2005). A further dimension to coping is direction of focus i.e. strategies directed

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towards a threat are described as ‘approach coping’ (e.g. problem-solving) and strategies directed away from a threat are labelled as ‘avoidance coping’ (e.g. denial) (Moos & Schaefer, 1993). This theoretical framework has been used widely to guide research into how people cope with a wide range of phenomena, including cancer.

Previous research has demonstrated that a wide range of coping styles and strategies are used by people living with various cancer diagnoses, including lung cancer, breast cancer, and gastrointestinal cancers (Al-Azri, Al-Awisi & Al-Moundhri, 2017; Nipp et al., 2016; Walker, Zona & Fisher, 2006). Both emotion-focused and problem-focused approach coping have been found to be related to improved psychological and physical wellbeing (Roesch et al., 2005). Avoidance coping conversely has been linked to higher levels of distress and lower mood and physical functioning (McCaul et al., 1999; Roesch et al., 2005). QoL has also been found to be significantly associated with coping strategies, with avoidant strategies found to be particularly detrimental to QoL in a sample of women with breast cancer (Kershaw, Northouse, Kritpracha, Schafenacker, & Mood, 2004). Emotion-focused strategies have been found to be used more by patients with advanced cancer diagnoses (Thomsen, Rydahl-Hansen & Wagner, 2010). Findings from a study by Nipp et al. (2016) suggest coping strategies employed are related to individual illness perceptions, with increased perception of chronicity found to lead to increased use of passive strategies such as anxious preoccupation and hopelessness.

Perceived capacity to cope with cancer and employ coping strategies have been demonstrated to be negatively correlated with uncertainty (Germino et al., 1998). The use of emotion-focused coping strategies, however, has been found to mediate between fear of uncertainty and emotional distress during and after cancer treatment (Mishel & Sorenson, 1991; Taha, Matheson & Anisman, 2012). The theme of coping with uncertainty has also been identified amongst patients with advanced illnesses (Kimbell, Murray, Macpherson &

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Boyd, 2016; Tejani, Kamen, Mohile & Gramling, 2014). While the experience of uncertainty has been identified as a challenge to coping across a range of cancer diagnoses, it is possible that it may be a particular issue for individuals diagnosed with cancer of unknown primary (CUP).

A diagnosis of CUP is given to individuals where a secondary cancer has been identified in the absence of an identifiable primary source (Varadhachary & Raber, 2014). Approximately 9000 people in the UK are diagnosed with CUP each year (Cancer Research UK, 2017), with figures suggesting CUP diagnoses make up 2-5% of all diagnosed cancers (Riihimäki, Hemminki, Sundquist, & Hemminki, 2013). The condition is associated with a poor prognosis, with a median survival rate of 3 months (Hemminki, Bevier, Hemminki, & Sundquist, 2012; van de Wouw, Janssen, Heijnen, Coebergh, & Hillen, 2002). The majority of patients are very frail at the time of diagnosis and unable to undergo any anti-cancer treatment (cytotoxic chemotherapy). While a minority of patients (15-20%) belong to clinico-pathological subsets with more favourable prognosis (favourable risk subsets), 80-85% of patients do not belong to those subsets and even if they are well enough to undergo chemotherapy the median survival is generally less than 1 year (Fizazi et al 2015).

To date very little research has been undertaken with people living with CUP, however existing studies has identified that CUP amplifies difficulties encountered across other cancer diagnoses due to elevated levels of uncertainty (La Pushin, 2009; Richardson et al., 2015). This uncertainty in CUP has been related to: a high volume of investigative testing (Symons, James & Brooks, 2009); indefinite prognosis and lack of clarity in treatment plan (Ryan, Lawlor & Walshe, 2013); and lack of continuity in care (Richardson et al., 2015; Wagland et al. ,2017). This increased uncertainty has been linked to increased depression and anxiety and decreased quality of life (Hyphantis et al., 2013). Therefore, increased

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uncertainty in CUP may make coping for individuals with this diagnosis particularly challenging.

Only a subgroup of CUP patients are medically stable 6 months beyond their diagnosis. This group of patients have had a prolonged period of coping with the uncertainty of CUP and potential related distress, however no research found in literature searches has as yet focused on this particular population. As such research addressing this gap in the literature is warranted to inform clinical practice around how this patient group can be best supported to cope with any distress stemming from uncertainty about their illness, the process of treatment, or any other CUP-related difficulties, potentially enhancing quality of life. The proposed study will aim to explore the coping experiences of this particular population.

### **Rationale**

The above background provides an overview of the relevant literature relating to coping in cancer patients and highlights the gap in this literature in relation to those living relatively longer-term with a diagnosis of CUP. As previous findings have highlighted that uncertainty has a detrimental impact on coping with cancer and that CUP is a diagnosis characterised by uncertainty, it is possible that for individuals with CUP, coping is even more challenging than it is for individuals with cancer of known primary site. As such, it is important to better understand the experience of individuals living for an extended period (6 months or more) with CUP and how they cope.

### **Aims**

The aim of the study is to explore the experiences of individuals coping longer-term with CUP. The intended outcome of the study will be to identify themes from participants' data relating to how they have coped over the time since their CUP diagnosis. It is hoped that this knowledge will indicate what kind of coping strategies are most or least helpful for people living with CUP and what potential support mechanisms may be beneficial.

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It is hoped that findings will be of use to inform services and staff how they can best support people living longer-term with CUP to cope throughout their time living with the condition. It may also help to identify what, if any, form of psychological support is perceived to be most helpful by this patient group.

### **Research Questions**

What are the coping experiences of people who are living longer term with CUP?

- Do these patients feel able to cope? What factors increase or decrease perceived coping capacity?
- Has their sense of ‘coping’ changed throughout their illness?
- Do patients feel that coping longer term with CUP is qualitatively different than coping with a cancer of known primary site?

### **Method**

The study will use Interpretative Phenomenological Analysis (IPA), a qualitative approach which provides both the methodology and analytic strategy as outlined by Smith and Osborne (2008).

### **Participants**

Participants will be recruited from across seven acute hospital trusts. [REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

### **Sampling**

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A purposive sampling strategy will be used in order to identify participants who will meet the outlined inclusion and exclusion criteria. The medical teams in the identified CUP services will be responsible for identifying potential candidates for participation and during this process will assess whether the criteria are met. The chief investigator will also ascertain that each participant meets inclusion and exclusion criteria during initial phone contact prior to interviews taking place.

The aim will be to recruit up to 10-12 participants. The size of the sample has been based upon the IPA's focus upon small, homogenous samples (Smith & Osborne, 2008). Typically, selection of sample size is based upon having enough participants to shed light upon the phenomenon of interest and identify convergent and divergent themes, yet not so many that the 'depth' necessary for IPA is lost (Pietkiewicz & Smith, 2012). Published IPA studies typically have samples of between 4-15 people. The aim of 10-12 participants for this study therefore falls within the usual boundaries for IPA studies and is estimated to be realistic for the scope of the study whilst offering the possibility of reaching data saturation (i.e. that no new themes are likely to emerge through further interviewing) (Brocki & Wearden, 2006).

Should more participants that this be interested in taking part, participants will be selected on a first-come-first-served basis. Exceptions to this may be made if there is a significant gender imbalance in the existing sample, for example if males are under-represented, potential male participants may be chosen ahead of females who expressed their interest sooner.

### **Inclusion and Exclusion Criteria**

Participants will be eligible for inclusion in the study if:

- They have received a diagnosis of CUP
- They received their CUP diagnosis over 6 months ago and are now deemed to be clinically stable by their medical team

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- They are currently receiving treatment or being actively monitored by the CUP service at any of the host NHS Trusts

(  
 [REDACTED]  
 [REDACTED]  
 [REDACTED]  
 [REDACTED]  
 [REDACTED]  
 [REDACTED]).

- They are aged 18 or over
- They are able to provide informed consent to participate

Participants will not be eligible for inclusion in the study if:

- They are acutely unwell or nearing the end of their life
- They do not speak English (unfortunately no funds are available for a translator as part of this study)
- They are under 18 years of age
- They lack mental capacity to provide informed consent to participate (e.g. due to a severe learning disability or dementia)

Smith and Osborne (2008) posit that the sample should be homogeneous in order to shed light on the phenomenon of interest, in this instance coping with CUP. Therefore, the inclusion and exclusion criteria aim to ensure participants recruited have had a relatively similar journey in terms of time passed since their CUP diagnosis and current clinical stability.

In order to make outcomes as useful as possible when considering the wider population, efforts will be made to recruit a relatively even gender mix if possible. Efforts

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will also be made to recruit participants from across the different host NHS trusts to ensure results are not representative of the experience of care in individual Trusts. The decision to involve seven NHS trusts in order to recruit a relatively small number of participants was made based on advice from the field supervisor Dr [REDACTED] and other oncologists working in CUP services that the number of patients meeting inclusion criteria for the study in each Trust is likely to be very small. Therefore, seven Trusts were selected to maximise recruitment opportunities, however, it is possible that participants will not be recruited from each Trust if no patients meet the criteria or are willing to be involved in the study.

One contact person (ordinarily a clinical nurse specialist) will be identified in each Trust who will act as the primary link with the chief investigator to facilitate recruitment.

### **Materials**

The following materials were produced by the chief investigator:

- Participant Information Sheet
- Professionals' Information Sheet
- Consent to be contacted form
- Consent form
- Interview Schedule
- Demographic Information Form

The consent form and participant information sheet were based on templates provided by the Health Research Authority and on guidance provided by the Doctorate in Clinical Psychology Programme at Lancaster University.

Questions for the interview schedule were developed by the chief investigator and guided by the research questions. Guidance provided by Smith and Osborne (2008) for the production of interview schedules for IPA research was followed.



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The demographic information form was created to capture relevant demographic data. Data gathered are age, time since diagnosis, gender, and ethnicity. These data are important variables for providing an accurate report on the study sample. Options for ethnic background were obtained from the Office for National Statistics' (ONS) recommendations for collection of ethnicity survey data in England.

### **Patient and public involvement**

As part of the process of developing the research materials, the chief investigator consulted with members of the Patient Cancer Care Improvement (PCCI) Group. The group is made up of service users who have been under the care of [REDACTED] for cancer treatment and is co-ordinated by staff from the on-site [REDACTED] [REDACTED] team.

A consultation session was held on the 12<sup>th</sup> September 2018. All members of the group were invited to attend. Two service users attended the session along with the [REDACTED] group co-ordinator. The service users were invited to provide feedback on the interview schedule, participant information sheet, consent to be contacted form, and consent form. Feedback was received regarding the accessibility of materials in terms of language, layout, font size etc., the sensitivity of and wording of the interview questions given the sensitive nature of the research, and the acceptability of the research from the service users' perspectives.

Based on feedback, a number of amendments were made to the materials to increase the likelihood that they will be easily understood by potential participants. Feedback from the service users was that they were in favour of the project and its intended aims to better understand patient experience.

### **Procedure**

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Potential participants will be identified by members of their CUP medical team (e.g. Clinical Nurse Specialist, Consultant Oncologist, Clinical Psychologists). An information sheet will be provided to the professionals in each of the seven CUP services outlining the study and the participant inclusion and exclusion criteria.

Once identified, potential participants will be provided with a participant information sheet during a routine appointment. If they are interested in taking part, they will be invited to fill out a 'Consent to be contacted' sheet with their contact details by the involved clinician, giving permission for the chief investigator to make contact. If the potential candidate ticks all the relevant boxes on this form and agrees to be contacted, their details (name and contact telephone number) will be provided by the Trust contact person to the chief investigator over the telephone. These contact details will be stored by the chief investigator on paper in the locked drawer in their home. Nobody else will have access to this drawer. The paper contact details will be shredded as soon as the interview has taken place. The original consent to be contacted form will be stored in the clinical records.

The potential participant will be given the participant information sheet to take home with them and refer to as necessary.

The decision for the researcher to contact participants rather than asking participants to call the researcher was made following recommendation from the Research and Development department at [REDACTED] who advised that in their experience this set up was preferable to service users/participants.

### **Consent**

Once an individual has provided initial 'consent to be contacted', the chief investigator will contact them on the given contact number for an informal discussion. An interval of at least one week will be left between the individual providing consent to be

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contacted and being called. This time is to allow the individual to thoroughly read the information sheet and formulate any questions they may like to ask.

The phone call will be made on a mobile telephone provided by Lancaster University specifically for research purposes. The number of the mobile phone will be provided to potential participants in advance on the information sheet. This decision was made based upon the advice of the Research and Development department at [REDACTED] who advised that in their experience, research participants often prefer not to answer the phone to an unfamiliar number.

Once reached by telephone, the individual will be given the opportunity to ask any questions about the study. If at this stage they are happy to participate, arrangements will be made with them over the phone to meet. Participants will be given the choice to meet either in their own homes or at their local hospital site.

At the start of the meeting, the chief investigator will go through the consent form with the participant, ensuring they understand each statement and answering any questions that arise. Participants will be reminded at this stage that there is no obligation for them to proceed with the interview if they are not fully comfortable and that they are free to stop the interview at any point. They will also be reminded that they are free to withdraw up until 2 weeks after the interview takes place. Following this time, the anonymised transcription will take place and withdrawal will no longer be possible. Reassurance can be provided at this stage, however, that all identifying information will be removed.

If the chief investigator has any doubts at any stage regarding the individual's capacity to provide consent, the process will be paused and the individual's clinical team will be consulted regarding the appropriateness of including the individual in the research. Only once it is clear that the individual has capacity to provide informed consent would

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undertaking the interview be re-visited. This would be contingent upon meeting criteria for capacity as laid out in the Mental Capacity Act (Department of Health, 2005).

Three copies of the consent form will be produced. The original copy will be retained in the patient's file, one copy will be given to the participant, and one copy will be retained by the chief investigator. Where the interview takes place in participants' homes, the consent form will be attached to the letter to the participant's Clinical Nurse Specialist in order for it to be retained in their clinical file. The chief investigator's copy will be scanned to make an electronic copy as soon as possible which will then be stored securely on the researcher's personal Lancaster University storage drive. This drive is secure and password protected. The transfer will be made via the Lancaster University VPN. The paper copy of the consent form will then be shredded by the chief investigator. The electronic version of the consent form will be stored for a maximum of six months after the completion of the study in line with the protocols of Lancaster University's doctorate in clinical psychology programme.

### **Data Collection**

Participants will be given a choice as to whether the interview is conducted at their local hospital site or in their own home. The decision to offer this choice was made in order to maximise participant comfort during the research process. If the participant chooses for the interview to be conducted in their own home, the researcher will follow the lone working policy of their employer, [REDACTED] in order to minimise any risk to the researcher. This includes assessing any risks posed by participants or the environment and making the time and location of any interviews known by a selected colleague as per [REDACTED]'s 'buddy system'. For any interviews with participants recruited via [REDACTED], their local lone working policy will also be adhered to. This involves a similar arrangement to [REDACTED]'s 'buddy-system' along with an additional risk assessment process and documentation needing to be completed prior to the interview. If

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the patient chooses for the interview to be conducted at the hospital site this will be arranged for the most convenient time for the participant. This may be prior to a medical appointment to minimise travel or at another time if the participant prefers. A room for this purpose will be booked on the hospital site for the researcher and participant to meet. Interviews will not be carried out directly following a medical appointment due to the potentially emotionally exhausting nature of such appointments and the potential for the specific appointment outcomes to influence the interview content, rather than offering a more general overview of the participant's experience since their diagnosis.

Data will be collected via semi-structured interviews lasting for around 1 hour. One interview will be completed with each participant. This approach is deemed the 'exemplary' method for IPA, allowing for in-depth exploration along with flexibility to respond with additional follow up questions or prompts in response to participant answers (Smith and Osborne, 2008). Interviews will be carried out in person by the chief investigator. If necessary or more appropriate (i.e. due to fatigue) the interview may be split over more sessions in order to make the process manageable for individual participants. This will be discussed with each participant when the interview is initially arranged and should any participants become fatigued/unwell during the interview process and wish to continue at another time. Additional interviews with participants may also be carried out if any additional themes/questions arise from interviews conducted later in the research process which it would be valuable to discuss with any participants interviewed prior to generate richer data. Participants will be asked on the consent form whether they are willing for the chief investigator to contact them following their interview in these circumstances. Participants will be made aware they are free to decline contact of this type and that contact would only be made within three months of their initial interview taking place.

Interviews will be audio recorded using a portable Dictaphone.

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The chief investigator will also go through the Demographic Information for Study Participants with each participant to gather key demographic information. The participant's name will not be included on this sheet. Information will be used to provide information on overall characteristics of the sample.

Following the interview, the chief investigator will send a copy of the 'Letter to Clinical Nurse Specialists' to the individual's CNS to advise of their participation in case of any additional support needs.

### **Storage of Data**

The recording file will be transferred onto the chief investigator's Lancaster University storage drive which is password protected and secured. The transfer will be made via Lancaster University's VPN. This transfer from the Dictaphone to the University drive will be made as quickly as practicably possible due to the Dictaphone not having the option to encrypt or password protect the recording. Once this is completed the recording will be deleted from the Dictaphone. For the short period of time prior to the transfer being made the Dictaphone will be stored as securely as possible by the chief investigator.

Following transfer of the recording to the University Drive, the recording will be transcribed verbatim, following the guidance from Smith and Osborne (2008). Participants' names and any other identifying information referred to (e.g. names of family members, town lived in) will be omitted from the transcripts to ensure participant anonymity. Once the recording has been transcribed it will be deleted from the Lancaster University storage drive.

During analysis electronic copies of transcripts will be stored on the researcher's personal University storage drive which is password protected and secured. Electronic transcripts will be stored separately to electronic consent forms so it is not possible to identify which transcript belongs to which participant.

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Once the study is complete, the anonymised transcripts will be encrypted and transferred electronically via the secured University VPN to the Research Coordinator of the Doctorate in Clinical Psychology at Lancaster University where the chief investigator is a student. The transcripts will then be stored by the Research Director for up to ten years (in line with the course protocol), at which point they will be deleted by the Research Director.

The Demographic Information for Study Participants form will be electronically scanned following each interview and the electronic copy will be stored on the chief investigator's secure university storage drive via the university VPN. The paper copy will then be shredded.

### **Proposed analysis**

The analytic strategy will be guided by the recommendations of Smith and Osborne (2008). This involves initially reading each transcript independently a number of times to generate initial themes. The initial themes are then organised into clusters of related themes. This process is then repeated for each transcript, with convergences and divergences between participants noted. Finally, the clusters of themes from across the participants are synthesised and organised hierarchically to produce main 'superordinate' themes and associated subordinate themes. In order to complete this process effectively, initial annotations and colour coding of themes will be done by hand. This will involve printing off copies of the anonymised transcripts. These copies will be stored securely in a locked drawer in the home of the chief investigator. Once this stage of the analysis is complete, the annotated paper transcripts will be scanned and the electronic copies will be securely stored on the researcher's personal Lancaster University storage drive. This means of storage is password protected and secure. The paper copies of transcripts will then be shredded by the chief investigator.

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Electronic software (Microsoft Excel) may also be used to undertake the analysis of themes. Any electronic documents relating to the analysis will be saved securely on the researcher's password protected personal University storage drive.

### **Practical concerns**

Room bookings for interviews where required will be made via staff contacts at each Trust site.

Costs of printing and photocopying will be covered by Lancaster University's Doctorate in Clinical Psychology programme along with mileage costs associated with the researcher's travel to interviews.

### **Ethical concerns**

A number of ethical issues may arise from undertaking the proposed research. The primary identified risk is of causing distress to participants through discussion of emotionally challenging topics. A risk assessment and management plan is included below.

#### **Assessment and Management of Risk**

Participants are made aware on the consent form that in the instance of the disclosure of risk confidentiality may not be maintained if other services or professionals need to be involved to ensure the safety of themselves or anybody else. This will be reiterated verbally at the beginning of the interview.

#### Risks to participants

Emotional distress:

Due to the sensitive nature of the research topic, it is possible that participants may experience some emotional distress as a result of participating. If this is to occur during the interview, the interview and digital recorder will be paused. The participant will be given the chance to speak with the chief investigator if they desire and given as much time as needed



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until their distress decreases. The option to cancel or rearrange the interview will be offered to the participant. If the participant is highly distressed, the chief investigator will liaise as soon as possible with their field supervisor regarding the patient's welfare. The participant will be made aware of this. Following this, support can be offered by the clinical team as necessary.

If the individual becomes distressed following the interview, a list of support resources is provided on the information sheet that they may find useful. This section also directs them to their clinical team who have a great amount of expertise in managing CUP and can provide emotional support. The individual will be made aware of these resources at the end of the interview.

### Risks to self:

If the participant discloses any thoughts or intent to harm themselves in anyway immediate support will be sought by the chief investigator from their field supervisor or academic supervisor. If an imminent risk of harm to self is identified (e.g. threats of suicide, acts of self-harm), the chief investigator may contact relevant emergency services to ensure the person's safety. If the risk is not imminent, discussion will take place between the individual, chief investigator, and the chief investigator's supervisors to devise an appropriate plan of action. This may include referral to mental health crisis services, involvement of family members or friends with the individual's consent, and support from the treating CUP service. The participant will be kept informed of who will need to know about their disclosure. The option to cancel or rearrange the interview will be offered to the participant.

### Physical Health:

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Due to the nature of the research, it is possible that participants may present as physically unwell at interview. To minimise this risk, participants will only be recruited where deemed to be medically stable by their medical team. However, it is recognised that this may not necessarily be static. If at interview it is evident that the participant is not physically well enough to engage in the interview process (e.g. fatigue, sickness, weakness etc.) the interview will be cancelled or postponed based on the participant's wishes. Any concerns regarding deterioration or sudden changes in physical health will be passed on to the participant's clinical nurse specialist to ensure any medical assistance required is made available. This will be discussed with the participant as appropriate. If it is apparent at interview that the participant is acutely unwell the researcher may contact the participant's medical team to seek advice or the participant's GP or ambulance services if they require immediate medical attention.

Risk from others:

If any risk to the participant from others is disclosed or apparent during the interview, the interview will be paused in order to address the risk as a priority. Again, the chief investigator will make contact with the research or field supervisor regarding appropriate action to be taken. This may include referral to safeguarding agencies, or police in instances of immediate risk of harm from others. The participant will be kept informed of who will need to know about their disclosure. The option to cancel or rearrange the interview will be offered to the participant.

Risks to researcher

Risks from others:

## ETHICS FORM

In carrying out interviews individually it is possible that the researcher may be vulnerable to risk of harm from participants should they become aggressive during the session. The likelihood of this is reduced where interviews are carried out on the hospital site where other professionals will be in the immediate vicinity. The risk, therefore, is greater when visiting individuals in their own homes. It is also possible that there may be risks in these instances of harm from other individuals (e.g. family members). There is also a potential risk on home-visits of environmental risks such as dogs. To minimise any risk the [REDACTED] lone worker policy will be followed by the chief investigator. For home visits to any participants recruited via [REDACTED], their local lone working policy will be followed and risk assessment documentation completed.

### Risk of emotional distress:

Due to the nature of the research area, it is possible that the chief investigator may experience some emotional distress as a result of carrying out the interviews with participants. In this instance, supervision can be sought by the chief investigator from the field supervisor or academic supervisor as required. The chief investigator also has access to an Employee Assistance Programme via their employer [REDACTED] should further emotional support be required.

### **Timescale**

Data collection will commence following the necessary ethical approvals being granted. It is anticipated that interviews will commence in January 2019 and will be completed by April 2018. The project will end in May 2019 when it will be submitted to the Doctorate in Clinical Psychology programme for marking. Results will be fed back to participants upon request (made on the consent form) following submission of report.

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Appendices

Appendix 4-A: Ethics Application

IRAS Form

Reference:  
5.11 19/NW/0096

IRAS Version

Welcome to the Integrated Research Application System

IRAS Project Filter

The integrated dataset required for your project will be created from the answers you give to the following questions. The system will generate only those questions and sections which (a) apply to your study type and (b) are required by the bodies reviewing your study. Please ensure you answer all the questions before proceeding with your applications.

Please complete the questions in order. If you change the response to a question, please select 'Save' and review all the questions as your change may have affected subsequent questions.

**Please enter a short title for this project** (maximum 70 characters)  
Coping longer-term with CUP

**1. Is your project research?**

Yes  No

**2. Select one category from the list below:**

- Clinical trial of an investigational medicinal product
- Clinical investigation or other study of a medical device
- Combined trial of an investigational medicinal product and an investigational medical device
- Other clinical trial to study a novel intervention or randomised clinical trial to compare interventions in clinical practice
- Basic science study involving procedures with human participants
- Study administering questionnaires/interviews for quantitative analysis, or using mixed quantitative/qualitative methodology
- Study involving qualitative methods only
- Study limited to working with human tissue samples (or other human biological samples) and data (specific project only)
- Study limited to working with data (specific project only)
- Research tissue bank
- Research database

**If your work does not fit any of these categories, select the option below:**

Other study

**2a. Please answer the following question(s):**

- a) Does the study involve the use of any ionising radiation?  Yes  No
- b) Will you be taking new human tissue samples (or other human biological samples)?  Yes  No
- c) Will you be using existing human tissue samples (or other human biological samples)?  Yes  No

**3. In which countries of the UK will the research sites be located?** (Tick all that apply)

- England
- Scotland

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- Wales  
 Northern Ireland

**3a. In which country of the UK will the lead NHS R&D office be located:**

- England  
 Scotland  
 Wales  
 Northern Ireland  
 This study does not involve the NHS

**4. Which applications do you require?**

- IRAS Form  
 Confidentiality Advisory Group (CAG)  
 Her Majesty's Prison and Probation Service (HMPPS)

**Most research projects require review by a REC within the UK Health Departments' Research Ethics Service.  
 Is your study exempt from REC review?**

- Yes  No

**5. Will any research sites in this study be NHS organisations?**

- Yes  No

**5a. Are all the research costs and infrastructure costs (funding for the support and facilities needed to carry out research e.g. NHS Support costs) for this study provided by a NIHR Biomedical Research Centre, NIHR Collaboration for Leadership in Health Research and Care (CLAHRC), NIHR Patient Safety Translational Research Centre or Medtech and In Vitro Diagnostic Cooperative in all study sites?**

Please see information button for further details.

- Yes  No

*Please see information button for further details.*

**5b. Do you wish to make an application for the study to be considered for NIHR Clinical Research Network (CRN) Support and inclusion in the NIHR Clinical Research Network Portfolio?**

Please see information button for further details.

- Yes  No

*The NIHR Clinical Research Network provides researchers with the practical support they need to make clinical studies happen in the NHS e.g. by providing access to the people and facilities needed to carry out research "on the ground".*

*If you select yes to this question, you must complete a NIHR Clinical Research Network (CRN) Portfolio Application Form (PAF) immediately after completing this project filter question and before submitting other applications. Failing to complete the PAF ahead of other applications e.g. HRA Approval, may mean that you will be unable to access NIHR CRN Support for your study.*

**6. Do you plan to include any participants who are children?**



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 Yes  No**7. Do you plan at any stage of the project to undertake intrusive research involving adults lacking capacity to consent for themselves?** Yes  No

*Answer Yes if you plan to recruit living participants aged 16 or over who lack capacity, or to retain them in the study following loss of capacity. Intrusive research means any research with the living requiring consent in law. This includes use of identifiable tissue samples or personal information, except where application is being made to the Confidentiality Advisory Group to set aside the common law duty of confidentiality in England and Wales. Please consult the guidance notes for further information on the legal frameworks for research involving adults lacking capacity in the UK.*

**8. Do you plan to include any participants who are prisoners or young offenders in the custody of HM Prison Service or who are offenders supervised by the probation service in England or Wales?** Yes  No**9. Is the study or any part of it being undertaken as an educational project?** Yes  No

Please describe briefly the involvement of the student(s):

The chief investigator is a trainee clinical psychologist undertaking this project in partial fulfilment of a doctorate in clinical psychology (DClinPsy) at Lancaster University.

While the HRA's UK policy framework for health and social care research (2017, file:///C:/Users/hayle/Downloads/uk-policy-framework-health-social-care-research.pdf) states that ordinarily students should not take the role of chief investigator, exceptions to this rule may be made "for an experienced care practitioner or manager undertaking an educational qualification for continuing professional development or a doctoral-level study while employed by a health or social care provider or a university, or for a researcher undertaking a doctoral-level study in receipt of a fellowship" (p.17). The student in question meets these requirements for the role of chief investigator.

**9a. Is the project being undertaken in part fulfilment of a PhD or other doctorate?** Yes  No**10. Will this research be financially supported by the United States Department of Health and Human Services or any of its divisions, agencies or programs?** Yes  No**11. Will identifiable patient data be accessed outside the care team without prior consent at any stage of the project (including identification of potential participants)?** Yes  No

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IRAS Form

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**Integrated Research Application System  
Application Form for Research involving qualitative methods only****IRAS Form (project information)**

Please refer to the *E-Submission* and *Checklist* tabs for instructions on submitting this application.

The Chief Investigator should complete this form. Guidance on the questions is available wherever you see this symbol displayed. We recommend reading the guidance first. The complete guidance and a glossary are available by selecting [Help](#).

Please define any terms or acronyms that might not be familiar to lay reviewers of the application.

**Short title and version number:** (maximum 70 characters - this will be inserted as header on all forms)  
Coping longer-term with CUP

Please complete these details after you have booked the REC application for review.

**REC Name:**  
Liverpool East

**REC Reference Number:**  
19/NW/0096

**Submission date:**  
28/01/2019

**PART A: Core study information****1. ADMINISTRATIVE DETAILS****A1. Full title of the research:**

Patients' experiences of coping longer-term with cancer of unknown primary

**A2-1. Educational projects**

Name and contact details of student(s):

**Student 1**

	Title	Forename/Initials	Surname
	Ms	Hayley	Slater
Address	[REDACTED]		
	[REDACTED]		
Post Code	[REDACTED]		
E-mail	h.slater1@lancaster.ac.uk		
Telephone	[REDACTED]		
Fax			

Give details of the educational course or degree for which this research is being undertaken:

Name and level of course/ degree:  
Doctorate in Clinical Psychology (DClinPsy)

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Name of educational establishment:  
Lancaster University

Name and contact details of academic supervisor(s):

**Academic supervisor 1**

	Title	Forename/Initials	Surname
	Dr	Anna	Daiches
Address	Department of Health Research Faculty of Health and Medicine Lancaster University		
Post Code	LA1 4YG		
E-mail	a.daiches@lancaster.ac.uk		
Telephone	01524 594406		
Fax			

**Academic supervisor 2**

	Title	Forename/Initials	Surname
	Dr	Anna	Duxbury
Address	Department of Health Research Faculty of Health and Medicine Lancaster University		
Post Code	LA1 4YG		
E-mail	a.duxbury@lancaster.ac.uk		
Telephone	01524 592 974		
Fax			

Please state which academic supervisor(s) has responsibility for which student(s):

*Please click "Save now" before completing this table. This will ensure that all of the student and academic supervisor details are shown correctly.*

Student(s)	Academic supervisor(s)
<b>Student 1</b> Ms Hayley Slater	<input checked="" type="checkbox"/> Dr Anna Daiches <input checked="" type="checkbox"/> Dr Anna Duxbury

A copy of a current CV for the student and the academic supervisor (maximum 2 pages of A4) must be submitted with the application.

**A2-2. Who will act as Chief Investigator for this study?**

- Student  
 Academic supervisor  
 Other

**A3-1. Chief Investigator:**

Date: 28/01/2019

5

251064/1328269/37/297

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	Title Forename/Initials Surname
	Dr Anna Daiches
Post	Clinical Director
Qualifications	MA, D Clin Psych
ORCID ID	
Employer	Lancashire Care NHS Foundation Trust
Work Address	Department of Health Research Faculty of Health and Medicine Lancaster University
Post Code	LA1 4YG
Work E-mail	a.daiches@lancaster.ac.uk
* Personal E-mail	a.daiches@lancaster.ac.uk
Work Telephone	00000000000
* Personal Telephone/Mobile	01524594406
Fax	00000000000

*\* This information is optional. It will not be placed in the public domain or disclosed to any other third party without prior consent.*

*A copy of a current CV (maximum 2 pages of A4) for the Chief Investigator must be submitted with the application.*

**A4. Who is the contact on behalf of the sponsor for all correspondence relating to applications for this project? This contact will receive copies of all correspondence from REC and HRA/R&D reviewers that is sent to the CI.**

	Title Forename/Initials Surname
	Ms Becky Gordon
Address	Research Services B14 Furness College Lancaster University
Post Code	LA1 4YT
E-mail	ethics@lancaster.ac.uk
Telephone	01524592981
Fax	

**A5-1. Research reference numbers. Please give any relevant references for your study:**

Applicant's/organisation's own reference number, e.g. R & D (if available):	not applicable
Sponsor's/protocol number:	not applicable
Protocol Version:	0.1
Protocol Date:	28/07/2018
Funder's reference number (enter the reference number or state not applicable):	not applicable
Project website:	n/a

**Additional reference number(s):**

Ref. Number Description	Reference Number
not applicable	not applicable

*Registration of research studies is encouraged wherever possible. You may be able to register your study through your NHS organisation or a register run by a medical research charity, or publish your protocol through an open*

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access publisher. If you have registered your study please give details in the "Additional reference number(s)" section.

**A5-2. Is this application linked to a previous study or another current application?**

Yes  No

Please give brief details and reference numbers.

n/a

**2. OVERVIEW OF THE RESEARCH**

*To provide all the information required by review bodies and research information systems, we ask a number of specific questions. This section invites you to give an overview using language comprehensible to lay reviewers and members of the public. Please read the guidance notes for advice on this section.*

**A6-1. Summary of the study.** Please provide a brief summary of the research (maximum 300 words) using language easily understood by lay reviewers and members of the public. Where the research is reviewed by a REC within the UK Health Departments' Research Ethics Service, this summary will be published on the Health Research Authority (HRA) website following the ethical review. Please refer to the question specific guidance for this question.

This study will seek to explore the experiences of coping of individuals who are living 'longer-term' with cancer of unknown primary (CUP) i.e. being maintained/stabilised on treatment over 6-months post-diagnosis. This group of patients represent a relatively small sub-group as, unfortunately, a CUP diagnosis is often received in the later stages of illness with a poor prognosis. Research with populations experiencing other cancer diagnoses has highlighted that a range of coping strategies are employed with direct impacts on psychological distress. Uncertainty has been identified as a factor which increases distress for those with cancer. Relatively little is known about the experiences of those diagnosed with CUP, which is a condition entailing a great deal of uncertainty in relation to prognosis, treatment, and illness progression and no research so far has focused specifically upon patients who are stable on treatment so far beyond their diagnosis, and as such have been living with CUP for a prolonged period. Therefore the current study will investigate coping experiences within this population. Data will be gathered via interviews with patients.

**A6-2. Summary of main issues.** Please summarise the main ethical, legal, or management issues arising from your study and say how you have addressed them.

*Not all studies raise significant issues. Some studies may have straightforward ethical or other issues that can be identified and managed routinely. Others may present significant issues requiring further consideration by a REC, HRA, or other review body (as appropriate to the issue). Studies that present a minimal risk to participants may raise complex organisational or legal issues. You should try to consider all the types of issues that the different reviewers may need to consider.*

**Purpose and Design:**

To understand the coping experiences of people living longer-term with CUP, it is necessary to gather first-hand accounts from patients themselves. As such, a qualitative methodological approach was most fitting for this aim and will allow the generation of rich, detailed data from participants through semi-structured interview conversations. The nature of the research topic (CUP) and interview process may inevitably lead to some conversations with participants that are emotive in nature. There is potential for this to cause distress to participants. Should this occur the participants will be given the option to pause or stop the interview. Participants will be offered time to talk to the chief investigator and discuss possible support options. The chief investigator is a trainee clinical psychologist who regularly has difficult and emotionally laden conversations of this nature with clients in their clinical work. Resources for further support are listed on the participant information sheet should they be required in the event of distress. If there are concerns for the participant's emotional well-being, the chief investigator will liaise with the field supervisor,

Dr [REDACTED] (Principal Clinical Psychologist) who is an experienced clinical psychologist working in cancer services to discuss what support may be appropriate. Should any participant indicate any thoughts or intentions of harming themselves in any way as a result of distress, confidentiality will be broken (as outlined on the consent form) in order to ensure the relevant services are involved to provide the participant with support.

Service users from the Patient Cancer Care Improvement Group at [REDACTED] were consulted regarding the content of the recruitment materials and interview questions regarding how distress could be minimised for participants through use of sensitive language. Feedback from the group members was that they were in favour of the project as a means to better understand and potentially provide recommendations to improve the experiences of

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CUP patients.

## Consent:

Potential participants will be identified by a member of medical staff from their CUP team. The CUP team will be made aware of the inclusion and exclusion criteria for the study so that appropriate participants can be identified. This information is outlined in the 'Professionals' information sheet'.

Potential participants will receive a copy of the participant information sheet and, if they are interested in participating, will be invited to fill in a 'consent to be contacted form' with their contact details (name and telephone number). Their contact details will then be passed on to the Chief Investigator by the CUP team. A period of 1 week will be left between the participant giving their permission to be contacted and contact being made to allow participants time to review the information sheet and consider any questions they may like to ask. Following this time period, the chief investigator will telephone the participant to informally discuss the study and answer any questions. If at this stage the participant is still willing to be part of the study a meeting for the interview will be arranged. Immediately before the interview the chief investigator will go through the consent form with the participant to ensure their understanding of each item. They will then be asked whether they are happy to proceed and sign the consent form. The participant will be reminded that they are under no obligation to participate and that the medical care they receive will not be impacted by their taking part. They will be reminded that they are free to withdraw at any time without giving reason up until two weeks following interview at which point the data will have been anonymously transcribed for inclusion in the analysis.

## Risks, burdens, and benefits:

There are no direct benefits associated with participation in the study. It is hoped that findings from the study will inform best practice for how services can support people living longer-term with CUP.

As discussed above, there is a possibility that interviews may involve the discussion of emotional content which may be distressing for participants. Measures will be taken to minimise and manage any distress that arises, including: informing participants we can pause or terminate the interview at any time and signposting participants to resources (included in the participant information sheet) for further support if indicated. The Chief Investigator may also liaise with the field supervisor, Dr [REDACTED] (Clinical Psychologist) around what specific local support may be available or any onward referrals that may be beneficial. The Patient Cancer Care Improvement Group at [REDACTED] provided consultation on the phrasing of interview questions in order to minimise the distress and wording may cause. Participants are made aware on the consent form that their clinical nurse specialist will be routinely made aware of their participation in the study in case of any further support being needed. Clinical nurse specialists will be alerted to their patient's participation by the 'letter to clinical nurse specialists' which will be sent out following the interview.

Should any risk to or from self or others be disclosed by participants during interviews the interview process may be paused or terminated to allow the arising issues to be appropriately managed. Participants will be made aware by the consent form, participant information sheet, and verbally that should any risks be identified their confidentiality may be breached in order for appropriate actions to be taken to ensure the safety of those involved in the disclosure. There may be some risk to the chief investigator associated with conducting interviews in patients' own homes. As such the [REDACTED] 'Lone Working' Policy guidelines will be followed. In the instance of home visits to any participants recruited via [REDACTED], risk assessment procedures will also be followed.

It is hoped that by focusing upon a sample population who are deemed to be clinically stable, the research will avoid placing undue burden upon those who are acutely or severely physically unwell who may find participation particularly challenging. However, due to their diagnosis, it is possible that participants may be experiencing fatigue or become unwell during interview. In these instances the interview will be terminated and, with participant consent, may be continued at another time. The chief investigator will discuss with participants when arranging interviews whether they would prefer to conduct the interview over two sessions to minimise the risk of fatigue or symptom exacerbation.

## Confidentiality:

The "Caldicott Principles" and Data Protection Act (1998) have been considered when designing this research project. No personal patient information will be available to the chief investigator until the patient gives their consent to be contacted and shows interest in participating in the study. At this stage, personal data gathered by the chief investigator will be kept to the minimum required, namely a name and contact telephone number. Should the individual wish for their interview to be conducted at their home address this information will be gathered over the telephone and stored with their 'consent to be contacted form'. This data will be stored securely in a locked drawer in the chief investigator's home and will be shredded as soon as the interview has taken place.

The interview will be audio recorded. The recording will be transferred as soon as practically possible to the chief investigator's secure storage space on the Lancaster University Network which is password protected. It will then be transcribed anonymously, using a pseudonym. Any identifying information (e.g. names of family members or home town) will be redacted to protect anonymity. The participant will be referred to only by the pseudonym throughout the

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analysis and write-up of the project. Once the interview is transcribed the recording will be deleted from the Lancaster University storage drive. The transcripts will be saved electronically in the drive. Upon submission of the project, transcripts will be securely electronically transferred to Lancaster University's Doctorate in Clinical Psychology who will retain them for up to ten years as per their assessment policy. Consent forms will be scanned to create an electronic copy, once this is completed the paper copy will be shredded. The electronic version will be stored on the Lancaster University server for a maximum of six months following project completion, in line with Lancaster University Doctorate in Clinical Psychology guidance.

Participants will be informed prior to the interview, both in writing (on consent form) and verbally, that their confidentiality may be breached if there are any concerns about risk to them or others. In this scenario the chief investigator would consult with their field supervisor regarding the best course of action, considering the participant's wishes where possible. The clinical nurse specialist of each participant will be made aware of their participation in the study by the 'clinical nurse specialist letter' which will be sent following the interview. This is to make the clinical nurse specialists aware of the possibility further support may be needed by participants following their interview.

**Conflict of Interest:**

There are no issues in relation to conflict of interest.

**Feedback to Participants:**

Participants will be asked to provide their postal address on their consent form should they wish to receive a summary of results from the study following completion.

**Grievances:**

Contact details for the chief investigator's supervisors is included in the participant information sheet should any participants wish to make a complaint regarding any aspect of the research process.

**3. PURPOSE AND DESIGN OF THE RESEARCH****A7. Select the appropriate methodology description for this research. Please tick all that apply.**

- Case series/ case note review
- Case control
- Cohort observation
- Controlled trial without randomisation
- Cross-sectional study
- Database analysis
- Epidemiology
- Feasibility/ pilot study
- Laboratory study
- Metanalysis
- Qualitative research
- Questionnaire, interview or observation study
- Randomised controlled trial
- Other (please specify)

n/a

**A10. What is the principal research question/objective? Please put this in language comprehensible to a lay person.**

What are the coping experiences of people who are living longer-term with CUP?

**A11. What are the secondary research questions/objectives if applicable? Please put this in language comprehensible to a lay person.**

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- Do these patients feel able to cope? What factors increase or decrease perceived coping capacity?
- Has their sense of 'coping' changed throughout their illness?
- Do patients feel that coping longer term with CUP is qualitatively different than coping with a cancer of known primary site?

**A12. What is the scientific justification for the research? Please put this in language comprehensible to a lay person.**

Research has demonstrated that people diagnosed with all forms of cancer may experience increased levels of emotional distress (Carlson et al., 2004; Zabora et al., 2001) and mental health difficulties (Singer, Das-Munshi and Brähler, 2010).

CUP is a relatively under-researched area given that it is one of the most lethal forms of cancer (Hemminki, Bevier, Hemminki, & Sundquist, 2012; van de Wouw, Janssen-Heijnen, Coebergh, & Hillen, 2002). A diagnosis of CUP is given when a secondary cancer is found without an identifiable primary source (Varadhachary & Raber, 2014). Due to this, the condition is often characterised by uncertainty in relation to cause, prognosis, and treatment (Ryan, Lawlor & Walshe, 2013; Symons, James & Brooks, 2009). This uncertainty has been shown to amplify the difficulties encountered across other cancer diagnoses for patients with CUP (La Pushin, 2009; Richardson et al., 2015).

Understandably, these emotional difficulties encountered as a result of living with cancer may impact on the individual's perceived coping capacity. Coping can be defined as "constantly changing cognitive and behavioural efforts to manage external and/or internal demands that are appraised as taxing or exceeding the resources of the person" (Lazarus & Folkman, 1984). Previous studies have demonstrated that people living with cancer employ a wide range of coping styles and strategies (Al-Azri, Al-Awisi & Al-Moundhri, 2017; Nipp et al., 2016), which may positively or negatively impact psychological wellbeing (Roesch et al., 2005). As yet, little research has been undertaken to investigate the coping experiences of people with CUP. However, findings showing that increased uncertainty negatively impacts upon ability to implement coping strategies (Germino et al., 1998) allows us to infer that 'coping' may be a particular challenge for people living with CUP.

While unfortunately a diagnosis of CUP often indicates poor prognosis and limited life expectancy (Greco et al., 2010), a subset of patients are medically stable over six months following diagnosis (Riihimäki, Hemminki, Sundquist, & Hemminki, 2013). This group of patients, therefore, has an extended period of living with and coping with CUP, and potentially the associated uncertainty and emotional distress. No research has previously been undertaken which focuses on the experiences of coping for this patient population and, therefore, it is believed that this research is warranted. It is hoped the study will increase understanding of patients' experiences and therefore how services can best support them throughout their time living with CUP.

**A13. Please summarise your design and methodology. It should be clear exactly what will happen to the research participant, how many times and in what order. Please complete this section in language comprehensible to the lay person. Do not simply reproduce or refer to the protocol. Further guidance is available in the guidance notes.**

The research will be qualitative in nature and will use interpretative phenomenological analysis (IPA) as the guiding approach and analytic strategy. This methodological approach was selected due to the focus on understanding the lived experience of individuals which best met the remit of the research questions.

Sample:

Participants will be recruited from across seven NHS Trust CUP services: [REDACTED]

[REDACTED] Seven Trusts were identified as, despite the relatively small sample size, it is anticipated that the number of people meeting inclusion criteria in each Trust may be very low, due to the nature of CUP. Relevant clinical staff will be provided with information about the study and the inclusion/exclusion criteria in order to identify appropriate candidates via the 'Professional's Information Sheet'.

Participants will need to have been diagnosed with CUP over six months before the interview and will need to be assessed to be 'medically stable' by their clinical team. These patients treated by CUP services come from the 80-85% of those diagnosed who do not belong to favourable risk subsets, for whom the median survival time is generally less than 1 year (Fizazi et al 2015).

Participants will need to be 18 years of age or older and have capacity to provide informed consent to participate. Unfortunately, patients that cannot speak English will not be able to participate as there are no funds available within the scope of this research to provide translation services.



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A sample size of 10-12 participants will be recruited in line with the recommendations for an IPA study (Smith & Osborne, 2008).

## Recruitment and consent:

Recruitment will commence once the necessary ethical approval has been granted. Patients identified as meeting the inclusion criteria will be provided with a participant information sheet by a member of their clinical team. If they are interested in participating, they will be asked to provide their name and contact number on the 'consent to be contacted' form. A period of one week will be left in between the participant providing these details and the chief investigator making contact to allow time to re-read the information sheet and generate any questions. Following this period, the chief investigator will contact the potential participant by telephone for an informal discussion about the study and to answer any questions. If at this stage the potential participant is still interested in participating, an interview will be scheduled. The participant will be given a choice between meeting in their own home or at their hospital site.

Immediately prior to the interview, the chief investigator will go through the consent form with the participant to ensure understanding of each item. It will be reiterated that the participant is under no obligation to complete the interview and that they are free to withdraw at any time until two weeks after the interview without giving any reason. The participant will be asked to sign the consent form if they are happy to continue.

## Interview:

Each participant will partake in one interview lasting for approximately one hour. Participants will be given the option to split the interview across multiple sessions if required in order to reduce risk of fatigue/exacerbation of any symptoms of physical illness.

The interview will be semi-structured, having topics related to the research questions, but also allowing for flexibility to explore any salient points made in more depth and make the interview more conversational and participant-led. The semi-structured interview is considered the best tool for gathering data for an IPA study (Smith & Osborne, 2008).

Before the interview commences participants will be reminded about the limits of confidentiality should there be any concerns for wellbeing and of their right to withdraw, as stated above. They will also be advised the interview may be paused at any time should they feel distressed or emotional. Participants will be signposted to the resources provided on the participant information sheet should they feel in need of further support.

Interviews will be audio recorded which patients are made aware of via the participant information sheet and consent form.

Participants will be asked to fill out their postal address on the consent form if they would like to receive a summary of the study results following completion of the project.

At the face to face interview, the chief investigator will also go through a brief demographic information questionnaire (Demographic Information Form) to gather the participant's age, time since CUP diagnosis, gender, and ethnicity. This will take no longer than five minutes and participants will be free to decline to give the information.

The recruitment materials and interview schedule were developed with consultation from service users from the Patient Cancer Care Improvement group.

Patients will be asked on the consent form whether they would be willing to partake in a follow up interview should any additional themes or questions arise later in the research process which may help to generate richer data. This contact would occur within three months of the initial interview. Patients will be made aware that they are free to decline to consent to this.

**A14-1. In which aspects of the research process have you actively involved, or will you involve, patients, service users, and/or their carers, or members of the public?**

- Design of the research
- Management of the research
- Undertaking the research
- Analysis of results
- Dissemination of findings
- None of the above

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*Give details of involvement, or if none please justify the absence of involvement.*

Service users from the Patient Cancer Care Improvement group which is facilitated by [REDACTED] at [REDACTED] were invited to consult on the study's recruitment materials and interview questions. The whole group was invited and two service users were able to attend. Feedback was provided regarding the language and terminology used, how 'reader-friendly' recruitment materials were, and whether interview questions were perceived as appropriate and sensitively phrased in order to minimise the likelihood of distress. Feedback from service users was favourable and the group members supported the study as an opportunity to better understand patient experiences and potentially provide recommendations which may lead to improvements for CUP patients.

All participants will be given the option to receive a summary of the study results following project completion.

## 4. RISKS AND ETHICAL ISSUES

## RESEARCH PARTICIPANTS

## A15. What is the sample group or cohort to be studied in this research?

Select all that apply:

- Blood
- Cancer
- Cardiovascular
- Congenital Disorders
- Dementias and Neurodegenerative Diseases
- Diabetes
- Ear
- Eye
- Generic Health Relevance
- Infection
- Inflammatory and Immune System
- Injuries and Accidents
- Mental Health
- Metabolic and Endocrine
- Musculoskeletal
- Neurological
- Oral and Gastrointestinal
- Paediatrics
- Renal and Urogenital
- Reproductive Health and Childbirth
- Respiratory
- Skin
- Stroke

Gender: Male and female participants

Lower age limit: 18 Years

Upper age limit: No upper age limit

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**A17-1. Please list the principal inclusion criteria (list the most important, max 5000 characters).**

Participants will be included based upon the following criteria:

- Diagnosis of CUP
- Clinically stable 6 months or more following diagnosis
- Receiving treatment or being actively monitored by Trust care teams
- 18 years or older

**A17-2. Please list the principal exclusion criteria (list the most important, max 5000 characters).**

- Participants will be excluded if for any reason they are not able to engage with the research process or give informed consent to participate e.g. not speaking English, significant learning disability or cognitive impairment

**RESEARCH PROCEDURES, RISKS AND BENEFITS****A18. Give details of all non-clinical intervention(s) or procedure(s) that will be received by participants as part of the research protocol. These include seeking consent, interviews, non-clinical observations and use of questionnaires.**

Please complete the columns for each intervention/procedure as follows:

1. Total number of interventions/procedures to be received by each participant as part of the research protocol.
2. If this intervention/procedure would be routinely given to participants as part of their care outside the research, how many of the total would be routine?
3. Average time taken per intervention/procedure (minutes, hours or days)
4. Details of who will conduct the intervention/procedure, and where it will take place.

Intervention or procedure	1	2	3	4
Consent gained from participant by clinical staff to be contacted by the chief investigator	1	0	5 minutes	Clinical staff team- likely to be clinical nurse specialists or consultant oncologists. Conversation to take place during routine contact.
Phone contact from chief investigator to answer any questions and, if agreed with participant, schedule interview slot.	1	0	15 minutes	Hayley Slater, Chief Investigator. Phone contact.
In person consent seeking immediately prior to interview. Opportunity to answer any questions.	1	0	5 minutes	Hayley Slater, Chief Investigator. Interviews will take place at hospital site or participants own home depending on preference.
Interview (one one-off interview, may be split across 2 sessions if this best meets participant needs to minimise fatigue, physical symptoms etc.)	1-2	0	1 hour	Hayley Slater, Chief Investigator. Will take place at hospital site or participants' own home depending on preference.
Follow up interview (in the event of any new themes/questions arising later in research process). As above, if the participant is experiencing fatigue etc. interview may be over 2 sessions.	1-2	0	1 hour	Hayley Slater, Chief Investigator. Will take place at hospital site or participants' own home depending on preference.

**A21. How long do you expect each participant to be in the study in total?**

Approximately 1 hour in a one-off interview. This may be split over 2 sessions lasting 20-30 minutes each in order to minimise fatigue for participants if appropriate.

Patients will be asked on the consent form and whether they would be willing to be contacted to partake in a follow-up interview should any new themes or questions arise later in the research process. This follow up interview would again be a maximum of 1 hour in duration. This interview will be arranged within three months of the initial interview occurring.

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**A22. What are the potential risks and burdens for research participants and how will you minimise them?**

*For all studies, describe any potential adverse effects, pain, discomfort, distress, intrusion, inconvenience or changes to lifestyle. Only describe risks or burdens that could occur as a result of participation in the research. Say what steps would be taken to minimise risks and burdens as far as possible.*

Participants will be asked questions about their experiences of CUP and how they have coped since their diagnosis. This is inevitably a highly sensitive area and there is a possibility that discussing these topics may be emotionally challenging or difficult for participants. Steps that have and will be taken to minimise the likelihood and severity of participant distress include:

- Consulting with service users regarding choice of language and interview questions to use language that is sensitive and least distressing
- Making participants aware prior to the interview that we can break and pause the interview at any point. They will also be made aware that at any point the interview can be terminated if preferred and they may withdrawn from the study any time until 2 weeks following the interview when transcription occurs. In the event that a participant wishes to withdraw from the study part way through an interview, their will not be included in the study.
- Participants will have time as required during or following the interview to talk through any issues that are raised with the chief investigator.
- Options for further support will be discussed with each participant. These are outlined on the participant information sheet and will be re-referred to at interview. If the participant is highly distressed, the chief investigator will consult with their field supervisor regarding what support may be available and any onward referrals for psychological support as indicated and desired by the participant. If there are any concerns for the participant's safety this will be immediately discussed with the field supervisor and acted on accordingly.

Measures will also be taken to promote participants' physical comfort and reduce risk of fatigue/exacerbation of physical symptoms. To do so participants will be given the option of completing the approximately 60 minute interview over 2 shorter sessions.

**A23. Will interviews/ questionnaires or group discussions include topics that might be sensitive, embarrassing or upsetting, or is it possible that criminal or other disclosures requiring action could occur during the study?**

Yes  No

*If Yes, please give details of procedures in place to deal with these issues:*

Yes, that topic of the research (CUP) is such that discussing their experience may be upsetting or distressing for participants. To manage this, participants will be made aware that interviews can be paused or terminated at any time. If upset or distressed, participants will have opportunity to talk with the chief investigator about any concerns. Resources for support will be provided for each participant on the participant information sheet. If the participant is highly distressed or feels in need of further support, the chief investigator will contact their field supervisor to seek advice and consider possible support options or onward referrals, considering the participant's preferences.

If any disclosures are to occur during the interview process, the chief investigator will contact their field supervisor for support regarding next steps. If the disclosure is of an urgent/emergency nature the chief investigator will contact emergency services as appropriate. All participants will be made aware prior to interview that confidentiality will be breached if there are any concerns for their safety or the safety of anybody else.

**A24. What is the potential for benefit to research participants?**

There are no direct benefits associated with participation in the study. Patients may find it helpful to talk openly about their experiences.

**A26. What are the potential risks for the researchers themselves? (if any)**

It is possible that the content of interview discussions may be upsetting for the chief investigator. If this is the case support will be sought from the field and clinical supervisors as required.

There may be risks to the chief investigator associated with lone working when conducting interviews in participants' own homes. To minimise this risk the Lone working Policy of [REDACTED] the chief investigator's employer, will be followed. This will mean that risks will be assessed by the chief investigator on arrival and interview will be immediately terminated if there are any concerns for safety. A 'buddy' system will also be put in place, with the chief investigator arranging with a peer for the peer to monitor their safety. The peer will be made aware

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of the location of the interview and expected duration. The chief investigator will contact the 'buddy' once the interview is complete and log their safety. If this contact is not made, the buddy will follow procedures to ensure that the chief investigator is safe and raise the alarm if there are any concerns.

In instances of home visits to any patients recruited via [REDACTED] Trust's local Lone Working Policy Guidelines will be followed in addition to established [REDACTED] Procedures. The advice given in both sets of guidelines are roughly similar, however, for home visits to patients of [REDACTED] an additional risk assessment form will be completed prior to any visits taking place.

## RECRUITMENT AND INFORMED CONSENT

*In this section we ask you to describe the recruitment procedures for the study. Please give separate details for different study groups where appropriate.*

**A27-1. How will potential participants, records or samples be identified? Who will carry this out and what resources will be used?** For example, identification may involve a disease register, computerised search of GP records, or review of medical records. Indicate whether this will be done by the direct healthcare team or by researchers acting under arrangements with the responsible care organisation(s).

Potential participants will be identified by clinical staff (e.g. clinical nurse specialists, medical oncologists) working in the CUP services where recruitment will take place. Relevant staff will be provided with a 'professionals' information sheet' listing inclusion and exclusion criteria along with information about the study to aid staff in selecting eligible participants.

Potential participants (i.e. meeting inclusion/exclusion criteria) will be asked during routine contact by the staff member whether they are willing to be contacted by the chief investigator to discuss the study, ask any questions, and, if willing, arrange an interview slot. The chief investigator will confirm that criteria are met during the preliminary telephone conversation prior to interview. Informed consent will be gathered by the researcher immediately prior to the interview taking place.

The chief investigator will not have any access to any personal information prior to participants providing details on the 'consent to be contacted form'. This form will ask for the participant's name and contact telephone number.

**A27-2. Will the identification of potential participants involve reviewing or screening the identifiable personal information of patients, service users or any other person?**

Yes  No

*Please give details below:*

n/a

**A28. Will any participants be recruited by publicity through posters, leaflets, adverts or websites?**

Yes  No

**A29. How and by whom will potential participants first be approached?**

By a clinical nurse specialist or other member of the individual's direct healthcare team. Clinical staff in the CUP teams will be provided with a 'professionals' information sheet' providing information about the study and outlining the inclusion and exclusion criteria in order to identify eligible patients. Patients will be approached by clinical staff during routine contact. They will be provided with the 'participant information sheet' and have chance to discuss the study with the member of staff. If they are interested in participating, they will be asked to complete the 'consent to be contacted' sheet in order for their details to be passed to the chief investigator.

Once these details are collected, a period of one week will be left in order to give patients time to read over the provided information and consider any questions. Following this, the chief investigator will contact potential participants on the provided telephone number. This telephone call will provide time to discuss the study and answer any questions. If patients are still interested in participating at this stage then an interview will be arranged during the call.

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The chief investigator will have no access to any personal records or information for any patients prior to participants agreeing to be contacted by the chief investigator.

**A30-1. Will you obtain informed consent from or on behalf of research participants?**

Yes  No

*If you will be obtaining consent from adult participants, please give details of who will take consent and how it will be done, with details of any steps to provide information (a written information sheet, videos, or interactive material). Arrangements for adults unable to consent for themselves should be described separately in Part B Section 6, and for children in Part B Section 7.*

*If you plan to seek informed consent from vulnerable groups, say how you will ensure that consent is voluntary and fully informed.*

Informed consent will be obtained from all study participants.

Patients meeting the study's inclusion and exclusion criteria will be identified by direct healthcare staff. They will be provided with a 'participant information sheet' during routine clinical contact. If they are interested in finding out more or participating, they will be asked by the member of clinical staff to complete a 'consent to be contacted' sheet, giving their name and contact number.

A time period of one week will then be left prior to contact to give patients time to re-read the 'participant information sheet' and consider and questions they may like to ask.

Following the one week period, the chief investigator will make contact with the potential participant to informally discuss the study and answer any questions. If at this stage the patient is happy to participate in the study, an interview slot will be arranged.

Immediately prior to the interview, the participant will be given time to ask any further questions. The chief investigator will go through the consent form with the participant, ensuring that the participant has a full understanding of each item on the form that they are consenting to. Participants will be reminded that they are under no obligation to participate in the study and that their participation has no impact on the medical care they receive. Participants will also be made aware that they are able to stop the interview or withdraw from the study without giving reason up until 2 weeks after the interview has taken place. At this stage their interviews will be transcribed and anonymised and they will be unable to withdraw, although every effort will be made to ensure all personal and identifiable information is removed.

As per the Mental Capacity Act (2005), all participants will be assumed to have capacity to provide informed consent. The chief investigator will be responsible for assessing during contact whether the individual has capacity to consent. The chief investigator is a trainee clinical psychologist with experience of seeking consent from a range of service users in clinical practice. If there is any reason to doubt that a participant does not have capacity to provide informed consent then the following steps will be taken:

- Discussion with the clinical team regarding their understanding of the individual's capacity and reason for putting them forward for the study
- Consideration of whether the individual is able to understand, weigh up, retain given information, and communicate their decision in line with the principles of the Mental Capacity Act (2005). This will be discussed by the chief investigator with their clinical and field supervisors to ensure appropriate assessment has been carried out with reasonable adjustments made to support understanding.
- If, based on the above criteria, the individual is not able to provide informed consent then they will be excluded from the study.

- All recruitment materials have been written in plain language with feedback given by service users during a consultation session to ensure that they are accessible and easy to understand.

*If you are not obtaining consent, please explain why not.*

n/a

Please enclose a copy of the information sheet(s) and consent form(s).

**A30-2. Will you record informed consent (or advice from consultees) in writing?**

Yes  No

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**A31. How long will you allow potential participants to decide whether or not to take part?**

One week will be left between potential participants agreeing to be contacted by the researcher and the researcher making telephone contact to allow time to read the information sheet. During the telephone contact potential participants will have opportunity to ask questions and, with their agreement a time slot for interview will be allocated at least another 24 hours later to allow more time for the potential participant to consider the given information and change their mind. Informed consent will be sought (written and verbal) immediately before interviews taking place.

If during the telephone call participants are still unsure about whether they would like to participate, they will be advised that they may continue to consider their answer and may contact the chief investigator on their research mobile phone if they have any further questions or decide they would like to participate.

Recruitment will begin once the relevant ethical approvals have been granted. The window for recruitment will have no fixed time limit and will end either once the target number of participants have been recruited or due to time constraints relating to the scheduled submission of the project. Participants will be recruited on a first come first served basis. Exceptions to this may be made only in the interest of maintaining gender balance within the sample, for example if there is a greater proportion of females recruited, a male participant may be selected ahead of further female participants if there are more participants interested than the sample limit of 12.

**A33-1. What arrangements have been made for persons who might not adequately understand verbal explanations or written information given in English, or who have special communication needs?(e.g. translation, use of interpreters)**

Unfortunately there are no funds available as part of this project for interpreter services and as such participants who do not speak English will be excluded. The process of translation may also impact the interpretative analytic process used in IPA and therefore is best avoided.

Consultation from a service user group was sought for feedback on participant materials to ensure that language and layout are understandable for patients.

**A35. What steps would you take if a participant, who has given informed consent, loses capacity to consent during the study? Tick one option only.**

- The participant and all identifiable data or tissue collected would be withdrawn from the study. Data or tissue which is not identifiable to the research team may be retained.
- The participant would be withdrawn from the study. Identifiable data or tissue already collected with consent would be retained and used in the study. No further data or tissue would be collected or any other research procedures carried out on or in relation to the participant.
- The participant would continue to be included in the study.
- Not applicable – informed consent will not be sought from any participants in this research.
- Not applicable – it is not practicable for the research team to monitor capacity and continued capacity will be assumed.

**Further details:**

If in between the initial permission to contact stage and the interview taking place there is reason to believe the individual may have come to lack capacity to consent or take part in the study they would be excluded from the study.

If the participant has capacity to consent immediately prior to interview and throughout the interview process but later comes to lack capacity, their data would still be included in the study.

All participant interview data will be anonymised using a pseudonym and and personal or identifiable details will be redacted.

*If you plan to retain and make further use of identifiable data/tissue following loss of capacity, you should inform participants about this when seeking their consent initially.*

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In this section, personal data means any data relating to a participant who could potentially be identified. It includes pseudonymised data capable of being linked to a participant through a unique code number.

## Storage and use of personal data during the study

**A36. Will you be undertaking any of the following activities at any stage (including in the identification of potential participants)? (Tick as appropriate)**

- Access to medical records by those outside the direct healthcare team
- Access to social care records by those outside the direct social care team
- Electronic transfer by magnetic or optical media, email or computer networks
- Sharing of personal data with other organisations
- Export of personal data outside the EEA
- Use of personal addresses, postcodes, faxes, emails or telephone numbers
- Publication of direct quotations from respondents
- Publication of data that might allow identification of individuals
- Use of audio/visual recording devices
- Storage of personal data on any of the following:
  - Manual files (includes paper or film)
  - NHS computers
  - Social Care Service computers
  - Home or other personal computers
  - University computers
  - Private company computers
  - Laptop computers

*Further details:*

Consent to be contacted form: The consent to be contacted form will be filled out by patients at the hospital site and retained in their clinical records. The participant's name and telephone number from the form will be provided via telephone to the chief investigator by the clinical staff. The chief investigator will keep the participant's name and phone number on a paper log sheet which will be kept in a locked drawer in the chief investigator's home. Nobody other than the chief investigator will have access to this drawer. Once the interview has taken place these details will be immediately shredded.

Consent form: The consent form will be completed immediately before the interview takes place. One copy of this form will be retained by the chief investigator, one copy will be retained by the patient, and one copy will be kept in the clinical file. Following the interview, the chief investigator will upload their copy to create an electronic document. The paper copy will then be shredded. The electronic copy of the consent form will be stored on the chief investigator's personal storage area on the Lancaster University server which is password protected and secure. The electronic consent form will be stored for a maximum of six months following completion of the study in line with Lancaster University's doctorate in clinical psychology data storage procedures. In the instance that an interview takes place in a participant's home, the file copy of the consent form will be attached to the letter to the clinical nurse specialist in order for it to be kept in their clinical record. This will be sent as soon as practically possible. Until this time, the consent form will be stored securely by the chief investigator in a locked drawer.

Interview audio recording: The audio recording of each interview will be uploaded as a file to the chief investigator's university storage area which is password protected and secure. This will be done as soon as practically possible following the interview. The recording will then be deleted from the Dictaphone. The recording file will be deleted once the interview has been transcribed by the chief investigator.

Interview transcript: The interview will be transcribed electronically by the chief investigator. The transcription will be anonymised and all personal or identifiable information will be redacted. The transcription will be stored electronically in the chief investigator's university storage area which is password protected and secure. The file will be saved separately to the consent forms so the two cannot be linked. During the analysis stage, paper copies of the



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transcription will be made in order for themes to be highlighted. These paper copies will be stored in a locked drawer in the chief investigator's home. Only the chief investigator has access to this drawer. Once this stage of the transcription is completed, the annotated transcripts will be scanned to create electronic files which will be uploaded to the chief investigator's university storage area which is password protected and secure. The paper copies will then be shredded.

Once the study is complete, the electronic transcripts will be transferred electronically via the Lancaster University VPN to the research coordinator of the doctorate in clinical psychology at Lancaster University. They will then be deleted from the chief investigator's university storage area. The files will be stored for a maximum of ten years by the research director, in line with the course protocol. They will then be deleted by the research director.

Demographic Information Form: This form will be scanned as an electronic copy as soon as practically possible following the interview. The electronic document will be stored in the chief investigator's secure, password-protected university storage drive. The hard copy will then be shredded. This document will be stored for a maximum of six months following completion of the study in line with Lancaster University's doctorate in clinical psychology data storage procedures.

**A37. Please describe the physical security arrangements for storage of personal data during the study?**

As stated in A36, electronic files (consent form, interview audio recordings, and interview transcripts) will be stored in the chief investigator's personal storage area on the Lancaster University server which is password protected and secure. As the audio recording device that will be used to encrypt interviews is not encrypted, audio files will be transferred to the secure storage space as quickly as practically possible then the recording will be deleted from the recording device. In the meantime the recording device will be stored securely by the chief investigator.

Paper documents (transcripts and participant contact details) will be stored for the minimum possible time in a locked drawer in the chief investigator's home. Nobody else has access to this drawer.

**A38. How will you ensure the confidentiality of personal data? Please provide a general statement of the policy and procedures for ensuring confidentiality, e.g. anonymisation or pseudonymisation of data.**

Participant data will be handled in line with the NHS Code of Confidentiality (2003) and Lancaster University's doctorate in clinical psychology data storage policy ([http://www.lancaster.ac.uk/shm/study/doctoral\\_study/dclinpsy/onlinehandbook/ethics\\_and\\_data\\_storage\\_advice/](http://www.lancaster.ac.uk/shm/study/doctoral_study/dclinpsy/onlinehandbook/ethics_and_data_storage_advice/))

Interview data will be anonymously transcribed using a pseudonym, following which original recordings will be deleted.

Participant information will be stored securely, held for the minimal necessary time, and securely disposed of (e.g. by shredding or deletion).

**A40. Who will have access to participants' personal data during the study? Where access is by individuals outside the direct care team, please justify and say whether consent will be sought.**

Personal data may be accessed by direct care staff during the recruitment process to verify whether patients meet the study inclusion and exclusion criteria.

The chief investigator will have access to patient's names and telephone numbers (once consent provided on the 'consent to be contacted' sheet) and then to data provided by the participant during interview (interview data and demographic information form).

The chief investigator's field and research supervisors may have access to the anonymised transcripts to support the process of data analysis.

**Storage and use of data after the end of the study****A41. Where will the data generated by the study be analysed and by whom?**

The data will be analysed by the chief investigator at their home address. Guidance will be obtained from the research supervisor and field supervisor in relation to analysis.

Paper copies of transcripts and participant contact details will be stored in a locked drawer in the chief investigator's home to which only the chief investigator has access. Electronic copies of materials for the analysis will be stored

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securely on the chief investigator's personal storage area on the Lancaster University server which is password protected.

**A42. Who will have control of and act as the custodian for the data generated by the study?**

	Title	Forename/Initials	Surname
	Dr	Bill	Sellwood
Post	Professor, Programme Director, Doctorate in Clinical Psychology, Lancaster University		
Qualifications	PhD		
Work Address	Division of Health Research Furness College, Lancaster University Lancaster		
Post Code	LA1 4YG		
Work Email	b.sellwood@lancaster.ac.uk		
Work Telephone	01524593998		
Fax			

**A43. How long will personal data be stored or accessed after the study has ended?**

- Less than 3 months  
 3 – 6 months  
 6 – 12 months  
 12 months – 3 years  
 Over 3 years

**A44. For how long will you store research data generated by the study?**

Years: 10  
Months:

**A45. Please give details of the long term arrangements for storage of research data after the study has ended. Say where data will be stored, who will have access and the arrangements to ensure security.**

Once the research has ended the interview transcripts will be encrypted and securely transferred by the chief investigator to the Lancaster University Doctorate in Clinical Psychology Research Coordinator. The chief investigator will send a separate email to the research coordinator with the password for the encrypted files, the end date of the study, and when files should be deleted. They will be stored for up to ten years as per the course's policy. Following this time they will be deleted by the Research Director. The course will store the files in a password-protected space on the University server.

**INCENTIVES AND PAYMENTS****A46. Will research participants receive any payments, reimbursement of expenses or any other benefits or incentives for taking part in this research?**

- Yes     No

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**A47. Will individual researchers receive any personal payment over and above normal salary, or any other benefits or incentives, for taking part in this research?**

Yes  No

**A48. Does the Chief Investigator or any other investigator/collaborator have any direct personal involvement (e.g. financial, share holding, personal relationship etc.) in the organisations sponsoring or funding the research that may give rise to a possible conflict of interest?**

Yes  No

## NOTIFICATION OF OTHER PROFESSIONALS

**A49-1. Will you inform the participants' General Practitioners (and/or any other health or care professional responsible for their care) that they are taking part in the study?**

Yes  No

*If Yes, please enclose a copy of the information sheet/letter for the GP/health professional with a version number and date.*

**A49-2. Will you seek permission from the research participants to inform their GP or other health/ care professional?**

Yes  No

*It should be made clear in the participant's information sheet if the GP/health professional will be informed.*

## PUBLICATION AND DISSEMINATION

**A50. Will the research be registered on a public database?**

Yes  No

*Please give details, or justify if not registering the research.*

The study has been registered with The National Cancer Research Institute (NCRI) as a piece of research which addresses one of the current 'Top 26 living with and beyond cancer research questions'. No registry reference number is provided by the NCRI. Web link: <https://www.ncri.org.uk/lwbc/>

*Registration of research studies is encouraged wherever possible.*

*You may be able to register your study through your NHS organisation or a register run by a medical research charity, or publish your protocol through an open access publisher. If you are aware of a suitable register or other method of publication, please give details. If not, you may indicate that no suitable register exists. Please ensure that you have entered registry reference number(s) in question A5-1.*

**A51. How do you intend to report and disseminate the results of the study? Tick as appropriate:**

- Peer reviewed scientific journals
- Internal report
- Conference presentation
- Publication on website
- Other publication
- Submission to regulatory authorities
- Access to raw data and right to publish freely by all investigators in study or by Independent Steering Committee

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on behalf of all investigators

No plans to report or disseminate the results

Other (please specify)

n/a

**A52. If you will be using identifiable personal data, how will you ensure that anonymity will be maintained when publishing the results?**

Pseudonyms will be used for participants and no clearly identifying details will be included. Any personal details that may identify the participant that are disclosed during the interview will be redacted to maintain anonymity. These may include hometown, names of friends or relatives, names of clinical staff, specifics of occupation etc.

**A53. Will you inform participants of the results?**

Yes  No

*Please give details of how you will inform participants or justify if not doing so.*

Patients will be asked on the consent form if they would like to receive a summary of results once the project is completed. If they would like to receive the results they will be asked to provide a postal address on the consent form.

**5. Scientific and Statistical Review****A54. How has the scientific quality of the research been assessed? Tick as appropriate:**

- Independent external review
- Review within a company
- Review within a multi-centre research group
- Review within the Chief Investigator's institution or host organisation
- Review within the research team
- Review by educational supervisor
- Other

*Justify and describe the review process and outcome. If the review has been undertaken but not seen by the researcher, give details of the body which has undertaken the review:*

The research project has been developed under the supervision of the chief investigator's research supervisor at Lancaster University and field supervisor who is a clinical psychologist working in cancer services. The research will also be assessed by the Lancaster University Examinations Board and the Doctorate in Clinical Psychology Research Team.

*For all studies except non-doctoral student research, please enclose a copy of any available scientific critique reports, together with any related correspondence.*

*For non-doctoral student research, please enclose a copy of the assessment from your educational supervisor/ institution.*

**A59. What is the sample size for the research? How many participants/samples/data records do you plan to study in total? If there is more than one group, please give further details below.**

Total UK sample size: 12

Total international sample size (including UK): 0

Total in European Economic Area: 0

*Further details:*

Between 10 and 12 participants will be recruited.

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**A60. How was the sample size decided upon?** *If a formal sample size calculation was used, indicate how this was done, giving sufficient information to justify and reproduce the calculation.*

This sample size is the largest recommended size for a study using IPA methodology (Smith and Osborne, 2008). The sample will be selected purposely to recruit a sample whose experience is relevant to the research questions.

**A62. Please describe the methods of analysis (statistical or other appropriate methods, e.g. for qualitative research) by which the data will be evaluated to meet the study objectives.**

Interpretative phenomenological analysis will be used to analyse qualitative data. This will involve manual analysis to generate hierarchical themes across the data.

**6. MANAGEMENT OF THE RESEARCH**

**A63. Other key investigators/collaborators.** *Please include all grant co-applicants, protocol co-authors and other key members of the Chief Investigator's team, including non-doctoral student researchers.*

	Title	Forename/Initials	Surname
Post			
Qualifications			
Employer			
Work Address			
Post Code			
Telephone			
Fax			
Mobile			
Work Email			
Post			
Qualifications			
Employer			
Work Address			
Post Code			
Telephone			
Fax			
Mobile			
Work Email			
Post	Dr	Craig	Murray
Qualifications	PhD		
Employer	Lancaster University		

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Work Address	Department of Health Research Faculty of Health and Medicine Lancaster University
Post Code	LA1 4YG
Telephone	01524 592754
Fax	
Mobile	
Work Email	c.murray@lancaster.ac.uk
	Title Forename/Initials Surname
	█ ████ ████
Post	Consultant Medical Oncologist
Qualifications	MD
Employer	██
Work Address	██████████ ██████████ ██████████
Post Code	██████
Telephone	██████████
Fax	
Mobile	
Work Email	██████████@██████████

## A64. Details of research sponsor(s)

## A64-1. Sponsor

## Lead Sponsor

## Status:

- NHS or HSC care organisation  
 Academic  
 Pharmaceutical industry  
 Medical device industry  
 Local Authority  
 Other social care provider (including voluntary sector or private organisation)  
 Other

*If Other, please specify: n/a*

## Commercial status:

Non-  
Commercial

## Contact person

Name of organisation Lancaster University  
 Given name Becky  
 Family name Gordon  
 Address Research Services, Lancaster University  
 Town/city Lancaster

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Post code	LA1 4YT
Country	UNITED KINGDOM
Telephone	01524592981
Fax	
E-mail	ethics@lancaster.ac.uk

**A65. Has external funding for the research been secured?***Please tick at least one check box.*

- Funding secured from one or more funders
- External funding application to one or more funders in progress
- No application for external funding will be made

What type of research project is this?

- Standalone project
- Project that is part of a programme grant
- Project that is part of a Centre grant
- Project that is part of a fellowship/ personal award/ research training award
- Other

Other – please state:  
n/a**A66. Has responsibility for any specific research activities or procedures been delegated to a subcontractor (other than a co-sponsor listed in A64-1) ? Please give details of subcontractors if applicable.**

- Yes  No

**A67. Has this or a similar application been previously rejected by a Research Ethics Committee in the UK or another country?**

- Yes  No

*Please provide a copy of the unfavourable opinion letter(s). You should explain in your answer to question A6-2 how the reasons for the unfavourable opinion have been addressed in this application.***A68-1. Give details of the lead NHS R&D contact for this research:**

	Title	Forename/Initials	Surname
Organisation			
Address			
Post Code			
Work Email			

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Telephone

Fax

Mobile

Details can be obtained from the NHS R&D Forum website: <http://www.rdforum.nhs.uk>

**A69-1. How long do you expect the study to last in the UK?**

Planned start date: 03/01/2019

Planned end date: 30/08/2019

Total duration:

Years: 0 Months: 7 Days: 28

**A71-1. Is this study?** Single centre Multicentre**A71-2. Where will the research take place? (Tick as appropriate)** England Scotland Wales Northern Ireland Other countries in European Economic Area

Total UK sites in study 7

**Does this trial involve countries outside the EU?** Yes No**A72. Which organisations in the UK will host the research? Please indicate the type of organisation by ticking the box and give approximate numbers if known:** NHS organisations in England 7 NHS organisations in Wales NHS organisations in Scotland HSC organisations in Northern Ireland GP practices in England GP practices in Wales GP practices in Scotland GP practices in Northern Ireland

Joint health and social care agencies (eg  
community mental health teams)

 Local authorities Phase 1 trial units Prison establishments Probation areas



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<p>Independent (private or voluntary sector) organisations</p> <p><input type="checkbox"/> Educational establishments</p> <p><input type="checkbox"/> Independent research units</p> <p><input type="checkbox"/> Other (give details)</p> <p>n/a</p> <p>Total UK sites in study: 7</p>
--

**A73-1. Will potential participants be identified through any organisations other than the research sites listed above?**

Yes  No

**A74. What arrangements are in place for monitoring and auditing the conduct of the research?**

The chief investigator will be supervised by the research supervisor and field supervisor which will include monthly supervisory contact. A research contract has been agreed between the three parties agreeing arrangements for monitoring and audit

**A76. Insurance/ indemnity to meet potential legal liabilities**

*Note: in this question to NHS indemnity schemes include equivalent schemes provided by Health and Social Care (HSC) in Northern Ireland*

**A76-1. What arrangements will be made for insurance and/or indemnity to meet the potential legal liability of the sponsor(s) for harm to participants arising from the management of the research? Please tick box(es) as applicable.**

*Note: Where a NHS organisation has agreed to act as sponsor or co-sponsor, indemnity is provided through NHS schemes. Indicate if this applies (there is no need to provide documentary evidence). For all other sponsors, please describe the arrangements and provide evidence.*

- NHS indemnity scheme will apply (NHS sponsors only)
- Other insurance or indemnity arrangements will apply (give details below)

Lancaster University legal liability cover will apply

*Please enclose a copy of relevant documents.*

**A76-2. What arrangements will be made for insurance and/ or indemnity to meet the potential legal liability of the sponsor(s) or employer(s) for harm to participants arising from the design of the research? Please tick box(es) as applicable.**

*Note: Where researchers with substantive NHS employment contracts have designed the research, indemnity is provided through NHS schemes. Indicate if this applies (there is no need to provide documentary evidence). For other protocol authors (e.g. company employees, university members), please describe the arrangements and provide evidence.*

- NHS indemnity scheme will apply (protocol authors with NHS contracts only)
- Other insurance or indemnity arrangements will apply (give details below)

Lancaster University legal liability cover will apply

*Please enclose a copy of relevant documents.*

**A76-3. What arrangements will be made for insurance and/ or indemnity to meet the potential legal liability of**

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**investigators/collaborators arising from harm to participants in the conduct of the research?**

*Note: Where the participants are NHS patients, indemnity is provided through the NHS schemes or through professional indemnity. Indicate if this applies to the whole study (there is no need to provide documentary evidence). Where non-NHS sites are to be included in the research, including private practices, please describe the arrangements which will be made at these sites and provide evidence.*

- NHS indemnity scheme or professional indemnity will apply (participants recruited at NHS sites only)  
 Research includes non-NHS sites (give details of insurance/ indemnity arrangements for these sites below)

n/a

*Please enclose a copy of relevant documents.***A78. Could the research lead to the development of a new product/process or the generation of intellectual property?**

- Yes  No  Not sure



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	Post Code Country	[Redacted] [Redacted] [Redacted]	Country
IN4	<input checked="" type="radio"/> NHS/HSC Site <input type="radio"/> Non-NHS/HSC Site	Organisation name Address Post Code Country	Forename Hayley Middle name Family name Slater Email h.slater1@lancaster.ac.uk Qualification (MD...) Country
IN5	<input checked="" type="radio"/> NHS/HSC Site <input type="radio"/> Non-NHS/HSC Site	Organisation name Address Post Code Country	Forename Hayley Middle name Family name Slater Email h.slater1@lancaster.ac.uk Qualification (MD...) Country
IN6	<input checked="" type="radio"/> NHS/HSC Site <input type="radio"/> Non-NHS/HSC Site	Organisation name Address Post Code Country	Forename Hayley Middle name Family name Slater Email h.slater1@lancaster.ac.uk Qualification (MD...) Country

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IN7

NHS/HSC Site  
 Non-NHS/HSC Site

Forename Hayley  
Middle name  
Family name Slater  
Email h.slater1@lancaster.ac.uk  
Qualification (MD...)  
Country

Organisation name [REDACTED]  
Address [REDACTED]  
Post Code [REDACTED]  
Country [REDACTED]

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**PART D: Declarations****D1. Declaration by Chief Investigator**

1. The information in this form is accurate to the best of my knowledge and belief and I take full responsibility for it.
2. I undertake to fulfil the responsibilities of the chief investigator for this study as set out in the UK Policy Framework for Health and Social Care Research.
3. I undertake to abide by the ethical principles underlying the Declaration of Helsinki and good practice guidelines on the proper conduct of research.
4. If the research is approved I undertake to adhere to the study protocol, the terms of the full application as approved and any conditions set out by review bodies in giving approval.
5. I undertake to notify review bodies of substantial amendments to the protocol or the terms of the approved application, and to seek a favourable opinion from the main REC before implementing the amendment.
6. I undertake to submit annual progress reports setting out the progress of the research, as required by review bodies.
7. I am aware of my responsibility to be up to date and comply with the requirements of the law and relevant guidelines relating to security and confidentiality of patient or other personal data, including the need to register when necessary with the appropriate Data Protection Officer. I understand that I am not permitted to disclose identifiable data to third parties unless the disclosure has the consent of the data subject or, in the case of patient data in England and Wales, the disclosure is covered by the terms of an approval under Section 251 of the NHS Act 2006.
8. I understand that research records/data may be subject to inspection by review bodies for audit purposes if required.
9. I understand that any personal data in this application will be held by review bodies and their operational managers and that this will be managed according to the principles established in the Data Protection Act 2018.
10. I understand that the information contained in this application, any supporting documentation and all correspondence with review bodies or their operational managers relating to the application:
  - Will be held by the REC (where applicable) until at least 3 years after the end of the study; and by NHS R&D offices (where the research requires NHS management permission) in accordance with the NHS Code of Practice on Records Management.
  - May be disclosed to the operational managers of review bodies, or the appointing authority for the REC (where applicable), in order to check that the application has been processed correctly or to investigate any complaint.
  - May be seen by auditors appointed to undertake accreditation of RECs (where applicable).
  - Will be subject to the provisions of the Freedom of Information Acts and may be disclosed in response to requests made under the Acts except where statutory exemptions apply. May be sent by email to REC members.
11. I understand that information relating to this research, including the contact details on this application, may be held on national research information systems, and that this will be managed according to the principles established in the Data Protection Act 2018.
12. Where the research is reviewed by a REC within the UK Health Departments Research Ethics Service, I understand that the summary of this study will be published on the website of the Health Research Authority (HRA) together with the contact point for enquiries named below. Publication will take place no earlier than 3 months after the issue of the ethics committee's final opinion or the withdrawal of the application.

**Contact point for publication**(Not applicable for R&D Forms)

*HRA would like to include a contact point with the published summary of the study for those wishing to seek further*

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*information. We would be grateful if you would indicate one of the contact points below.*

- Chief Investigator
- Sponsor
- Study co-ordinator
- Student
- Other – please give details
- None

**Access to application for training purposes** (Not applicable for R&D Forms)

*Optional – please tick as appropriate:*

I would be content for members of other RECs to have access to the information in the application in confidence for training purposes. All personal identifiers and references to sponsors, funders and research units would be removed.

This section was signed electronically by Dr Anna Daiches on 28/03/2019 12:35.

Job Title/Post:           Clinical Director  
Organisation:            Lancaster University  
Email:                     a.daiches@lancaster.ac.uk

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**D2. Declaration by the sponsor's representative**

*If there is more than one sponsor, this declaration should be signed on behalf of the co-sponsors by a representative of the lead sponsor named at A64-1.*

I confirm that:

1. This research proposal has been discussed with the Chief Investigator and agreement in principle to sponsor the research is in place.
2. An appropriate process of scientific critique has demonstrated that this research proposal is worthwhile and of high scientific quality.
3. Any necessary indemnity or insurance arrangements, as described in question A76, will be in place before this research starts. Insurance or indemnity policies will be renewed for the duration of the study where necessary.
4. Arrangements will be in place before the study starts for the research team to access resources and support to deliver the research as proposed.
5. Arrangements to allocate responsibilities for the management, monitoring and reporting of the research will be in place before the research starts.
6. The responsibilities of sponsors set out in the UK Policy Framework for Health and Social Care Research will be fulfilled in relation to this research.

*Please note: The declarations below do not form part of the application for approval above. They will not be considered by the Research Ethics Committee.*

7. Where the research is reviewed by a REC within the UK Health Departments Research Ethics Service, I understand that the summary of this study will be published on the website of the National Research Ethics Service (NRES), together with the contact point for enquiries named in this application. Publication will take place no earlier than 3 months after issue of the ethics committee's final opinion or the withdrawal of the application.
8. Specifically, for submissions to the Research Ethics Committees (RECs) I declare that any and all clinical trials approved by the HRA since 30th September 2013 (as defined on IRAS categories as clinical trials of medicines, devices, combination of medicines and devices or other clinical trials) have been registered on a publicly accessible register in compliance with the HRA registration requirements for the UK, or that any deferral granted by the HRA still applies.

This section was signed electronically by An authorised approver at ethics@lancaster.ac.uk on 29/03/2019 17:32.

Job Title/Post: Head of Research Quality and Policy  
 Organisation: Lancaster University  
 Email: b.gordon@lancaster.ac.uk



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**D3. Declaration for student projects by academic supervisor(s)**

1. I have read and approved both the research proposal and this application. I am satisfied that the scientific content of the research is satisfactory for an educational qualification at this level.
2. I undertake to fulfil the responsibilities of the supervisor for this study as set out in the UK Policy Framework for Health and Social Care Research.
3. I take responsibility for ensuring that this study is conducted in accordance with the ethical principles underlying the Declaration of Helsinki and good practice guidelines on the proper conduct of research, in conjunction with clinical supervisors as appropriate.
4. I take responsibility for ensuring that the applicant is up to date and complies with the requirements of the law and relevant guidelines relating to security and confidentiality of patient and other personal data, in conjunction with clinical supervisors as appropriate.

**Academic supervisor 1**

This section was signed electronically by Dr Anna Duxbury on 31/03/2019 14:02.

Job Title/Post: Clinical Psychologist/ Clinical Tutor  
Organisation: Lancaster University  
Email: a.duxbury@lancaster.ac.uk

**Academic supervisor 2**

This section was signed electronically by Dr Anna Daiches on 28/03/2019 12:37.

Job Title/Post: Clinical Director  
Organisation: Lancaster University  
Email: a.daiches@lancaster.ac.uk

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**Appendix 4-A: Research Ethics Committee Favourable Opinion Letter****North West - Liverpool East Research Ethics Committee**

Barlow House  
 3rd Floor  
 4 Minshull Street  
 Manchester  
 M1 3DZ

**Please note: This is the favourable opinion of the REC only and does not allow you to start your study at NHS sites in England until you receive HRA Approval**

10 May 2019

Dr Anna Daiches  
 Clinical Director  
 Lancashire Care NHS Foundation Trust  
 Department of Health Research  
 Faculty of Health and Medicine  
 Lancaster University  
 LA1 4YG

Dear Dr Daiches

<b>Study title:</b>	<b>Patients' experiences of coping longer-term with cancer of unknown primary</b>
<b>REC reference:</b>	<b>19/NW/0096</b>
<b>Protocol number:</b>	<b>not applicable</b>
<b>IRAS project ID:</b>	<b>251064</b>

Thank you for your correspondence of 10 May 2019, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Chair, together with the lead reviewer.

We plan to publish your research summary wording for the above study on the HRA website, together with your contact details. Publication will be no earlier than three months from the date of this opinion letter. Should you wish to provide a substitute contact point, require further

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information, or wish to make a request to postpone publication, please contact [hra.studyregistration@nhs.net](mailto:hra.studyregistration@nhs.net) outlining the reasons for your request.

### **Confirmation of ethical opinion**

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

### **Conditions of the favourable opinion**

The REC favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission must be obtained from each host organisation prior to the start of the study at the site concerned.

*Management permission should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements. Each NHS organisation must confirm through the signing of agreements and/or other documents that it has given permission for the research to proceed (except where explicitly specified otherwise).*

*Guidance on applying for HRA and HCRW Approval (England and Wales)/ NHS permission for research is available in the Integrated Research Application System, at [www.hra.nhs.uk](http://www.hra.nhs.uk) or at <http://www.rdforum.nhs.uk>.*

*Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.*

*For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.*

*Sponsors are not required to notify the Committee of management permissions from host organisations*

### Registration of Clinical Trials

All clinical trials (defined as the first four categories on the IRAS filter page) must be registered on a publically accessible database within 6 weeks of recruitment of the first participant (for medical device studies, within the timeline determined by the current registration and publication trees).

There is no requirement to separately notify the REC but you should do so at the earliest opportunity e.g. when submitting an amendment. We will audit the registration details as part of the annual progress reporting process.

To ensure transparency in research, we strongly recommend that all research is registered but for non-clinical trials this is not currently mandatory.

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If a sponsor wishes to request a deferral for study registration within the required timeframe, they should contact [hra.studyregistration@nhs.net](mailto:hra.studyregistration@nhs.net). The expectation is that all clinical trials will be registered, however, in exceptional circumstances non registration may be permissible with prior agreement from the HRA. Guidance on where to register is provided on the HRA website.

**It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).**

**Ethical review of research sites**

## NHS sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

**Approved documents**

The final list of documents reviewed and approved by the Committee is as follows:

<i>Document</i>	<i>Version</i>	<i>Date</i>
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [Employer indemnity insurance]	0.1	24 January 2019
GP/consultant information sheets or letters [Professionals Information Sheet]	0.1	07 December 2018
Interview schedules or topic guides for participants [Interview Schedule]	0.1	11 July 2018
IRAS Application Form [IRAS_Form_10052019]		10 May 2019
Letter from sponsor [Letter from sponsor]	0.1	24 January 2019
Non-validated questionnaire [Demographic Information Sheet]	0.1	07 December 2018
Non-validated questionnaire [Demographic Information sheet]	0.2	11 March 2019
Other [Lone working- ██████████]		13 January 2019
Other [Risk assessment- ██████████]		13 January 2019
Other [Lone Working- ██████████]		13 January 2019
Other [Employer professional negligence insurance]	0.1	24 January 2019
Other [Letter to Clinical Nurse Specialist]	0.2	11 March 2019
Other [Re-submission cover letter]		28 March 2019
Participant consent form [Participant Consent Form]	0.2	11 March 2019
Participant consent form [Consent to be contacted]	0.2	11 March 2019
Participant information sheet (PIS) [PIS]	0.3	11 March 2019
Research protocol or project proposal [Protocol]	0.1	28 July 2018
Summary CV for Chief Investigator (CI) [CI CV]		11 March 2019
Summary CV for student [Student CV]		13 January 2019
Summary CV for supervisor (student research) [Supervisor CV]		13 January 2019
Summary CV for supervisor (student research) [Anna Duxbury CV]	0.1	11 February 2019

**Statement of compliance**

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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.

### **After ethical review**

#### Reporting requirements

The attached document "*After ethical review – guidance for researchers*" gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The HRA website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

### **User Feedback**

The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website:

<http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance/>

### **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/>

<b>19/NW/0096</b>
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<b>Please quote this number on all correspondence</b>
---

With the Committee's best wishes for the success of this project.

Yours sincerely



**Signed on behalf of the Chair, Miss Kimberley Saint**

Email:nrescommittee.northwest-liverpooleast@nhs.net

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**Appendix 4-C: Health Research Authority Approval Letter**

Dr Anna Daiches  
Clinical Director  
Lancashire Care NHS Foundation Trust  
Department of Health Research  
Faculty of Health and Medicine  
Lancaster University  
LA1 4YG

Email: [hra.approval@nhs.net](mailto:hra.approval@nhs.net)  
[Research-permissions@wales.nhs.uk](mailto:Research-permissions@wales.nhs.uk)

10 May 2019

Dear Dr Daiches

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

**Study title:** Patients' experiences of coping longer-term with cancer  
of unknown primary  
**IRAS project ID:** 251064  
**REC reference:** 19/NW/0096  
**Sponsor** Lancaster 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.

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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 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 **251064**. Please quote this on all correspondence.

Yours sincerely,  
Chris Kitchen

Email: [hra.approval@nhs.net](mailto:hra.approval@nhs.net)

**List of Documents**

The final document set assessed and approved by HRA and HCRW Approval is listed below.

<i>Document</i>	<i>Version</i>	<i>Date</i>
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [Employer indemnity insurance]	0.1	24 January 2019
GP/consultant information sheets or letters [Professionals Information Sheet]	0.1	07 December 2018
HRA Schedule of Events [SoE]	1	15 February 2019
HRA Statement of Activities [SoA]	1	15 February 2019
Interview schedules or topic guides for participants [Interview Schedule]	0.1	11 July 2018
IRAS Application Form [IRAS_Form_10052019]		10 May 2019
Letter from sponsor [Letter from sponsor]	0.1	24 January 2019
Non-validated questionnaire [Demographic Information Sheet]	0.1	07 December 2018
Non-validated questionnaire [Demographic Information sheet]	0.2	11 March 2019
Other [Lone working- ██████████]		13 January 2019
Other [Risk assessment- ██████████]		13 January 2019
Other [Lone Working- ██████████]		13 January 2019
Other [Employer professional negligence insurance]	0.1	24 January 2019
Other [Letter to Clinical Nurse Specialist]	0.2	11 March 2019
Other [Re-submission cover letter]		28 March 2019
Participant consent form [Participant Consent Form]	0.2	11 March 2019
Participant consent form [Consent to be contacted]	0.2	11 March 2019
Participant information sheet (PIS) [PIS]	0.3	11 March 2019
Research protocol or project proposal [Protocol]	0.1	28 July 2018
Summary CV for Chief Investigator (CI) [CI CV]		11 March 2019
Summary CV for student [Student CV]		13 January 2019

ETHICS FORM

IRAS project ID	251064
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**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
<p>This is a non-commercial study with multiple participating NHS organisations. There is one site type involved in the study.</p>	<p>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.</p>	<p>A Statement of Activities has been submitted and the sponsor is not requesting and does not expect any other site agreement to be used.</p>	<p>No application for external funding has been made. As per the Statement of Activities, no funding will be provided to the participating organisation.</p>	<p>A Local Collaborator is expected to be in place at the participating organisation. As per the Statement of Activities, the sponsor will not provide additional training.</p>	<p>For research team members that do not have existing contractual relationships with the participating organisation, Letters of Access should be in place if the activities undertaken at the NHS site involve contact with patients (e.g. to take consent), on the basis of Research Passports (if University employed) or NHS to NHS confirmation of pre-engagement checks letters (if NHS employed). The pre-engagement checks should include standard DBS checks and Occupational Health Clearance. No specific pre-engagement checks are required to have taken place if the members of the research team are only accessing</p>



## ETHICS FORM

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patients' data.

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**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 stated that they do not intend to apply to the CRN Portfolio.

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**Appendix 4-D: Initial Response from the Research Ethics Committee****Health Research Authority****North West - Liverpool East Research Ethics Committee**

Barlow House  
3rd Floor  
4 Minshull Street  
Manchester  
M1 3DZ

11 March 2019

Ms Hayley Slater



Dear Ms Slater

<b>Study Title:</b>	<b>Patients' experiences of coping longer-term with cancer of unknown primary</b>
<b>REC reference:</b>	<b>19/NW/0096</b>
<b>Protocol number:</b>	<b>not applicable</b>
<b>IRAS project ID:</b>	<b>251064</b>

The Research Ethics Committee reviewed the above application at the meeting held on 21 February 2019. Thank you for attending to discuss the application.

**Provisional opinion**

The Committee is unable to give an ethical opinion on the basis of the information and documentation received so far. Before confirming its opinion, the Committee requests that you provide the further information set out below.

Authority to consider your response and to confirm the Committee's final opinion has been delegated to the Chair and Dr Supriya Kapas.

**Further information or clarification required**

1. Amend the IRAS form to change the Academic Supervisor to Chief Investigator, entering details of the Academic Supervisor and re-authorising the IRAS form.
2. In the Informed Consent Form,
  - a. Include the below point in relation to audits, "I understand that relevant sections of my medical notes and data collected during the study may be looked at by doctors from the research group, from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records."

## ETHICS FORM

- b. Make clear that points, 7, 8 and 9 are optional by indicating each as **(Optional)**.
3. Either correct the Consent to Contact form to ensure consistency of version numbers and dates with corresponding documents or make this part of the form blank, to be added when the form is completed.
4. Correct the recipient of the GP letter and:
  - a. Correct tense to ensure clarity.
5. Remove patient identifiable information from the demographic information sheet.

**If you would find it helpful to discuss any of the matters raised above or seek further clarification from a member of the Committee, you are welcome to contact Gemma Warren.**

When submitting a response to the Committee, the requested information should be electronically submitted from IRAS. Please refer to the guidance in IRAS for instructions on [how to submit a response to provisional opinion electronically](#).

Please submit revised documentation where appropriate underlining or otherwise highlighting the changes which have been made and giving revised version numbers and dates. You do not have to make any changes to the REC application form unless you have been specifically requested to do so by the REC.

The Committee will confirm the final ethical opinion within a maximum of 60 days from the date of initial receipt of the application, excluding the time taken by you to respond fully to the above points. A response should be submitted by no later than 10 April 2019.

#### **Extract of the meeting minutes**

##### **Care and protection of research participants; respect for potential and enrolled participants' welfare and dignity**

The Committee picked up on the assessor's comments on the storage of identifiable data and confirmed that it was not appropriate to keep identifiable data at the researchers' home.

*Ms Slater confirmed that she would be working from home but that the intention was to take in documents by the next day. Ms Slater agreed that it was not a long term storage solution to store identifiable documents at home and instead would be given to the clinical nurse specialist as soon as possible.*

The Committee was satisfied.

The Committee wished to clarify that the number provided in order to contact the researcher was not her personal telephone number.

*Ms Slater confirmed that it was a study specific phone.*

The Committee was reassured.

## ETHICS FORM

**Informed consent process and the adequacy and completeness of participant information**

The Committee noted that points 7, 8 and 9 were optional and should be demarcated as such.

The Committee noted that there was no consistency between consent to contact version numbers and dates. The Committee suggested leaving these blank to add corresponding version numbers and dates when they are used.

The Committee asked that information regarding the possibility of audits conducted for regulatory purposes was advised in the Participant Information Sheet.

**Suitability of the applicant and supporting staff**

The Committee agreed that the Academic Supervisor should take the role of the Chief Investigator in line with section 9.3 of the UK Policy Framework for Health and Social Care Research.

*Ms Slater explained that Lancaster University encourages students to be Chief Investigators where they are working clinically.*

The Committee agreed that they would much prefer an academic supervisor take the role of Chief Investigator to ensure proper supervision.

**Other general comments**

The Committee noted that the GP letter should be addressed to the Clinical Nurse Specialist as they were to be the recipient of this letter and tense was changed to ensure clarity.

The Committee noted that the IRAS form referred to the creation of intellectual property and the Committee wished to clarify whether Ms Slater thought that Intellectual property would be generated.

*It was Ms Slater's belief that intellectual property would be generated where there was a unique outcome from the study.*

The Committee confirmed that this did not constitute intellectual property and that this question in the IRAS form no longer applied.

The Committee noted that the demographic information sheet had identifiable patient information and asked that this was removed.

Please contact the REC Manager if you feel that the above summary is not an accurate reflection of the discussion at the meeting.

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**Documents reviewed**

The documents reviewed at the meeting were:

<i>Document</i>	<i>Version</i>	<i>Date</i>
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [Employer indemnity insurance]	0.1	24 January 2019
GP/consultant information sheets or letters [Professionals Information Sheet]	0.1	07 December 2018
GP/consultant information sheets or letters	0.1	06 December 2018
Interview schedules or topic guides for participants [Interview Schedule]	0.1	11 July 2018
IRAS Application Form [IRAS_Form_28012019]		28 January 2019
IRAS Checklist XML [Checklist_12022019]		12 February 2019
Letter from sponsor [Letter from sponsor]	0.1	24 January 2019
Non-validated questionnaire [Demographic Information Sheet]	0.1	07 December 2018
Other [Lone working- ██████████]		13 January 2019
Other [Risk assessment- ██████████]		13 January 2019
Other [Lone Working- ██████████]		13 January 2019
Other [Employer professional negligence insurance]	0.1	24 January 2019
Participant consent form [Consent form]	0.1	01 December 2018
Participant consent form [Consent to contact]	0.1	07 December 2018
Participant information sheet (PIS) [PIS]	0.1	11 July 2018
Research protocol or project proposal [Protocol]	0.1	28 July 2018
Summary CV for Chief Investigator (CI) [CI CV]		13 January 2019
Summary CV for student [Student CV]		13 January 2019
Summary CV for supervisor (student research) [Supervisor CV]		13 January 2019
Summary CV for supervisor (student research) [Anna Duxbury CV]	0.1	11 February 2019

**Membership of the Committee**

The members of the Committee who were present at the meeting are listed on the attached sheet

**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.

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19/NW/0096

Please quote this number on all correspondence

Yours sincerely

A handwritten signature in black ink, appearing to read 'K Saint', is enclosed in a light grey rectangular box.

pp

**Miss Kimberley Saint  
Chair**

Email: [nrescommittee.northwest-liverpooleast@nhs.net](mailto:nrescommittee.northwest-liverpooleast@nhs.net)

*Enclosures: List of names and professions of members who were present at the meeting and those who submitted written comments.*

*Copy to: Ms Becky Gordon  
Ms Helen Spickett, Blackpool teaching Hospitals NHS Foundation Trust*

**Appendix 4-E: Re-Submission of Ethics Application Covering Letter**

Miss Hayley Slater

[REDACTED]  
[REDACTED]  
[REDACTED]  
[REDACTED]

28<sup>th</sup> March 2019

Dear RES Committee North West – Liverpool East members,

Re: IRAS Project ID: 251064 (Coping longer-term with CUP)

I wish to inform you that all requested changes discussed at our meeting on 21<sup>st</sup> February 2019 have now been made and the amended IRAS application has been submitted as per the recommendations outlined in the committee’s provisional response letter.

Please note that one further change has also been made to the participant information sheet. A line has been added to inform participants that their demographic data will be taken at the interview meeting and that this will be optional. We discussed this verbally at the meeting, however, it was not recorded in the recommendations. I do hope that this acceptable.

Yours sincerely,

Hayley Slater

Trainee Clinical Psychologist

Lancaster University

**Appendix 4-F: Information Sheet for CUP Professionals**

Coping longer-term with CUP (IRAS ID 251064)

**Information Sheet for CUP Professionals**

Version 0.1, created 07/12/2018

Study title:

**Patients' experiences of coping longer-term with cancer of unknown primary**

Hello,

I am hoping that you may be able to help with the recruitment of participants for the above study. My name is Hayley and I am a final year trainee clinical psychologist on the doctorate in clinical psychology programme at Lancaster University. The research is being carried out as part of my final thesis project and is being supervised by Dr [REDACTED] [REDACTED] (Principal Clinical Psychologist, [REDACTED]) and Dr [REDACTED] [REDACTED] (Medical Oncology Consultant, [REDACTED]).

The aim of the study is to understand how people cope following their diagnosis of CUP. The study will focus on the sub-group of patients who are medically stable six months or more following their diagnosis. This sample represents a distinct population whose needs may be quite different from other patients with CUP and other diagnoses of cancer. In better understanding this group's experiences, it is hoped that we can come to understand the best way to support patients during this really difficult time.

The research is taking place across seven acute hospital trusts:

[REDACTED]  
[REDACTED]  
[REDACTED]

Through conversations with members of the CUP network, it is clear that the potential pool of participants who are medically stable 6 months after their CUP diagnosis is small. Due to this, any help from yourself with identifying and recruiting any eligible patients will be hugely appreciated.

Further information about the study is included in the attached Participant Information Sheet.

**How you can help**



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I would really appreciate you familiarising yourself with the inclusion and exclusion criteria listed below in order to identify any patients you are working with who meet these criteria. Once any patients are identified, I would ask that you take an appropriate opportunity (e.g. at a routine appointment) to discuss the possibility of participating and share the 'Participant Information Sheet' with them. Once they have become familiar with this information, please ask the patient whether they would be willing to be contacted by the lead researcher (Hayley) to discuss further and, if the patient is happy to proceed, ask that they fill in the 'Consent to be Contacted' form (attached). At this stage they are under no obligation to take part and will have the chance to ask Hayley any questions about the process.

Any completed 'Consent to be contacted' forms should be given to

(service contact) who will pass the patient's details on to the researcher.

### Participant inclusion criteria

- They received their CUP diagnosis over 6 months ago and are now deemed to be clinically stable by their medical team
- They are currently receiving treatment or being actively monitored by the CUP service at any of the host acute NHS Trusts
- They are aged 18 or over
- They are able to provide informed consent to participate

### Participant exclusion criteria

- They are acutely unwell or nearing the end of their life
- They do not speak English (unfortunately no funds are available for a translator as part of this study)
- They are under 18 years of age
- They lack mental capacity to provide informed consent (e.g. due to a learning disability or dementia)

Thank you for your time in reading this information and your support in recruiting potential participants. If you have any questions about any elements of the research please send me an email ([h.slater1@lancaster.ac.uk](mailto:h.slater1@lancaster.ac.uk)).

Kind regards,

Hayley Slater  
Trainee Clinical Psychologist

ETHICS FORM

Lancaster University

**Appendix 4-G: Participant Information Sheet**



Participant Information Sheet (Version 0.3, amended 11/03/2019)

Study title:

**Patients' experiences of coping longer-term with cancer of unknown primary**

We are hoping that people may be able to help us with our research to understand how people living longer-term with cancer of unknown primary (CUP) cope. We would be interested in talking to anybody that has been living with CUP for six months or longer about their experiences.

The research is being done by a trainee clinical psychologist and will count towards their professional accreditation.

**Why is this research being done?**

We would like to better understand how people living with CUP manage in what can be a very distressing situation, involving lots of uncertainties. The research will aim to get an understanding of people's experiences of living and coping with a diagnosis of CUP for 6 months or more. We hope that by better understanding the experiences of individuals, we can improve the support that we offer to patients during this time.

**What would taking part involve?**

You will be asked to take part in an interview lasting for around 1 hour. During this interview you will be asked questions about your experiences since being diagnosed with CUP. You can answer the questions in as much or as little detail as you wish. You will also be asked whether you would be willing to participate in a follow up interview within three months of your first interview.

You can choose whether the interview takes place at your home or at the hospital at a time that is convenient for you. The conversation will be audio recorded.

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You will be asked to provide some optional demographic data, including your age, the date of your diagnosis, and your ethnic group.

The recording will then be typed out and analysed. At this stage your personal details will be removed so nobody apart from the researcher will know it is you.

It is possible that the research findings may be published once the research is completed.

Your choice to participate will have no impact upon the treatment you receive from your healthcare team.

Your clinical nurse specialist will be made aware that you are participating in the study.

### **What are the possible benefits of taking part?**

There are not likely to be any specific benefits to taking part. You may find it helpful to have an opportunity to talk openly about your experiences. You may also like to think that sharing your experience could lead to improvements in support for other people in your position in the future.

### **What are the possible disadvantages and risks of taking part?**

It is possible that some of the things we talk about may be upsetting. If you find that you do become distressed during the interview we can stop at any time. If you feel you would benefit from some additional support, the researcher will liaise with their supervisor who is a clinical psychologist working in CUP services. They will discuss the kind of support that might be available via your medical team to help at this time. There is also some information at the bottom of this information sheet about other services which could offer further emotional or practical support.

While the information you share will be kept confidential, if the researcher has any concerns about your safety or anybody else's safety from your conversation they may need to involve other professionals.

### **What if I change my mind?**

You are free to withdraw from the study at any time until 2 weeks after the interview has been carried out.

### **What happens to my information if I take part?**

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The audio recording of the interview will be securely stored. It will be deleted once it has been typed out. The typed transcript of the interview will also be stored securely and a pseudonym will be used so that you will not be identifiable. Paper copies of transcripts may be made for the analysis process. These will be stored securely and shredded once analysis is completed. Only the chief investigator and the research supervisors will have access to the interview recording and transcripts. Once the project is complete, the transcripts will be stored electronically by Lancaster University for a minimum of ten years. Lancaster University will act as the data controller for any personal information collected during the study. Anonymous quotes will be used in the write up of the study which will be shared with the medical team and may also be published in an academic journal or conference presentation. Electronic copies of the consent form that you sign will be stored securely and separately from the audio data so that your identity cannot be linked to the interview data. The paper copy will be shredded immediately once the electronic version is made.

Under the GDPR you have certain rights when personal data is collected about you. You have the right to access any personal data held about you, to object to the processing of your personal information, to rectify personal data if it is inaccurate, the right to have data about you erased and, depending on the circumstances, the right to data portability. Please be aware that many of these rights are not absolute and only apply in certain circumstances. If you would like to know more about your rights in relation to your personal data, please speak to the researcher on your particular study.

For further information about how Lancaster University processes personal data for research purposes and your data rights please visit our webpage: [www.lancaster.ac.uk/research/data-protection](http://www.lancaster.ac.uk/research/data-protection)

### **What if I am not interested in taking part?**

You do not need to take any further action.

### **What if I am interested in taking part?**

Please fill in the attached 'Consent to be contacted' form and hand it to a member of your healthcare team. This form will be kept in your clinical records and your

## ETHICS FORM

details will be passed on to the lead researcher, Hayley Slater (Trainee Clinical Psychologist) who will contact you around one week later to have an informal conversation about whether you would like to take part in the study. This one week gap is to allow you time to re-read this information and consider your decision and any questions. **If you consent to being contacted, Hayley will call you on the telephone number 07508375668.** The call will give you opportunity to ask any questions about the study before you make your decision. If you decide at this stage that you are willing to participate, Hayley will arrange for you to meet to carry out the interview. This will be arranged at a convenient time for you either at home or at the hospital. If you decide at this stage not to participate then you will not be contacted again and the care from your medical team will not be impacted.

**Who has reviewed the project?**

This study has been reviewed and approved by the NHS Research Ethics Committee.

**Where can I obtain further information about the study if I need it?**

If you have any questions about the study, please contact the chief investigator:

Hayley Slater  
Trainee Clinical Psychologist  
Telephone: 01524 592754  
Email: h.slater1@lancaster.ac.uk  
Clinical Psychology  
Division of Health Research  
Lancaster University  
Lancaster  
LA1 4YG

You may also contact the chief investigator's supervisors:

Dr Anna Daiches  
Clinical Director  
Telephone: 01524 594406  
Email: a.daiches@lancaster.ac.uk  
Clinical Psychology  
Division of Health Research  
Lancaster University  
Lancaster  
LA1 4YG

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Dr Anna Duxbury  
Clinical Tutor  
Telephone: 01524 592 974  
Email: a.duxbury@lancaster.ac.uk  
Clinical Psychology  
Division of Health Research  
Lancaster University  
Lancaster  
LA1 4YG

Dr [REDACTED]

**Complaints**

If you wish to make a complaint or raise concerns about any aspect of this study and do not want to speak to the researcher, you can contact:

Professor Catherine Walshe, Head of the Division of Health Research  
Telephone: 01524 510124  
Email: c.walshe@lancaster.ac.uk  
Division of Health Research  
Lancaster University  
Lancaster  
LA1 4YG

If you wish to speak to someone outside of the Clinical Psychology Doctorate Programme, you may also contact:

Professor Roger Pickup  
Tel: +44 (0)1524 593746  
Associate Dean for Research Email: r.pickup@lancaster.ac.uk

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Faculty of Health and Medicine  
(Division of Biomedical and Life Sciences)  
Lancaster University  
Lancaster  
LA1 4YG

**Thank you for taking the time to read this information sheet.**

**Resources for further support:**

In the event that you feel distressed or in need of further support following your interview, or at any time in the future, the resources listed below may be useful.

Your medical team

You may find it helpful to discuss any issues that come up with a member of your medical team (e.g. your clinical nurse specialist). They can provide specialist support and, if appropriate, may be able to refer you to a psychologist who specialises in working with people living with cancer.

Macmillan Cancer Support

Information and support for anybody living with cancer

Telephone: 0808 808 0000 Website: [www.macmillan.org.uk](http://www.macmillan.org.uk)

(Calls are free from mobile and UK landline phones. Lines are open 9am-8pm Monday to Friday).

Maggie's

Face to face [REDACTED] and online support centres offering support to people with cancer

Telephone: [REDACTED] Website: [www.maggiescentres.org](http://www.maggiescentres.org)

(Calls are free from most UK landline and mobile phone providers).

CancerHelp

Non-clinical service offering support, counselling, relaxation-based activities, and day services. [REDACTED]

[REDACTED]

**Appendix 4-H: Consent to be Contacted Form**

Coping longer-term with CUP (IRAS ID 251064)

**Consent to be contacted form**

Version no. 0.2, amended 11/03/2019

Study title: Patients' experiences of coping longer-term with cancer of unknown primary

**Patient Declaration**

Please tick box

I have read the participant information sheet (version \_\_\_\_\_, dated \_\_\_\_\_) about the above study and may be interested in participating.

I give my consent to be contacted by the lead researcher, Hayley Slater (trainee clinical psychologist) for an informal conversation to ask any questions and discuss whether I am willing to take part in the research.

I am aware that I am free to choose not to participate in the research at any time until 2 weeks after the interview takes place and that the decision will not impact on the care I receive.

Name:

Signature:



## ETHICS FORM

The best number(s) to contact me on:

Date:

**Appendix 4-I: Consent Form**

Coping longer-term with CUP (IRAS ID  
251064)

**PARTICIPANT CONSENT FORM**

Version 0.2, amended 11/03/2019

Title of Project:

**Patients' experiences of coping longer-term with cancer of unknown primary**

Name of Researcher: Hayley Slater (Trainee Clinical Psychologist)

Please  
tick box

- 1) I confirm that I have read the information sheet dated \_\_\_\_\_ (version \_\_\_\_\_) for the above study. I have had the opportunity to consider the information, ask questions, and have had these answered satisfactorily.
- 2) I understand that my participation is voluntary and that I am free to withdraw at any time until 2 weeks after the interview without giving any reason. My medical care or legal rights will not be affected if I withdraw.
- 3) I understand that the interview will be recorded and then transcribed without my details.
- 4) I understand that the recording will be kept until transcribed and will then be deleted. The anonymous transcripts will be held by Lancaster University for up to 10 years.
- 5) I understand that anonymous quotations from my interview may be included in the write up of the study which will be shared with my medical team and may also be published in academic journals or conference presentations.

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6) I understand that my information will remain confidential and anonymous unless the researcher has any concerns about my safety or the safety of others. In this instance the researcher may need to discuss the concerns with their supervisor and/or other relevant professionals.

7) I agree to my clinical nurse specialist being informed of my participation in the study. **Optional**

Their name is:

8) I would like to receive a summary of the study results upon completion **Optional**

9) I would be willing to be contacted to participate in a follow up interview within the next three months **Optional**

10) I understand that relevant sections of my medical notes and data collected during the study may be looked at by doctors from the research group, from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.

11) I agree to take part in the above study.

\_\_\_\_\_  
Name of Participant

\_\_\_\_\_  
Date

\_\_\_\_\_  
Signature

\_\_\_\_\_  
Name of Person  
taking consent

\_\_\_\_\_  
Date

\_\_\_\_\_  
Signature

ETHICS FORM

If you selected the option to receive a summary of the study results upon completion, please provide your postal address below.

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**Appendix 4-J: Interview Schedule:**

Interview schedule (Version 0.1, created 11/07/2018)

- **Could you tell me about what things have been like for you since your diagnosis of CUP?**

*Prompts: response to diagnosis, now*

- **What is your understanding of the diagnosis?**

*Prompts: Anything not understood/unclear; had you heard of CUP before?*

- **On a day-to-day basis, how do you deal with having CUP?**
- **Since your diagnosis has there been times when you have felt more or less able to cope?**

- **Has there been any things which have helped you to cope?**

*Prompts: personal qualities and strengths, actions, external resources*

- **Have any things made coping more challenging?**
- **Are there any things that you think would help you feel more able to manage?**

- **Has the way you've dealt with CUP been similar or different to how you have dealt with any other difficult things in your life?**
- **Do you think that knowing the primary site of your cancer would make things different in any ways?**

*Prompts: would anything be easier/more difficult*

**Appendix 4-K: Demographic Information Sheet**

Coping longer-term with CUP (IRAS ID 251064)



**Demographic Information for study participants**

Version 0.2, amended 11/03/2019

Age: -----

Date of CUP diagnosis: -----

Gender:	Male	Female	Other	Prefer not to say
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

What is your ethnic group:

**White**

- 1. English/Welsh/Scottish/Northern Irish/British
- 2. Irish
- 3. Gypsy or Irish Traveller
- 4. Any other White background, please describe  -----

**Mixed/Multiple ethnic groups**

- 5. White and Black Caribbean
- 6. White and Black African
- 7. White and Asian
- 8. Any other Mixed/Multiple ethnic background, please describe  -----

**Asian/Asian British**

- 9. Indian
- 10. Pakistani
-

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11. Bangladeshi

12. Chinese

13. Any other Asian background, please describe \_\_\_\_\_

**Black/ African/Caribbean/Black British**

14. African

15. Caribbean

16. Any other Black/African/Caribbean background, please describe  \_\_\_\_\_

**Other ethnic group**

17. Arab

18. Any other ethnic group, please describe  \_\_\_\_\_

## ETHICS FORM

**Appendix 4-L: Letter to Clinical Nurse Specialists**

Coping Longer-Term with CUP (IRAS ID 251064)

CNS Letter, Version 0.2, amended 11/03/2019



Dear *Clinical Nurse Specialist*,

Re: *Participant Name*

This letter is to make you aware that the above patient has participated today in a research study entitled "Patients' experiences of coping longer-term with cancer of unknown primary (CUP)".

As per the information you have previously received, this involved a face-to-face interview lasting for approximately 1 hour in duration. There is a possibility that a further interview may take place at a later date with the patient's consent.

It is possible that the process of talking about individuals' experiences of CUP may be upsetting or distressing. All participants have been provided with a list of resources in case of any distress and advised that their CUP team are there to support them.

If you have any queries please do not hesitate to contact me on the details below.

Yours sincerely,

Hayley Slater

Trainee Clinical Psychologist

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Email: h.slater1@lancaster.ac.uk