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The experience of patients with oesophageal cancer receiving chemoradiotherapy treatment: a qualitative study embedded in the SCOPE2 trial

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Title page

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Data availability statement

The data that support the findings of this study are available on request from the corresponding author. Personal data are not publicly available due to privacy or ethical restrictions.

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Contribution Statement

TC Chief Investigator responsible for overall trial design and oversight of study progress.

AN designed and oversaw qualitative evaluation.

ML oversaw the qualitative study.

DHH drafted the results and manuscript.

DH-H & ML collected and analysed qualitative data.

SB was the study manager and contributed to trial study design, qualitative recruitment and quantitative data.

LN contributed to trial study design, study management (including study documentation) and monitoring oversight.

MH contributed to the trial design.

All authors contributed to revisions of the manuscript and approved the final version.

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Trial Registration

NCT02741856; ISRCTN: 97125464

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethics approval statement

SCOPE2 has full ethical approval from Wales Research Ethics Committee 3 (dated 22nd January 2016, with subsequent approval of each amendment; REC reference 15/WA/0395), and is conducted in accordance with The Medicines for Human Use (Clinical Trials) Regulations 2004 (SI2004/1031) and subsequent amendments, and the Declaration of

Helsinki 1996. Written informed consent has been obtained from all study participants, with separate consent obtained for participants in the Qualitative interview study.

Patient consent statement

Participants consented to the use of anonymised extracts in the study report and publications.

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Abstract

Objectives

This qualitative study explored patients' experiences and perceptions of the SCOPE2 trial. SCOPE2 studied radiotherapy dose escalation in patients with inoperable oesophageal cancer treated with (dCRT) definitive chemo-radiation.

Setting

UK

Participants

SCOPE2 trial participants, were invited to take part in interviews from across five clinical sites. Participants self-selected to take part in up to three interviews across four different time points: baseline (before treatment) and at 2-3 months, 3-6 months or 6 months+ after baseline. There were five female and five male interview participants.

Interventions

Participants were randomised to standard dose dCRT prescribed carboplatin/paclitaxel or cisplatin/capecitabine, or an escalated dose dCRT prescribed carboplatin /paclitaxel or cisplatin/capecitabine.

Methods

This qualitative study used semi-structured longitudinal interviews to explore the impact of treatment, patient outlook and quality of life, impact of the COVID-19 pandemic and potential improvements. Findings were presented in real-time to the trial team to inform of any potential improvements. Interview data were thematically analysed.

Results

Ten patients participated in 16 longitudinal interviews. Three participants were accompanied by companions. Participants experienced side-effects from radiotherapy and chemotherapy including nausea, throat pain, difficulties eating and regaining appetite, thrombosis and fatigue, although most of these symptoms gradually improved. Participants required more ongoing information and support regarding treatment side-effects, prognosis and cancer status in order to improve their overall quality of life. Best practice examples involved key contacts providing practical advice and signposting support.

Conclusion

Participants of the SCOPE2 trial reported short and longer-term side-effects from chemoradiotherapy, but these usually lessened over time. Participants attempted to be positive about their survival prospects by readjusting their expectations, priorities and lifestyles. Providing patients with ongoing opportunities to discuss detailed and timely information regarding treatment side-effects, aftercare and cancer status could improve the overall health and wellbeing of patients during oesophageal cancer trials and pathways.

Article Summary

Strengths and limitations of this study

- A limited number of qualitative studies use longitudinal interviews to gather real-time patient experiences during clinical trials. This study highlighted patients' ongoing trial and treatment experiences and the opportunity for trial improvements through longitudinal interviews.
- Semi-structured interviews provided rich data regarding patient experience before and during the COVID-19 pandemic, across different time points from participants across a range of age groups and genders.
- Recruitment to this qualitative study was slow and the small numbers of participants recruited restricted the breadth of experiences explored across different trial arms and the additional impact of higher dose of radiotherapy on patients.
- Lack of integration of qualitative study into the main trial recruitment limited opportunities for participant recruitment.
- Participants were self-selecting for interview, and needed to be well enough to be interviewed, thereby introducing a level of participant bias.

The experience of patients with oesophageal cancer receiving chemoradiotherapy treatment: a qualitative study embedded in the SCOPE2 trial

BACKGROUND

Oesophageal cancer (OC) has a relatively poor prognosis, as curative surgery is appropriate for only around 20% of the patient population (1) (2). Definitive chemoradiotherapy (dCRT) is offered as an alternative for patients who are unsuitable for surgery and is considered more effective than radiotherapy or chemotherapy alone. However, despite improved survival outcomes anticancer treatments may increase toxicities (3) and thus further diminish the patient's quality of life. (4)

The SCOPE2 trial builds on the SCOPE1 phase 2/3 trial (2013) which highlighted the survival and long-term toxicity benefits of standard (dCRT), as well as improved quality of life (5). However, SCOPE1 did not capture the experiences of the trial or treatments from the patients' perspectives. Subsequently, the SCOPE2 trial embedded a qualitative component which examined real-time experiences of a subgroup of trial participants.

SCOPE2 is a randomised Phase 2/3 trial for locally advanced non-metastatic oesophageal cancer patients. It examines radiotherapy dose escalation (standard dose of 50GY versus high dose of 60GY) and the effects of standard chemotherapy drugs (cisplatin and capecitabine, or carboplatin and paclitaxel). Additionally, it embedded a Phase 2 trial whereby patients who had not responded to the first two weeks of chemotherapy (as assessed by a second a positron emission tomography (PET) scan) could be randomised to either continue this chemotherapy regimen or switch to alternative one (6).

Previous qualitative studies embedded into cancer trials have provided in-depth insights into the experiences of patients with cancer relating to trial processes, their treatments, and their recovery (7) (8). In an OC trial (ROCS), real-time reporting of patient perspectives prompted trial amendments to increase recruitment, and highlighted existential concerns around the issues of physical and social eating, along with the burden of side-effects of radiotherapy and hospital appointments (8). In ROCS patients who received chemoradiotherapy treatment experienced longer term toxicity and a high symptom burden including dysphagia, lack of appetite, fatigue, dyspnoea (difficulty breathing) and pain, having a significant impact on physical functioning and quality of life.

This qualitative study was integrated within the SCOPE2 trial to provide an in-depth understanding of patients' and their companions' first-hand experiences of the demands of the trial and treatments, which are not captured through other trial data. The ongoing needs of participants were reported to the trial team in real-time with the aim of informing practice.

Aims

The aim of the qualitative component of the SCOPE2 trial was to explore patients' experiences and perceptions of the trial and treatment of escalated definitive chemoradiotherapy (dCRT) compared with standard dose, and of the two PET driven drug regimes.

Objectives:

1. To assess patient experience and perceptions of each dCRT arm of the trial.
2. To consider how participants' views change over time spent on treatment.

3. To examine the personal impact of treatment on participants' health and wellbeing.

Qualitative findings discussing the trial conduct, recruitment, and reasons for declining the trial are available elsewhere including in a full qualitative report.

METHODOLOGY

Study Design

This was a multicentre, longitudinal qualitative study of a sample of clinical trial participants with potentially curable OC. Qualitative methods were selected to understand the nuanced and individual experiences of participants.

Recruitment

The qualitative study took place between July 2017 and December 2021. Due to the COVID-19 pandemic the trial was closed to recruitment between March and August 2020 and the qualitative study between March and October 2020. The main trial began in 2016 and is due to finish recruitment in 2023. SCOPE2 has full ethical approval from Wales Research Ethics Committee 3.

Participants were recruited from five different sites across the UK and were informed of the optional qualitative interview study at the point of consent into the main trial or during the following 24 months. Patients were provided with a qualitative study information sheet and the qualitative study team were informed of the patient's contact details via secure email if patients provided written consent. Otherwise, patients provided their contact details to the

qualitative team using a reply slip and a stamped addressed envelope. The qualitative researchers contacted trial participants directly to arrange an interview and requested signed consent at the time of interview. Companions who accompanied patients during interviews provided written consent. All consent forms were held securely by the qualitative research team. Each participant was invited to participate in a maximum of three interviews.

An initial sample size of 30-40 participants was based on researcher judgement and theoretical saturation (9). However, recruitment to the qualitative study was delayed pre and post pandemic, as permissions to recruit to the qualitative element were granted separately to the main trial. Additional barriers limiting recruitment included lack of available staff for recruitment, the health of participants and delays due to the COVID-19 pandemic. These themes are more fully reported in the qualitative report.

Data collection

Qualitative researchers (DHH and ML) conducted semi-structured interviews. These researchers have experience in thematic analysis, as well as interviewing participants concerning sensitive subjects including cancer. They collected and analysed the data through a critical lens of researchers working outside the main trial team, and focused on understanding participants' lived experience of participants.

Interviews were conducted face to face before social restrictions were imposed in March 2020, and by telephone thereafter. Participants were invited to be interviewed up to three

times across four different time points: baseline (before treatment), 2-3 months, 3-6 months, or 6 months+ after baseline.

Before contacting participants for initial or follow up interviews, the qualitative researcher consulted the site's nurse to confirm that the patients remained in the trial and were well enough to be interviewed. Participants were self-selecting after being invited to participate in the interviews and were not offered payment for participation.

A semi-structured interview schedule was used to ensure a degree of consistency across the interviews, whilst still allowing for information to be elicited iteratively as interviews progressed. A revised version of the interview schedule was used after October 2020, which included questions regarding the impact of COVID-19 on the participants' experiences. Questions relating to this article are highlighted in interview schedule supplements 2, 3. Topics covered in the interviews, in line with the aims above included:

- Impact of treatment on function, health and wellbeing
- Personal needs and expectations
- Patients' and companions' perceptions of the trial and future aspirations

Interviews were audio recorded and transcribed verbatim by members of the team and an external transcription company.

Data Analysis

Longitudinal interviews were used as they provide opportunities to gain an understanding of the patient's experience over a period and draw attention to the processes and factors that influence change for the patient (10). Data were analysed thematically (11)(Braun & Clarke,

2012). This analysis was an iterative process, involving coding and interpretating data separately, then jointly identifying concepts and developing codes. The main researcher coded all data using the NVivo 12 software program, with 20% double-coded by the other researcher to ensure rigour. The researchers jointly developed a framework for analysis, through a process of cross-checking and deliberation of themes.

Real-time participant experience in relation to trial processes and treatment protocols was presented during trial meetings to allow necessary protocol amendments to improve trial conduct and patient experience. Initial findings were presented to the Trial Management Group and the qualitative lead for comment and reflection before being finalised.

Further details about how this study was conducted are available in the COREQ checklist supplement 1.

Public and Patient Involvement

The trial was overseen by a Trial Management Group which included two patient representatives known as Research Partners recruited through the Involving People Network. The research partners provided review and input into assessments of trial documentation, in particular patient facing documents, assisted with Scientific Milestone Reports, and contributed to TMG meetings. A PPI representative also reviewed final qualitative summary findings.

https://research.publichealthnetwork.cymru/en/news-and-funding/learn-more-about-involving-people-network/

RESULTS

Participants characteristics

Ten participants took part in a total of sixteen longitudinal interviews (Table 2). There were five female and five male interview participants, and three participants were accompanied by companions. The age range was 57-82 years and mean age was 70 years old. Five participants received the second PET scan (as part of the PET sub-study) while five did not receive this second scan (Table 1). Demographic participant data and information regarding participant interviews are available in (Table 2). Demographic information was collected and reported descriptively but was not used as sampling criteria.

Participants were interviewed from across all four treatment arms of the trial: standard dose dCRT prescribed carboplatin/paclitaxel (Arm 1); standard dose dCRT prescribed cisplatin/capecitabine (Arm 2); escalated dose dCRT prescribed carboplatin /paclitaxel (Arm 3); and escalated dose dCRT prescribed cisplatin/capecitabine (Arm 4) (Table 1). All interviews were conducted within seven months after baseline. Chemoradiotherapy was completed within twelve weeks.

Table 1: Participants' information and interviews

Patient	Arm	Companion accompanied	Baseline	Between 2- 3 months after baseline	3-6 months after baseline	6 months+ after baseline	Second PET scan at day 14
Participant 1	2	X		X	X		
Participant 2	2				X		X
Participant 3	1	X		X			X
Participant 4	1			X	X	X	
Participant 5	1				X		
Participant 6	4		X		X	X	
Participant 7	2				X	X	X
Participant 8	3				X		X
Participant 9	2					X	X

Participant 10	4	X	X				

Table 2: Number of participants interviewed pre and post pandemic

Data collection period	Number of participants interviewed	Number of Interviews
Pre-March 2020 (In-person interviews prior to Covid-19 pandemic)	4	7
Post-October 2020 (Telephone interviews after qualitative study suspension from March 2020 to October 2020 due to Covid-19 pandemic)	6	9
Total	10	16

Qualitative findings

The experiences of participants were captured throughout the trial, which highlighted changes at different time points in participants' perspectives, and the impact of treatment regimes on quality of life, including daily, family and social life (12) (13). The following results highlight the findings from the interviews, relating to the following key themes: impact of treatments; information and support needs post-treatment; patient outlook and quality of life; impact of COVID-19 and potential improvements. A hierarchy of themes and subthemes are presented in Table 3. A discussion of these findings is outlined below, examples of illustrative quotations are outlined in Supplement 4.

Table 3: Themes

Themes	Subthemes	Secondary subtheme
Experiences of treatment	Impact of treatment	

	Side-effects from treatments	Side-effects from chemotherapy Side-effects from radiotherapy
	Recovery after chemoradiotherapy	
Longer-term impact of treatments	Information and support needs after treatment	
Patient outlook and quality of life after treatments	Psycho-social impact Gradual improvements to quality of life Adaptation and normality Positive outlook after treatment	
Impact of COVID-19	Vulnerability and isolation	
Potential Improvements	Sharing information among peers Follow up information	

Experiences of treatment

Participants described the impact of receiving the treatment (radiotherapy and chemotherapy) including side-effects, and improvements to health. They emphasised how information provision and support from clinical trial and NHS staff before, during and after their treatments impacted on their overall psychological, as well as physical wellbeing.

Impact of treatment

Initial treatments and support provided by clinical teams earlier in the trial were described as having resulted in small improvements for some participants' cancer symptoms. These symptoms mainly related to difficulties eating.

Side-effects from treatments

Participants experienced short and longer-term side-effects from the trial treatments including pain, dysphagia, tiredness, and thrombosis. Several participants experienced multiple side-effects including pain and fatigue, or general degradation in their health, although most participants felt that these subsided over time.

Side-effects from chemotherapy

Participants described common side-effects they experienced after receiving chemotherapy including muscular fatigue, pain, and neuropathy in their feet. While most of these were expected, they were at times unprepared for certain symptoms.

Four patients reported that during the trial their chemotherapy treatment had been changed or stopped due to pre-existing conditions, side-effects that they had experienced or that the treatment was not positively affecting their cancer outcomes. This demonstrates the complexities patients and clinicians may face when weighing up the side-effects of different chemotherapy regimens.

Side-effects from radiotherapy

The experience of receiving radiotherapy was reported by most participants as being physically and psychologically arduous. Difficulty and pain swallowing experienced after radiotherapy were the main side-effects described by several participants.

Recovery after chemoradiotherapy

After the completion of chemoradiotherapy, during the recovery period, participants experienced symptoms which ranged from mild to severe, having physical and psychological

outcomes. Nausea, as well as fluctuations in appetite, weight and energy levels were reported by participants, often relating to pain and issues swallowing. Some participants recalled having to adapt to the fatigue caused by difficulty sleeping and pneumonia. Participants' symptoms tended to lessen over time, and when they had received support to reduce these symptoms, they usually recalled noticeable improvements. It was not always possible to differentiate between the longer-term impact of chemotherapy or radiotherapy treatments, as participants described their symptoms more generally.

Post-treatment issues relating to bowel function included constipation and diarrhoea. Other symptoms were also reported including low immunity and hair loss.

Longer-term impact of treatments

Participants reflected on their cancer treatment journey and how their symptoms had changed over time, including facing adversity throughout treatment regimens and gradual improvements.

In some instances, participants described the reality of the unexpected longer-term side-effects of the illness and treatment, emphasising the need for ongoing support and updates from healthcare professionals.

Information and support needs after treatment

Concerns were raised by several participants and their companions regarding what would happen post-treatment, as they felt that there was less information and support available than before and during their treatment. Participants expressed a need for further and more

timely information and updates from healthcare professionals regarding potential longer-term side-effects, including recovery timescales post-treatment.

Participants described difficulties with eating and dietary needs, and expressed the importance of being provided with relevant information regarding how the disease or treatments impacted on these fundamental needs.

Several participants described the high level of personal support from clinical and third sector services, including key workers, which made a significant impact on their trial and treatment experience. They described the support and information they received relating to their quality of life and practical needs.

Patient outlook and quality of life after treatments

Psycho-social impact of treatments

The psycho-social impact that some patients described in the first few months post-treatment included disinterest or lack of energy to participate in previously enjoyed hobbies and social activities.

Gradual improvements to quality of life

Participants explained how the treatment had impacted on their quality of life overall. Most felt that their physical health post-treatment had placed restrictions and strains on their everyday routines. At times they felt they had relied heavily on their family for support with daily activities. However, gradual improvements to participants' health and well-being

related to readapting and regaining their capacity to participate in previous routines and social activities.

Adaptation and normality

Regaining a sense of normality was important but complicated for some participants when re-adapting to life after treatment, as their daily lives had been significantly impacted by their experiences of cancer and treatment. Several participants explained that they struggled to readjust to life after treatment, due to the change in outlook that they needed to make, or the extra support that they had received on the trial, which was no longer available.

Positive outlook after treatment

Several participants described how they attempted to sustain a positive outlook about their survival prospects and their circumstances overall. Thus, being provided with adequate support and updated information aided their positive outlook.

Impact of the COVID-19 pandemic

Vulnerability and isolation

Some participants reflected on how the pandemic may have intensified the sense of isolation and stress that other patients felt during their treatment process, although these participants did not feel personally affected in this way.

The pandemic caused an increased sense of vulnerability and cautiousness amongst cancer

patients. However, the comprehensive social restrictions put into place for infection control, and the vaccination programme at times allayed some of their fears and eased the sense that these participants missed out on their usual social activities.

Potential Improvements

Sharing information among peers

Opportunities for participants and their caregivers to share information regarding their experiences of cancer and their treatment pathway through peer support networks were suggested, as a means of improving patient knowledge.

Follow up information

Follow up information regarding the participants' current cancer status, as well as results from the trial, were desired by a participant, who felt that they were unsure about their personal outcomes or how this related to the wider trial.

DISCUSSION

Main Findings

This qualitative study captured the experiences and perceptions of SCOPE2 trial participants, using longitudinal interviews. These interviews highlighted participants' changing practical, physical, and psychosocial needs. Expected and unexpected side-effects from the radiotherapy, and both sets of chemotherapy treatments, were described by participants at different time points, although most of these symptoms lessened over time. Participants attempted to be positive about their survival prospects and applied coping strategies by

readjusting their expectations and priorities, focusing on regaining a sense of 'normality'. The need for improved information and communication regarding the longer-term side-effects of chemoradiotherapy, aftercare, and cancer status was highlighted as necessary to improve overall patient experience and quality of life.

Strengths and limitations compared with other studies

The integration of longitudinal qualitative research into this trial, has provided novel and nuanced insights into participants' perceptions and experiences of the trial and chemoradiotherapy before and during the COVID-19 pandemic. These insights are not comprehensively captured through other types of data collection (quantitative and clinical data) during clinical trials. Using longitudinal interviews and real-time reporting has also informed the trial team of patients' ongoing information and support needs. As a result of this, a newsletter has been planned to report trial updates to participants. However, some quantitative (14) or combined qualitative and quantitative studies (15) which examined patients' experiences or quality of life after oesophageal cancer treatment recruited higher numbers of participants. These were able to compare the broader range of patients' experiences of chemoradiotherapy. Nonetheless, these studies did not explore the range of trial and treatment experiences through longitudinal data collection.

Comparison with the existing literature

Consistent with earlier qualitative studies, participants experienced varying side-effects from the chemoradiotherapy treatments across the trial arms, which ranged from mild to severe. Shorter-term symptoms included pneumonia, fatigue, difficulty sleeping and pain swallowing, reflect symptoms reported more generally among oesophageal cancer patients

(16). Longer-term gastrointestinal effects were also reported, including nausea, satiety and diarrhoea, poor appetite, and weight loss, reflecting side-effects after surgery reported in other studies (17)(18). However, it was at times difficult to differentiate between whether the side-effects reported were a result of radiotherapy or chemotherapy, a combination of both treatments or the underlying cancer.

Participants' perceptions of their treatment and side-effects changed over time and they attempted to be positive about their survival prospects by readjusting their expectations and priorities (19). Similar coping strategies and approaches to resilience and adaptation have been identified in studies that highlight the changing emotions that patients deal with when facing the uncertainties of life-threatening illnesses (20)(21). Participants reflected on the importance of regaining a sense of 'normality', in terms of the physical, social and psychological impact, as their daily lives had been significantly disrupted by the cancer and its treatment, but for the most part were improving over a period of months (22) (23).

Participants described varying levels of uncertainty and a lack of knowledge regarding potential longer-term side-effects from treatment. This reflects previous research findings illustrating the need to provide timely and appropriate patient communication and information, particularly relating to treatment aftercare, which can reduce anxiety and increase patients' well-being and their sense of agency (24) (16). In contrast, best practice examples were described as key contacts organising appointments and providing signposting to appropriate information, which reduced psychological and physical burdens on the participants during a time when they were acutely ill. These findings illustrate how the COVID-19 pandemic had varying effects on participants when receiving cancer treatment. Some participants felt that due to social restrictions the impact on their social

activities was less than it usually would have been pre-pandemic, while others felt a heightened sense of social isolation and reduced opportunities for peer support.

Implications for policy makers and future research

OC cancer clinical pathways need to provide opportunities for patients to discuss, revisit information and ask questions before, during and after their treatments, in order to enhance patient satisfaction with their trial, treatment and recovery experiences. Consistent signposting to charities and peer support could also enable patients to access relevant and timely support. Future trials and pathways should ensure ongoing access to support through the provision of a key contact for the patient. Sharing updates regarding the progress of the trial where possible, would also be useful for participants. A more integrated approach to qualitative studies embedded in trials including incorporating real-time reporting in future trials could provide improved opportunities for recruitment and patient experience. Future studies could follow up with patients over an extended period, in order to gain an understanding of the longer-term effects of chemoradiotherapy.

CONCLUSION

Qualitative study participants of the SCOPE2 trial were generally positive about the impact of their treatments and recovery experiences, despite experiencing a range of short and longer-term side-effects, some of which were unexpected. Future trials and cancer services should consider patients' needs for ongoing information and support regarding treatment aftercare, longer-term side-effects, prognosis, and cancer status to improve their overall health and wellbeing.

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Supplement 2

Consolidated criteria for reporting qualitative studies (COREQ): 32-item checklist

No	Item	Guide questions/description
Domain 1: Research team and reflexivity		
Personal Characteristics		
1.	Interviewer/facilitator	Which author/s conducted the interview or focus group? Dr Daniella Holland-Hart Dr Mirella Longo
2.	Credentials	What were the researcher's credentials? *E.g. PhD, MD* PhD
3.	Occupation	What was their occupation at the time of the study? Research Associate, Cardiff University
4.	Gender	Was the researcher male or female? Female
5.	Experience and training	What experience or training did the researcher have? All researchers hold extensive expertise in doing interviews. They all hold an updated GCP certificate and NVivo training and hold PhD's.
Relationship with participants		
6.	Relationship established	Was a relationship established prior to study commencement? No relationship but the researchers used their research experience and training to introduce the research study and mitigate

No	Item	Guide questions/description
		the asymmetry of information between the two parties.
7.	Participant knowledge of the interviewer	What did the participants know about the researcher? e.*g. personal goals, reasons for doing the research* Reasons for doing the research
8.	Interviewer characteristics	What characteristics were reported about the interviewer/facilitator? e.g. *Bias, assumptions, reasons and interests in the research topic* Research expertise
Domain 2: study design		
Theoretical framework		
9.	Methodological orientation and Theory	What methodological orientation was stated to underpin the study? *e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis* Thematic analysis, the conceptual thematic framework used in the study is described in the methodology section.
Participant selection		
10.	Sampling	How were participants selected? *e.g. purposive, convenience, consecutive, snowball* The sample were self-selecting
11.	Method of approach	How were participants approached? e.*g. face-to-face, telephone, mail, email* Face to face through the research nurse. Then via phone from the researchers.
12.	Sample size	How many participants were in the study? 10

No	Item	Guide questions/description
13.	Non-participation	How many people refused to participate or dropped out? Reasons? One patient was too unwell to participate in interviews after consenting.
Setting		
14.	Setting of data collection	Where was the data collected? e.*g. home, clinic, workplace* At home or via telephone.
15.	Presence of non-participants	Was anyone else present besides the participants and researchers? Companions were present in some interviews.
16.	Description of sample	What are the important characteristics of the sample? *e.g. demographic data, date* Gender, age.
Data collection		
17.	Interview guide	Were questions, prompts, guides provided by the authors? Was it pilot tested? Interview schedules included prompts, which were tested by a senior qualitative researcher (AN).
18.	Repeat interviews	Were repeat interviews carried out? If yes, how many? No repeat interviews were carried out but follow up interviews were carried out.
19.	Audio/visual recording	Did the research use audio or visual recording to collect the data? All interviews were audio recorded.
20.	Field notes	Were field notes made during and/or after the interview or focus group? Field notes were not made during the interviews.
21.	Duration	What was the duration of the interviews or focus group? Mean average 44 minutes

No	Item	Guide questions/description
22.	Data saturation	Was data saturation discussed? Yes, this was discussed within the team. However, we were unable to reach saturation due to the limited number of interviews.
23.	Transcripts returned	Were transcripts returned to participants for comment and/or correction? No this was not done.
Domain 3: analysis and findings		
Data analysis		
24.	Number of data coders	How many data coders coded the data? 2 data coders (DHH) and (ML)
25.	Description of the coding tree	Did authors provide a description of the coding tree? A coding tree is available but not described in the paper. However, the main themes and sub-themes are outlined in Table 4.
26.	Derivation of themes	Were themes identified in advance or derived from the data? Derived from the data itself
27.	Software	What software, if applicable, was used to manage the data? NVivo 12
28.	Participant checking	Did participants provide feedback on the findings? The patients did not comment but were offered a summary of findings.
Reporting		
29.	Quotations presented	Were participant quotations presented to illustrate the themes / findings? Was each quotation identified? e.*g. participant number*

No	Item	Guide questions/description
		All main themes were illustrated by quotes. The patients are identified by a number and at what stage the interview took place.
30.	Data and findings consistent	Was there consistency between the data presented and the findings? All main themes were illustrated by quotes, supplementary materials provide further evidence of these points and consistency.
31.	Clarity of major themes	Were major themes clearly presented in the findings? Major themes formed the basis of the presentation of the qualitative analysis, reflecting the purpose of the overall study (i.e. patient experience of the trial and treatments) and derived from the data itself.
32.	Clarity of minor themes	Is there a description of diverse cases or discussion of minor themes? Sub themes are also discussed, and examples of divergence between participants are outlined in the main text and additional quotations.

16.0 Embedded Qualitative Study Design

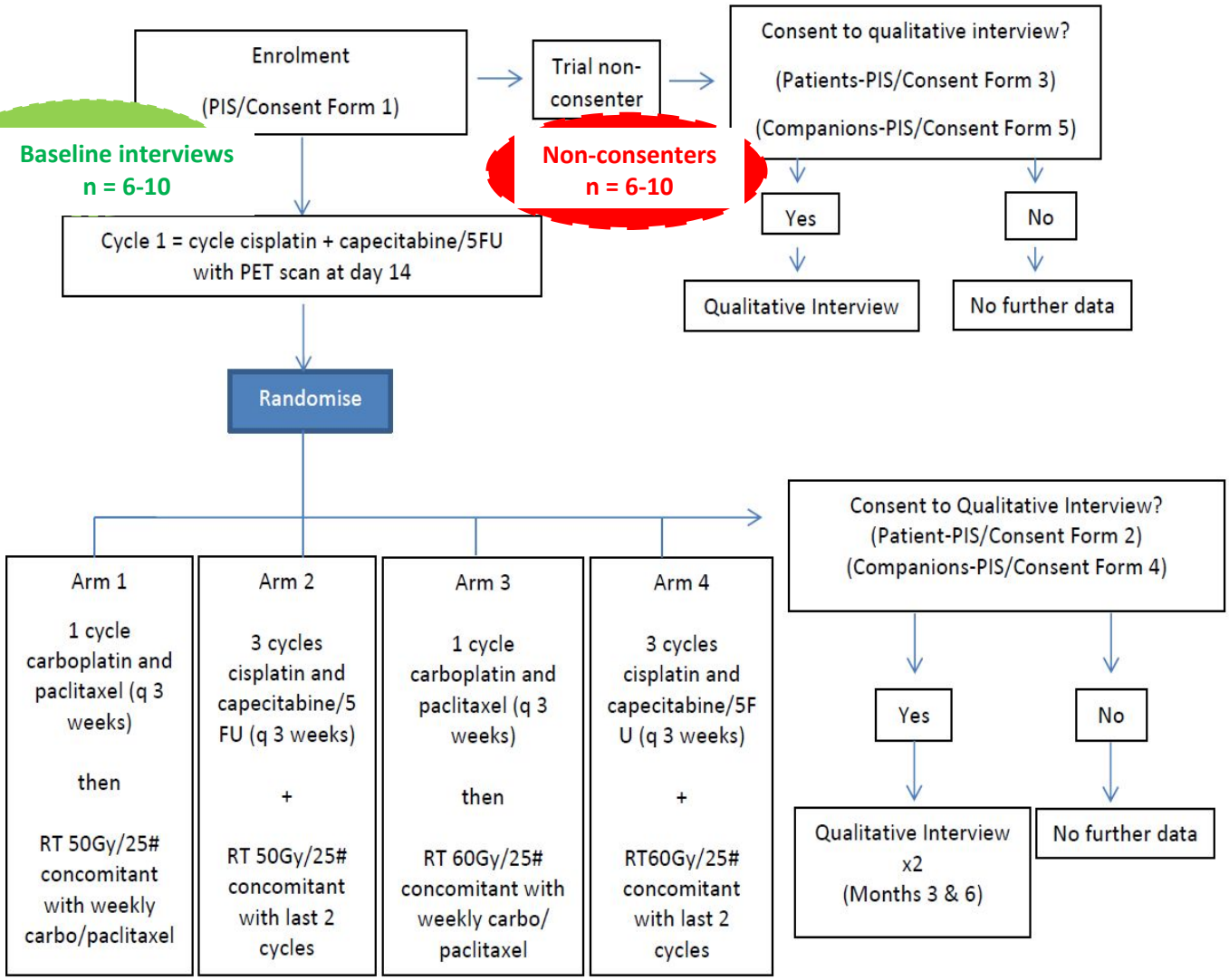
16.1 Rationale

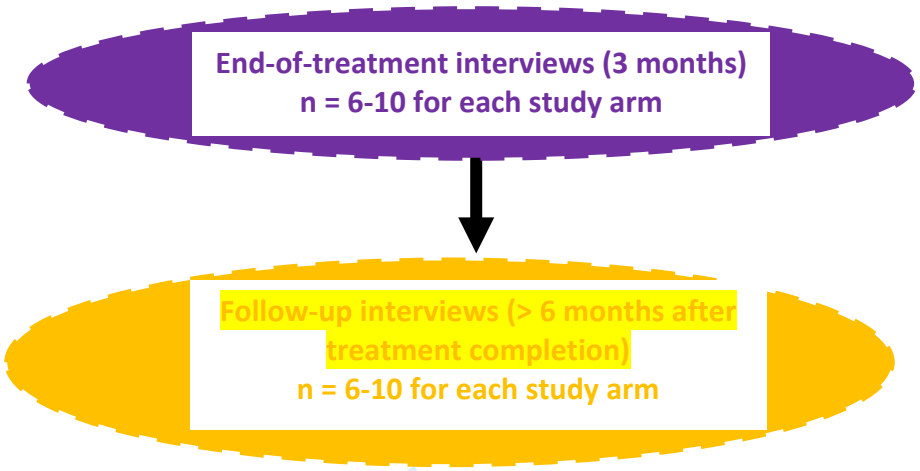
The qualitative component of the SCOPE 2 trial will explore patient experiences and perceptions of participating in a trial of escalated definitive chemoradiotherapy (dCRT) compared with standard dose, and of the two PET driven drug regimes.

16.2 Embedded qualitative study aims [AS PER PROTOCOL]

1. To assess patient experience and perceptions of each dCRT arm of the trial
2. To compare patient views across the dCRT arms of the trial
3. To consider how participants' views change over time spent on treatment
4. To examine the personal impact of treatment on patients' health and wellbeing
5. To understand patients' reasons for declining the trial

Qualitative interviews flowchart





BEFORE THE INTERVIEW

Rapport building

- Thank you for inviting me into your house

Introduction

- Thank you for agreeing to help me with this project – give a few details about the trial (e.g. name, centres, etc)
- I would also like to emphasise that only the study research team will see the information you give me.
- Your name will never be attached to any of them.
- As I mentioned I record the conversation to ease the analysis.
- However, in order for me to do this I need you to have your written consent
- Consenting the companion. As explained your …… can make any point or comment during the interview. However, again for us to be able to use the information given we need to consent ……. as well.
- Last but not least, if anything is not clear, please stop me at any time
- State the purpose of the interview

NON-CONSENTERS INTERVIEW GUIDE

Today we are going to talk about your experience of being invited to take to the SCOPE trial. The interview should take between 30 and 45 minutes. If you need a break at any time please let me know. Are you comfortable to carry on with the interview? (Reassure participants that this is not a test of knowledge – people remember different things)

Specific questions

1. When did you first hear about the trial?
    i. Who explained it to you?

2. What information were given to you?
    i. What did you think the aim of the trial was?
    ii. What was your understanding of the randomisation process?
    iii. Did you discuss the information given with others?
    iv. Did you feel you had enough time to think about the information given?

3. Can you tell me why you preferred not to participate in the trial?
    i. Did you feel that the trial was not what you expected?
    ii. Did you feel supported when making this decision?
    iii. Did you have any concern about turning the trial down?

4. Do you (or someone close to you) have any previous experience of being in a trial?

5. Do you (or someone close to you) have any experience of radiotherapy?
    i. Experience of chemotherapy?

6. Is there anything we could do to make it easier for patients to take part to a similar trial in future?

Concluding questions

7. I have been asking you many questions, is there anything you would like to ask me?

CONSENTERS BASELINE: INTERVIEW GUIDE

Today we are going to talk about how you have been feeling lately and how you feel about taking part in the trial. The interview should take between 30 and 45 minutes. If you need a break at any time please let me know. Are you comfortable to carry on with the interview?
(Reassure participants that this is not a test of knowledge – people remember different things)

Specific questions

1. When did you first hear about the trial?
    i. Who explained it to you?

2. What information did you receive?
    i. What did you think the aim of the trial was?
    ii. What was your understanding of the randomisation process?
        a. (Try to explore understanding of equipoise)
        b. (How they feel about uncertainty if raised)
    iii. Did you discuss the information given with others?
    iv. Did you feel you had enough time to think about the information given?

3. Can you tell me why you decided to participate in the trial?
    i. What were your main motives for joining
    ii. Did you feel supported when making this decision?

4. How are you feeling?

Concluding questions

5. I have been asking you many questions, is there anything you would like to ask me?

FOLLOW UP ARMS 1 TO 4 – TIME 1 (2-3 months): INTERVIEW GUIDE

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Introduction

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- Last but not least, if anything is not clear, please stop me at any time

Today we are going to talk about how you have been feeling lately, your experience about the treatment you received and how you feel about taking part in the trial. The interview should take between 30 and 45 minutes. If you need a break at any time please let me know. Are you comfortable to carry on with the interview? (Reassure participants that this is not a test of knowledge – people remember different things)

Specific questions

Joining the trial

1. How have you found being part of a clinical trial so far?
   i. Is what you expected?
   ii. Anything particularly positive?
   iii. Anything negative or that could be improved?
2. Have you had any questions or concerns since you have been on the trial?
   i. Did you speak to somebody about these concerns?

Treatment allocation

3. Have you had all your treatment?
4. What treatment were you on?
5. Have you been given information on how the treatment is working for you on the current state of your illness?
   i. What was your reaction to this information?
   ii. What did you think of the way the information was given to you?
6. How long have you been on your treatment?

7. Is this the treatment that you preferred?
   i. With hindsight, would you have preferred a different treatment?

ii. How did you feel after your PET scan (*avoid this question if the patient was ineligible for pet scan – check with the RN*) (logistics, side effects)

Treatment experiences

8. How have you been feeling
   i. Symptoms
   ii. Psychologically
   iii. Coping (If there are psychological difficulties or coping difficulties, how have they been addressed? Has the participant talked to anyone? Who supports them?)
9. Are you experiencing any symptoms at the moment? How do you manage them (medications, complementary therapies)?
10. Have you been getting any side effects from the treatment you received?

Impact of treatment on quality of life

11. How has your treatment affected your daily life?
    i. What has it stopped you doing? (try to tease out aspects around the logistics of the treatment [e.g. time away from home] and side effects from drugs [side effects/fatigue])
    ii. How have these symptoms affected you family and social life?
12. How is your quality of life since starting the treatment?
13. Does your treatment affect your family/social life?
    i. Time away from home
    ii. Side effects/fatigue

Accessing other services

16. Have been accessing other services? (eg Macmillan or Marie Curie)
    iii. Is there any other kinds of support you feel would benefit you?
    iv. Would you know how to access it?

Concluding questions

17. I have been asking you many questions, is there anything you would like to ask me?

FOLLOW UP ARMS 1 TO 4 – TIME 2 (6 months): INTERVIEW GUIDE

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Specific questions

The trial follow up

1. What is your understanding of how long you will be in the trial and what happens next?
   i. Follow up at 9, 12, 16, 20, 24 months
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2. How do you feel about the health care support you have been getting since you joined the trail?
   i. Is this what you expected?

Post-treatment experiences

3. What treatment were you on?
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8. How did you feel about having a second PET scan? (*avoid this question if the patient was ineligible for pet scan – check with the RN*) (logistics, side effects)

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12. How would you say that any symptoms and side effects you've experienced changed over the course of your illness?
13. Do you feel better or worse now than you did at the time of the diagnosis
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    ii. Mentally
14. How have you learned to manage your illness?

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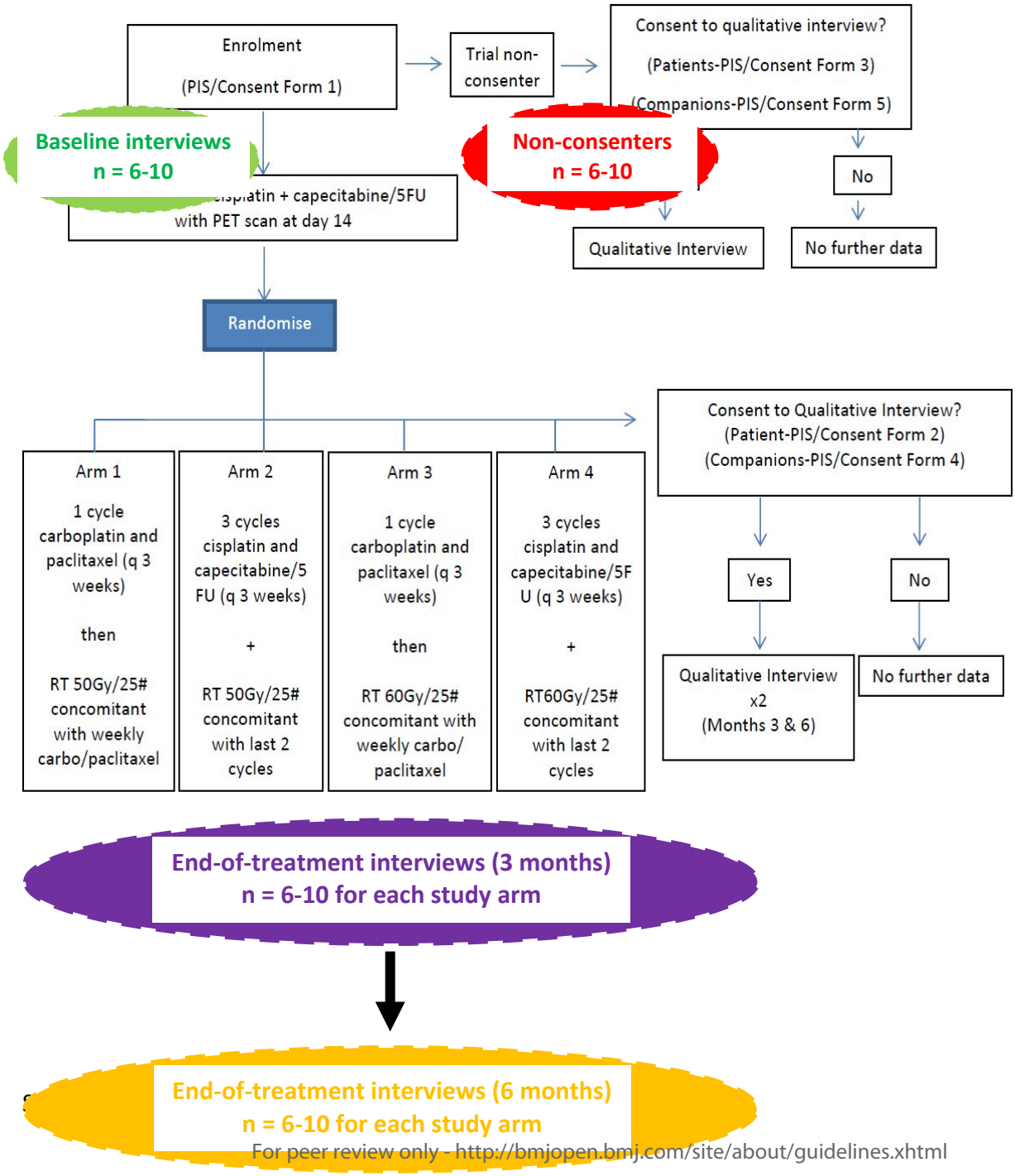

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5. Do you (or someone close to you) have any experience of radiotherapy?
    i. Experience of chemotherapy?

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        a. (Try to explore understanding of equipoise)
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        c. (understanding the different arms of the trial)
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    i. What were your main motives for joining?
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FOLLOW UP ARMS 1 TO 4 – TIME 1 (3 months): INTERVIEW GUIDE

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    ii. How did you feel after your PET scan (*avoid this question if the patient was ineligible for pet scan – check with the RN*) (logistics, side effects)

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12. How is your quality of life since starting the treatment?
13. Does your treatment affect your family/social life?
    i. Time away from home
    ii. Side effects/fatigue
    iii. Withdrawal

Impact of Coronavirus

14. Do you feel that the coronavirus has had any impact on your treatment or recovery?

i. How has the coronavirus affected your quality of life?

ii. Has the coronavirus had an impact on your care or support?

Accessing other services

15. Have been accessing other services? (eg Macmillan or Marie Curie)
    i. Is there any other kinds of support you feel would benefit you?
    ii. Would you know how to access it?

Concluding questions

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FOLLOW UP ARMS 1 TO 4 – TIME 2 (6 months): INTERVIEW GUIDE

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    i. Is this what you expected?

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4. How long were you on your treatment?
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13. Do you feel better or worse now than you did at the time of the diagnosis
    i. Physically
    ii. Mentally
14. How have you learned to manage your illness?

Impact of coronavirus

15. Do you feel that the coronavirus has had any impact on your treatment or recovery?
    i. How has the coronavirus affected your quality of life?
    ii. Has the virus had an impact on your care or support?

Accessing other services

16. Have you been accessing other services? (eg Macmillan or Marie Curie)
    i. Is there any other kinds of support you feel would benefit you?
    ii. Would you know how to access it?

Concluding questions

17. I have been asking you many questions, is there anything you would like to ask me?

Table 4: Illustrative Quotations

Key Themes	Illustrative Quotations
Experiences of treatment	
Impact of treatment	
Initial treatments and support provided by clinical teams earlier in the trial were described as having resulted in small improvements for some participants' cancer symptoms. These symptoms mainly related to difficulties eating.	*I know when I started I had difficulty swallowing obviously with the oesophagus tumour and it was sort of every meal, every few mouthfuls was getting difficult and I did feel in about two weeks into the first cycle, I was pretty much able to swallow normally. So, something positive is happening'*. **Participant 4 (2-3 months)**
	I had a tube fitted in my arm yesterday, ready for the chemo on Friday, and I've got a feeding tube, so I don't have to worry about not getting enough nutrition in, so I think a lot of worries I had at the beginning have faded. **Participant 6 (Baseline)**
Side-effects from treatments	
Side-effects from chemotherapy Participants described common side-effects they experienced after receiving chemotherapy including muscular fatigue, pain and neuropathy in their feet, while most of which were expected some they were unexpected.	*The side effects I've I had are quite sore feet at one stage when I was on the chemotherapy, which was difficulty walking.* **Participant 7 (3 months)**
	Cos everybody expected when I stopped the chemo, especially me, I thought that was it (laughs), you know stop the chemo and that's fine. And, then I stopped the chemo and I got ill (laughs). **Patient 6 (6 months)**
	During the 1st cycle … the pain in my feet and little bit sort of pins and needles like that, I think that's the worst side effect that I have experienced... Tiredness, you know, just feel worn out… the other thing that I get is almost like fatigue in my thighs… I think one day where I felt sick which is just cleaning my teeth. **Participant 4 (Baseline)**
Four patients reported that during the trial their chemotherapy treatment had been changed or stopped due to pre-existing conditions, side-effects that they had experienced or that it was not making enough of a difference to their cancer	*I found the capecitabine taking those every day I think they were the hardest of the drugs that I was taking… I did notice with them the nausea and the sickness and the fatigue was massive. When, they put me on [another chemotherapy drug] … I felt it was much gentler… unfortunate[ly] for me… having a blood clot… I think that was the worst thing… the blood clot was harder to recover from than the cancer (laughs)'.* **Participant 4 (3 months)**

outcomes. One participant described the unforeseen development of thrombosis after switching the types of chemotherapy they received due the initial side-effects. This demonstrates the complexities some patients face when weighing up the side-effects of different chemotherapy regimens.	*Companion: The last week of September that he couldn't eat… and that's why they stopped the treatment too early… and that tails off then because he has a dose of steroids and it boosted his appetite and It boosted everything.* *Patient: There were huge difference because of steroids… that was before all the, the pneumonia came on… that was again the weeks following the treatment which I be as happens.* **Participant 1 (6 months)** *After they took the test at the end of just one cycle and they said it didn't made enough difference so it was being changed*. **Participant 3 (2-3 months)** *The first chemo I was on, they had to change... I've got… Neuropathy. So, they changed it. And, another one was because of my kidneys. They changed that to a different one right at the very beginning. I didn't even go on it, which was much better as well because it was less traumatising and stressful for me. They definitely knew what they were doing*. **Participant 5 (3 months)**
Side-effects from radiotherapy The experience of receiving radiotherapy was reported by most patients as being physically and psychologically arduous. Difficulty and pain swallowing experienced after radiotherapy were the main side-effects described by several patients.	*Because of what the radiotherapy does, it sort of burns all the inside and it's very difficult to swallow… but that was the worst thing to be perfectly honest with you, the thing is I would like to able to eat like I used to, but at the moment I can't but I am getting there… definitely turns better now.* **Participant 2 (2- 3 months)** *With the radiotherapy… I was completely and utterly flat out, nothing mattered at all... You can't win it at any point… you can't concentrate or want anything, you feel bad if there is no pain, nevertheless you feel dreadful.* **Participant 1 (6 months)** *Once radiotherapy started I could feel then that the inflamed and the tumour and the oesophagus, I could feel that it sort of was creeping back to where I was before and it just got a little harder to swallow but not to the extent that I couldn't eat.* **Participant 4 (6 months)** *It's worse right now but then we've only just finished radiotherapy, it's very tender right now, it's burning from inside out… the consultant did say... I've been trying to get on pulses, semi solids... It's not how thin or thick it is it's the texture of it, whether it'll slide down or it won't slide down, so every now and again I experiment sending something down there. Sometimes I can do it but this particular week it's been*

difficult, but the consultant explained to me "I'm full up of chemo and I'm full up of radiotherapy and everything's pretty raw right now". **Participant 8 (3 months)**

I just have a slight problem with swallowing sometimes but that they say that's to do with the radiation but it didn't stop me eating what I want, I just have to make sure I chew it properly that's all. **Participant 9 (6 months)**

Recovery after chemoradiotherapy

After the completion of chemoradiotherapy, during the recovery period, participants experienced symptoms which ranged from mild to severe, having physical and psychological outcomes. Nausea, as well as fluctuations in appetite, weight and energy levels were reported by participants, often relating to pain and issues swallowing. Some participants recalled having to adapt to the fatigue caused by difficulty sleeping and pneumonia. Participants' symptoms tended to lessen over time, and when they had received support to reduce these symptoms they usually recalled noticeable improvements. It was not always possible to differentiate between the longer-term impact of chemotherapy or radiotherapy treatments, as participants described their symptoms more generally.

I lost my appetite a bit, but, … that's come back now, and … I am starting to regain weight… I still have problems digesting food … some foods just get stuck in my oesophagus, and that is still a little bit painful. **Participant 7 (3 months)**

I had pneumonia… I started with the infection as soon as I finished the chemo… I was in hospital for a week. And, I had about four different courses of antibiotics and they just weren't working on the pneumonia. And, I felt worse with that than I had been through all the treatment. And I was just starting to get better before we went away… within days I suddenly was much, much, much better. **Participants 6 (6 months)**

I had trouble sleeping for quite some time and that sorted itself out now and can sleep perfectly well now without any paracetamol at all, so night-time is good. **Participant 1 (2-3 months)**

*The treatment make[s] you very tired… I have to rest a lot and whilst I think to myself I feel really good today lets go out. When I have out a couple of hours I have to come home, even now you know it tires me, but that's fine. Things improve on a daily basis and hopefully it will continue to improve***. Participant 2 (3-6 months)**

I had some constipation, I have to admit and that's been an issue throughout… I had to listen to my body and you know rather than fighting sleep, rather than thinking that you know I am going to battle this , sometimes you just got to shut your eyes and think you know what I will sleep all day, doesn't matter. **Participant 4 (2-3 months)**

The fatigue, the tiredness… did seem to last a little bit longer than I really anticipated… you know some days I didn't feel like lifting my head off the pillow… I think the fatigue was a biggest one for me. **Participant 4 (6 months)**

I'm getting stronger in myself as well, so. And, the treatment has gone and I'm getting taste back, so I can taste things better than I did. You know cos just drinking. Just drinking water, it wasn't very nice, but it's alright now. **Participant 5 (2-3 months)**

I had nausea, tiredness has been the biggest one for me… it's slowly improving, I'm not dropping off to sleep as I'm talking to people type of thing now, but that was happening, (chuckling)… I've started to eat again, tiredness is the main thing, but nothing that I can't cope with and was expected, they told me that I would be, my body's going to, gotta kind of repair itself a bit now. I'm still taking the anti-nausea medications, but I have reduced them… I've still got the RIG feeder so, I'm trying to wean myself, at the moment, off it. So, I'm starting to try and take some of my medications orally, instead of through the tube. I'm on a lot less medication than I was. **Participant 6 (3 months)**

I was sleeping up to 17 hours a day … which is… I've spoke to the people down there and they say that's a natural side effect, but it happens. **Participant 7 (3 months)**

Longer-term impact of treatments

Participants reflected on their cancer treatment journey and how their symptoms had changed over time, including facing adversity throughout treatment regimens gradual improvements.

At the time during the treatment … I've felt really, really, really ill, worse than before I started the treatment… The treatment was tough… I have [had] a lot of symptoms, side-effects from it. But those have finished now, so obviously things are improving… when it finished, I was having problems… but each day I'm getting better. **Participant 5 (3 months)**

I'm just feeling better every day and my eating is improving all the time. **Participant 6 (6 months)**

I feel a lot better. Obviously the time I was diagnosed it was a bit of a bolt out of the blue and I was left you know in big, big shock. So, the fact that they've now said to me that the cancer's gone, it's obviously a huge relief. ***Participant* 7 (6 months)**

In some instances, however, participants described the reality of the unexpected longer-term side-effects of the illness and treatment, emphasising the need for

I was quite euphoric all the way through the treatment and it was after the treatment ended that I sort of thought it's all over now. The fatigue, the tiredness [will] all be going and it did seem to last a little bit longer than I really anticipated and unfortunately the wound with the blood clot still hasn't healed. **Participant 4 (6 months)**

ongoing support and updates from healthcare professionals.

Patient: No interest at all in checking my general condition which could have changed because of the treatment …
Companion: And you just hope that all the drugs are compatible. They all interact with each other and that is another hurdle. Who knows?...
Patient: It's thousands of, it's thousand of trials. How can you do it, interaction of drugs is a massive problem being tackled all the time. **Participant 1 (2-3 months)**

Information and support needs after treatment

Concerns were raised by several participants and their companions regarding what would happen post-treatment, as they felt that there was less information and support available than before and during their treatment. A need for further and more timely information and updates from healthcare professionals regarding potential longer-term side-effects including rare events such as blood clots and recovery timescales post-treatment was also expressed by participants.

We actually felt we have huge information on side effects during treatment but virtually nothing on after [treatment]. **Companion of Participants 1 (2-3 months)**

When it comes to this particular type of blood clot I had, there was nothing, no description there and I suppose if I could sort of say anything about the website- that's the one thing they missed because all the symptoms I read about were symptoms that were associated the side effects of the drugs as well. **Participant 4 (6 months)**

The fortnight before we draw the line for the end of treatment as to how things are likely to move on and likely tests and however… some sort of framework… As it is, we haven't got any date at all for anything beyond next Friday, week Friday, nothing at all… We didn't have a cohesive view on the whole thing presented by one person anyway, it was bits and pieces. **Participant 1 (2-3 months)**

Companion: Its general advice be kind to yourself for few months (coughs) and then you should begin to feel stronger or sleep more than you would have done so that your body recover. So the body has had fair hammering… It isn't just the 10 weeks when you take the chemotherapy challenge is it? It's much bigger picture. **Participant 1 (2-3 months)**

It's all been a bit strange because, I had to come off the initial chemotherapy drugs. It was sort of we will have to take you off the trial but still keep collecting the data from the trial and I understood that because… I think trials have to be very specific and if you stay outside the guidelines then it does blur the data… I don't know whether I will be monitored a little bit extra. I don't know whether I am assuming when I go back to check up in six months there would be the same questionnaires and the same sort of things. **Participant 4 (6 months)**

Participants described difficulties with eating and dietary needs, and expressed the importance of being provided with relevant information regarding how the disease or treatments impacted on these fundamental needs.	*I have phone calls from the clinical nurse… sometimes just to ask how I am, he's helped to make appointments for me when I've had problems making them myself. And he's managed to make everything seamless from one thing to another, which I greatly appreciated, because I was a bit all over the place, especially at the beginning of diagnosis… if [clinical nurse] thought that maybe I wasn't getting something, that the Oncologist was saying to me… maybe sometimes I was lacking a bit of understanding and he always made sure that I left that room, understanding everything.* **Patient 6 (3 months)** *One thing that I asked all along was really about how much I could eat, we have been asking, haven't we? You sort of [know] it is going to get more difficult, is my throat going to be smaller, will it get bigger again, how much will I be able to eat? Will I be able to eat properly at the end and I think that all out questions have been like that.* **Participant 3 (2-3 months)**
Several participants described a high level of personal support from clinical and third sector services, which made a significant impact on their trial experience. They described how they had received support relating to their quality of life and practical needs, which they may not have accessed from healthcare professionals.	*Age Connect, Age Concern one of those we have used their advice a few times. Just popped in and seen them… has been very, very good as a system for us.* **Participant 4 (6 months)** *The medical staff have really been great, and ... I've got all the information … all I need to do is pick the phone up and I know I can speak to somebody with any questions … have been in contact and … am on various forums with Macmillan, … which … my wife and I have accessed quite frequently … just to view other peoples' experiences, which has been good, because obviously whatever side effects you're having, there's always somebody else who's had them as well… it reinforces and puts you at ease really to see other people have gone … through the same thing.* **Patient 7 (3 months)** *Somebody did contact us from Macmillan right at the very, very start. He went through all sort of social things like… carers allowance and things like that and that's one of the things that I got to say that we were very, very grateful for… The information was fantastic and you know lots of the sites were really really good… I think I read along from the Macmillan website because that was quite sympathetic.* **Participant 4 (2-3 months)**
Patient outlook and quality of life Psycho-social impact of treatments The psycho-social impact that some patients experienced in the first few months following treatment included disinterest or	*Things that I would have done, I am a cellist, I play cello and other things and no way completely uninterested, stopped, books and all I read stopped.* **Participant 1 (2-3 months)**

lack of energy to participate in hobbies and social activities that they had previously.	*I suppose it has affected my social life … I don't really [go out]… at the moment, I've only just started going out perhaps socially a little bit more.* **Patient 7 (3 months)** *In my previous life basically, I was able to do a bit… of online communicating with people not that I felt like chatting to them but you know, I could keep [up] with things… to be one by phoning them, or writing to them, or visiting.* **Participant 3 (2-3 months)**
Gradual improvements to quality of life Participants explained how the treatment had impacted on their quality of life overall. Their physical health post-treatment had placed restrictions and strains on their everyday routines. At times they felt they had relied heavily on their family for support with daily activities. Gradual improvements to participants' health and well-being related to readapting and regaining their capacity to participate in previous routines and social activities.	*My wife has done everything for me and is very, very protective… I think it would have been lot tougher if I had been on my own. My daughter stepped in and did all the … she moved heaven and earth to make sure that for the last three months she was available... There were days when I [said] "it's okay, let me drive" and getting back into that was a biggish step but now I'm back into driving.* **Participant 4 (6 months)** *I've seen a daily improvement, day on day something else seems to improve… I could eat things today that I couldn't eat yesterday. It's an ongoing thing but it's an onwards and upwards kind of feeling. Today I'm going to my granddaughter's birthday and tomorrow I'm going out with friends. I couldn't do that a couple of months ago… starting to get back to normal now.* **Participant 5 (3 months)** *I say we are completely together, and I have completely depended on (names wife)… I been thinking very much about this, see people on a walk, people who are old, and they have nobody at home and they have to go back to an empty house as well and that's terrible you know at the end of the day its absolutely awful and I have been much aware of this and seen this kind of and there are simply people who are by themselves… how would I have coped that it not been for the kind of relationship*. **Participant 1 (3 months)** *My middle daughter, the nurse, when I needed or didn't know what I was doing at the very beginning, she came with me to the, to the clinics and to the meetings… and asked the questions that I didn't know what to ask or wasn't aware to ask at the time*. Participant **8 (3 months)** *It's been very tiring … my wife and I, we do like to do a little bit of walking and that. I obviously haven't been able to do anything like that.* **Participant 7 (3 months)**
Adaptation and normality	

Regaining a sense of normality was important but complicated for several participants when re-adapting to life after treatment, as their daily lives had been significantly impacted by their experiences of cancer and treatment. Some participants explained that they struggled to readjust to life after treatment, due to the change in outlook that they needed to make or the extra support that they had been provided with during their trial until that point but was no longer receiving.

I think there was a feeling of… as if you were left on your own. You get that initial feeling because the 12 weeks of treatment were so intense… we were in the hospital everyday, sometimes twice a day and then you know it's off you go then. It been couple of months now rest, recuperate relax, get back to normal life and I found that quite a strange statement and I got to admit that's perhaps the hardest thing to do now was getting back to normal life. **Participant 4 (6 months)**

The days and the nights are not the same at all and you don't see people and you miss all your normal, normal things that you do certain days and certain, lose all your points (laughs). **Participant 1 (6 months)**

I have found that because we actually went in on Saturday night, the first time it was to a function, a dinner and I said "I am coming but I don't know how long I can stay" and we stayed until 12'oclock, had a really nice time and then the next day I went out again to a food… had a fabulous weekend it was really nice, to break the mould to being ill…. I probably paid for that because I had couple days where I have needed to rest a lot, you know, that's fine. **Participant 2 (3-6 months)**

I do think back fondly because you sort of make acquaintances with people… I saw the same people 5 weeks, every day of the week. We got to know each other, we got to chat, we got to talk about our cancer, we got to talk about our treatments and how tired we were. You know we got to sympathise and carers got a chance to talk to carers and have laugh and have a little fun and have a giggle and what you have been doing today, bit of gardening you know those sort of things and roaring with laughter sometimes so that's, that's how I have handled it. **Participant 4 (6 months)**

Well you got to keep cheerful. It's not… been easy. It's been bit of a struggle getting back to normality but… we getting there…. It been couple of months now rest, recuperate relax, get back to normal life and I found that quite a strange statement and I got to admit that's perhaps the hardest to do now was getting back to normal life… I am sort of getting to the point where I am starting to feel better my wife is noticing that I am feeling better … I do a little bit of help around the house and do little things… So that's the thing now getting back to normality. **Participant 4 (6 months)**

I am getting back to normality then. **Participant 7 (3 months)**

I'll tell you one thing that I don't know whether you come across this a lot, but when I went to see the consultant he told me that the cancer had gone I expected to feel quite elated, but I didn't… if anything I felt sort of a bit down and I don't know why… And, my wife felt the same as well. **Participant 7 (6 months)**

Physically, I probably feel better, I feel good, no problems… I am getting back to normal, I am really where I was before the treatment. My social life and my family life, yes, is back to where it was, it's normal, quite happy it didn't make any different after the treatment. **Participant 7 (6 months)**

Positive outlook after treatment

Several participants described how they attempted to sustain a positive outlook about their survival prospects and their circumstances overall, as a coping mechanism. Thus, being provided with adequate support and information aided their positive outlook.

Things improve on a daily basis and hopefully it will continue to improve. I don't like it (laughs)… yeah a lot (laughs), yeah but that's fine you know, there will come a day when I will be fine and I will be able to go [out] again, so I will just wait for that day. **Participant 2 (3-6 months)**

Mentally… I have got no problems at all, never had, also with treatment I didn't have any difficulties that way, I knew what was happening, I was aware of it, and all it was about just waiting for the outcome. **Participant 9 (6 months)**

We are not doom mongers… I don't particularly think it will [be] good, it will [be] bad. It will be as it is. I really don't think I am bothered in that sort of sense at all what's going to happen. It's just a treatment. **Participant 1 (2-3 months)**

I… try to keep healthy, try to keep active you know and I also try to have a very positive outlook ... I think that's the huge thing during the situation is to be positive, to be hopeful. I constantly say to people I have not got the time to worry, I haven't got the energy to worry. I need all my energy now to look after myself to get better. Its pointless panicking, its pointless crying, its pointless breaking down and saying what if and why and I think a big part was accepting that, yes I got cancer, yes I going to have to go through the treatment… I think a lot of the stories about the treatment were horrendous. I haven't felt that as yet. **Participant 4 (2-3 months)**

I feel a lot better. Obviously the time I was diagnosed it was a bit of a bolt out of the blue and I was left you know in big, big shock. So, the fact that they've now said to me that the cancer's gone, it's obviously a huge relief. **Participant 7 (6 months)**

Impact of COVID-19 pandemic

Vulnerability and isolation

Some participants reflected on how the pandemic may have intensified the sense of isolation and stress that other patients felt during their treatment process, although these participants did not feel personally affected in this way.	*When you were sat in radiotherapy and chemo, some people probably needed somebody with them in chemo, I didn't… but there were people that were a lot sicker than I was I suppose pre- Covid you could have a friend with you to keep you company through the day*. **Participant 8 (3 months)** *It's not nice sometimes when you've got to go through things on your own, where you like having your partner sitting outside the door, but I don't think it's affected my treatment.* **Participant 6 (3 months)** *When we were filling in the clinic surveys… isolation wouldn't have been isolation if it hadn't have been for Covid… Covid had an influence on everything… From times of clinic, to staff levels to… it was an influence on everything.* **Participant 8 (3 months)**
The pandemic caused an increased sense of vulnerability and cautiousness amongst cancer patients. However, the comprehensive social restrictions put into place for infection control, and the vaccination programme at times, eased the sense that some of these participants missed out on their usual social activities.	*I haven't been out since the beginning of Covid… it's been isolation the way… if everybody else wouldn't have been in isolation as well, I suppose it would've affected me more, but because everybody else was in isolation… I don't suppose it bothered me that much, no, I was quite comfy that everybody else was stuck in as well*. **Participant 8 (3 months)** *Everybody's been really cautious around me; you know any family members that were coming here were doing lateral flow tests before. And, I still wear a mask wherever I go… we went away on holiday other people weren't wearing masks, when they were going to the bars or the restaurants, but I was. There is a bit of anxiety, but I'm double vaccinated. I still go to shops and stuff but I do get a bit of a rumbly tummy if I'm around people and they've not got masks on.* **Participant 6 (6 months)** *I've read … which could have made me more vulnerable to Covid, to counter that … I had my two vaccines … quite quickly because… of the cancer I've had, so that most probably countered that bit … the stress of that … against catching the Covid.* **Participant 7 (3 months)** *You've gotta wear masks and things like that… So, obviously you couldn't go out as much… Whilst you're going through treatment I didn't wanna go anywhere anyway, so the… Coronavirus didn't affect me, very, very little.* **Participant 7 (6 months)**
Potential Improvements	
Sharing information among peers Opportunities for participants and their caregivers to share information regarding	*I think there should be opportunities where people that have been through [cancer treatment]… share maybe positive experiences, can also point people in the direction you know? ... I think there is an*

their experiences of cancer and their treatment pathway through peer support networks were suggested as a means of improving patient knolwedge.

Follow up information

Follow up information regarding the participants' current cancer status, as well as results from the trial, were desired by a participant, who felt that they were unsure about their personal outcomes or how this related to the wider trial.

opportunity there maybe a support network of people's needs, need to be arranged. **Participant 4 (6 months)**

Did they tell me it was a 70/60 chance… they said to me they can burn it away… if it's not burnt away why not, you know what I mean? I think it should be followed up and I suppose my question to follow onto that would be, would we, the participants be able to see the outcome of your survey? **Participant 8 (3 months)**

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TITLE PAGE

The experiences of patients with oesophageal cancer receiving chemoradiotherapy treatment: a qualitative study embedded in the SCOPE2 trial.

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Abstract

Objectives

This qualitative study explored patients' experiences and perceptions of the SCOPE2 trial. SCOPE2 studied radiotherapy dose escalation in patients with inoperable oesophageal cancer treated with dCRT definitive chemotherapy.

Setting

Recruitment at five clinical sites in England and Wales, UK.

Participants

SCOPE2 trial participants, were invited to take part in interviews from across five clinical sites. Participants self-selected to take part in up to three interviews across four different time points: baseline (before treatment) and at 2-3 months, 3-6 months or 6 months+ after baseline. There were five female and five male interview participants.

Interventions

Participants were randomised to standard dose dCRT prescribed carboplatin/paclitaxel or cisplatin/capecitabine, or an escalated dose dCRT prescribed carboplatin /paclitaxel or cisplatin/capecitabine.

Methods

This qualitative study used semi-structured longitudinal interviews to explore the impact of treatment, patient outlook and quality of life and the impact of the COVID-19 pandemic. Interview data were thematically analysed.

Results

Ten patients participated in 16 longitudinal interviews. Three participants were accompanied by companions. Participants experienced side-effects from radiotherapy and chemotherapy including nausea, throat pain, difficulties eating and regaining appetite, thrombosis and fatigue, although most of these symptoms gradually improved. Participants required more ongoing information and support regarding treatment side-effects, and cancer status in order to improve their overall quality of life. Best practice examples involved key contacts providing practical advice and signposting support.

Conclusion

Participants of the SCOPE2 trial reported short and longer-term side-effects from chemoradiotherapy, but these usually lessened over time. Participants attempted to be positive about their survival prospects by readjusting their expectations, priorities and lifestyles. Providing patients with ongoing opportunities to discuss detailed and timely information regarding treatment side-effects, aftercare and cancer status could improve the overall health and wellbeing of patients during oesophageal cancer trials and pathways.

Article Summary

Strengths and limitations of this study

- This study highlighted patients' ongoing trial and treatment experiences and the opportunity to inform trial conduct through longitudinal interviews.
- Semi-structured interviews provided rich data regarding patient experience before and during the Covid-19 pandemic, across different time points from participants across a range of age groups and genders.
- Recruitment to this qualitative study was slow and the small numbers of participants recruited restricted the breadth of experiences explored across different trial arms and the additional impact of higher dose of radiotherapy on patients.
- Lack of integration of qualitative study into the main trial recruitment limited opportunities for participant recruitment.
- Participants were self-selecting for interview, and needed to be well enough to be interviewed, thereby introducing a level of participant bias.

The experiences of patients with oesophageal cancer receiving chemoradiotherapy treatment: a qualitative study embedded in the SCOPE2 trial.

BACKGROUND

Oesophageal cancer (OC) has a relatively poor prognosis, as curative surgery is appropriate for only around 20% of the patient population (1) (2). Definitive chemoradiotherapy dCRT is offered as an alternative for patients who are unsuitable for surgery and is considered more effective than radiotherapy or chemotherapy alone(3). However, despite improved survival outcomes anticancer treatments may cause toxicities (4) and thus further diminish the patient's quality of life. (5)

The SCOPE2 trial builds on the SCOPE1 phase 2/3 trial (2013) which highlighted the survival and long-term toxicity benefits of standard dCRT, as well as improved quality of life (6). However, SCOPE1 did not capture the experiences of the trial or treatments from the patients' perspectives. Subsequently, the SCOPE2 trial embedded a qualitative component which examined real-time experiences of a subgroup of trial participants.

SCOPE2 is a randomised Phase 2/3 trial for locally advanced non-metastatic oesophageal cancer patients. It examines radiotherapy dose escalation (standard dose of 50GY versus high dose of 60GY) and the effects of standard chemotherapy drugs (cisplatin and capecitabine, or carboplatin and paclitaxel). All patients were randomised in to one of four arms. Additionally, it embedded a Phase 2 trial whereby patients who had not responded to the first two weeks of chemotherapy (as assessed by a second a positron emission tomography (PET) scan) could be randomised to either continue this chemotherapy regimen or switch to alternative one (7).

Previous qualitative studies embedded into cancer trials have provided in-depth insights into the experiences of patients with cancer relating to trial processes, their treatments, and their recovery (8) (9). In an OC trial (ROCS), real-time reporting of patient perspectives prompted trial amendments to increase recruitment and highlighted existential concerns around the issues of physical and social eating, along with the burden of side-effects of radiotherapy and hospital appointments (9). In ROCS, patients were randomised to receive a stent or a stent plus radiotherapy. Those who received chemoradiotherapy treatment experienced longer-term toxicity and a high symptom burden including dysphagia, lack of appetite, fatigue, dyspnoea (difficulty breathing) and pain, having a significant impact on physical functioning and quality of life.

This qualitative study was integrated within the SCOPE2 trial to provide an in-depth understanding of a sub-set of patients' and their companions' first-hand experiences of the demands of the trial and treatments, which are not captured through other trial data. The ongoing needs of participants were reported to the trial team with the aim of informing practice.

Aims

The aim of the qualitative component of the SCOPE2 trial was to explore patients' experiences of chemoradiotherapy and perceptions of participating in the trial. SCOPE2 escalated definitive chemoradiotherapy dCRT compared with standard dose, and of the two drug regimens based on the outcomes of PET scans.

Objectives:

1. To assess patient experience and perceptions of each dCRT arm of the trial.
2. To consider how participants' views change over time spent on treatment.
3. To examine the personal impact of treatment on participants' health and wellbeing.

Qualitative findings discussing the trial conduct, recruitment, and reasons for declining the trial are available in a full qualitative report, available on request.

METHODOLOGY

Study Design

This was a multicentre, longitudinal qualitative study of a sample of clinical trial self-selecting participants with potentially curable OC. Qualitative methods were chosen to explore the nuanced and individual experiences of participants.

Public and Patient Involvement

The trial was overseen by a Trial Management Group which included two patient representatives known as Research Partners recruited through the Involving People Network (10) The research partners provided review and input into assessments of trial documentation, in particular patient facing documents, assisted with Scientific Milestone Reports, and contributed to TMG meetings. A PPI representative also reviewed final qualitative summary findings.

Ethics approval statement

SCOPE2 has full ethical approval from Wales Research Ethics Committee 3 (dated 22nd January 2016, with subsequent approval of each amendment; REC reference 15/WA/0395) and is conducted in accordance with The Medicines for Human Use (Clinical Trials) Regulations 2004 (SI2004/1031) and subsequent amendments, and the Declaration of Helsinki 1996. Written informed consent has been obtained from all study participants, with separate consent obtained for participants in the Qualitative interview study.

Recruitment

The qualitative study took place between July 2017 and December 2021. Due to the Covid-19 pandemic the trial was closed to recruitment between March and August 2020 and the qualitative study between March and October 2020. The main trial began in 2016 completed recruitment December 2023 and closed in February 2024.

SCOPE2 trial participants were invited to take part in interviews from across five clinical sites (hospitals) in England and Wales, which had signed up to the qualitative study. Potential participants were informed of the optional qualitative interview study at the point of consent into the main trial or at any point during the following 24 months after recruitment to the main trial. Initially, patients were invited for interviews up to six months after baseline, but due to slow recruitment ethical approval was obtained to expand the timescale for recruitment to interviews up to 24 months after baseline. This coincides with trial follow up periods. Patients were provided with a qualitative study patient information sheet (PIS) and consent was obtained once the patient had sufficient time to review the PIS. The qualitative study team were informed of the patient's contact details via secure email if patients provided written consent. Otherwise, patients provided their contact details to the qualitative team using a reply slip and a stamped addressed envelope. The qualitative

researchers contacted trial participants directly to arrange an interview and requested signed consent at the time of interview (face to face or via post). Participants were offered the opportunity to ask any questions before consenting. Companions who accompanied patients during interviews provided written consent, in order to capture additional information that they discussed. All consent forms were held securely by the qualitative research team. Each participant was invited to participate in a maximum of three interviews and were not offered payment.

Patients eligible for the trial who chose not to consent, were also invited to participate as non-consenters in the qualitative study, to explore their experiences of being invited to take to the SCOPE2 trial. The results of these interviews are not discussed in this paper, as they focus on trial conduct but are available in the qualitative report.

An initial sample size of 24-40 participants (6-10 per arm) was based on researcher judgement and theoretical saturation (11). However, due to time and financial limitations, the qualitative study finalised data collection in 2021. Barriers to recruitment are discussed in the limitations section and are more fully discussed in the qualitative report.

Data collection

The qualitative researchers conducted semi-structured interviews. These researchers have experience in thematic analysis, as well as interviewing participants concerning sensitive subjects including cancer. They collected and analysed the data through a critical lens of researchers working outside the main trial team and focused on understanding the lived experience of participants.

Interviews were conducted face to face at participant's homes or at the hospital before social restrictions were imposed in March 2020 due to the Covid pandemic, and by telephone thereafter. Participants were invited to be interviewed up to three times across four different time points: baseline (consent to the trial before treatment), 2-3 months, 3-6 months, or 6 months+ after baseline. This reflected the key time points in the trial before, during and after treatment. Demographic information was collected and is reported descriptively but was not used as sampling criteria.

Before contacting participants for initial or follow up interviews, the qualitative researcher consulted the site's nurse to confirm that the patients remained in the trial and were well enough to be interviewed. Due to the short timeframe between recruitment and treatment, or consent processes, it was not always possible to interview all participants at baseline, in these instances participants were asked to recall their experiences of trial recruitment in later interviews.

A semi-structured interview schedule was used to ensure a degree of consistency across the interviews, whilst still allowing for information to be elicited iteratively as interviews progressed (Supplement 1). A revised version of the interview schedule (v.30, Protocol 7.0) was used after February 2021, which included questions regarding the impact of Covid-19 on the participants' experiences (Supplement 2). These schedules include questions for participants at baseline and another set for those after treatment. Guide questions were tailored appropriately to each timepoint. Questions relating to this article are highlighted in interview schedule supplements. Topics covered in the interviews, in line with the aims above included:

- Impact of treatment on physical function, health and wellbeing.
- Personal needs and expectations.
- Patients' and their companions' perceptions of the trial and their future aspirations.

Interviews were audio recorded and transcribed verbatim by members of the team or an external transcription company.

Data Analysis

Longitudinal interviews were used to provide opportunities to gain an understanding of the patient's experience over time and draw attention to the processes and factors that influence change for the patient at different time points (12). This qualitative study does not aim to be fully generalisable but to provide in-depth insights into patient experiences of chemoradiotherapy. Data were analysed thematically (13)(Braun & Clarke, 2012). This analysis was an iterative process, involving inductive coding and interpretating data separately, then jointly identifying concepts and developing codes. The main researcher coded all data using the NVivo 12 software program, with 20% double-coded transcripts by the other researcher to ensure rigour. The researchers jointly developed a framework for analysis, through a process of cross-checking and deliberation of themes. Themes were generated, reviewed and categorised into key themes and sub-themes.

Additional details about how this study was conducted are available in the COREQ checklist supplement 3.

RESULTS

Participants characteristics

Ten participants took part in a total of sixteen longitudinal interviews (Table 1). There were five female and five male interview participants, and three participants were accompanied by companions. The age range was 57-82 years and mean age was 70 years old. Five participants received the second PET scan (as part of the PET sub-study) while five did not receive this second scan (Table 1).

Participants were interviewed from across all four treatment arms of the trial: standard dose dCRT prescribed carboplatin/paclitaxel (Arm 1); standard dose dCRT prescribed cisplatin/capecitabine (Arm 2); escalated dose dCRT prescribed carboplatin /paclitaxel (Arm 3); and escalated dose dCRT prescribed cisplatin/capecitabine (Arm 4) (Table 2). All interviews were conducted within seven months after baseline. Chemoradiotherapy was completed within twelve weeks.

Table 1: Number of participants interviewed pre and post pandemic.

Data collection period	Number of participants interviewed	Number of Interviews
Pre-March 2020 (In-person interviews prior to Covid-19 pandemic)	4	7
Post-October 2020 (Telephone interviews after qualitative study suspension from March 2020 to October 2020 due to Covid-19 pandemic)	6	9
Total	10	16

Table 2: Participants' information and interviews

Participant	Arm	Companion accompanied	Second PET scan at day 14	Baseline interview	Between 2- 3 months after baseline	3-6 months after baseline	6 months+ after baseline
P 1	2	X			✓	✓	
P 2	2		X			✓	
P 3	1	X	X		✓		
P 4	1				✓	✓	✓
P 5	1					✓	
P 6	4			✓		✓	✓
P 7	2		X			✓	✓
P 8	3		X			✓	
P 9	2		X				✓
P 10	4	X		✓			

Qualitative findings

The experiences of participants were captured throughout the trial, which highlighted changes at different time points in participants' perspectives, and the impact of treatment regimens on quality of life, including daily, family and social life (14) (15). The following results highlight the findings from the interviews, relating to the following key themes: impact of treatments; treatment impact over time, patient outlook and quality of life, and impact of Covid-19. A hierarchy of themes and subthemes are presented in Table 3. A discussion of these findings is outlined below, with illustrative quotations. A comprehensive outline of all relevant quotations is available in Supplement 4.

Table 3: Themes

Themes	Subthemes	Secondary subtheme
Experiences of treatment	Impact of treatment	

	Side-effects from treatments	Side-effects from chemotherapy Side-effects from radiotherapy
	Recovery after chemoradiotherapy	
Treatment impact over time	Information and support needs after treatment	
Patient outlook and quality of life after treatments	Psycho-social impact Gradual improvements to quality of life Adaptation and normality Positive outlook after treatment	
Impact of Covid-19	Vulnerability and isolation	

Experiences of treatment

Participants described the impact of receiving the treatment (radiotherapy and chemotherapy) including side-effects, and improvements to health. They emphasised how information provision and support from clinical trial and NHS staff before, during and after their treatments impacted on their overall psychological, as well as physical wellbeing.

Impact of treatment

Initial chemoradiotherapy and support provided by clinical teams earlier in the trial were described as having resulted in small improvements for some participants' cancer symptoms. These cancer symptoms mainly related to difficulties eating.

> When I started, I had difficulty swallowing obviously with the oesophagus tumour and it was sort of every meal, every few mouthfuls were getting difficult and I found in about two weeks into the first cycle, I was pretty much able to swallow normally. So, something positive is happening'. **Participant 4 (2-3 months)**

> I had a tube fitted in my arm yesterday, ready for the chemo on Friday, and I've got a feeding tube, so I don't have to worry about not getting enough nutrition in, so I think a lot of worries I had at the beginning have faded. **Participant 6 (Baseline)**

Side-effects from treatments

Participants experienced short and longer-term side-effects from the trial treatments including pain, dysphagia, tiredness, and thrombosis. Several participants experienced multiple side-effects including pain and fatigue, or general degradation in their health, although most participants felt that these subsided over time.

> During the 1st cycle … the pain in my feet and little bit sort of pins and needles like that, I think that's the worst side effect that I have experienced... Tiredness, you know, I just feel worn out… the other thing that I get is almost like fatigue in my thighs… I think one day where I felt sick which is [from] just cleaning my teeth. **Participant 4 (Baseline)**

Side-effects from chemotherapy

Participants described common side-effects they experienced after receiving chemotherapy including muscular fatigue, pain, and neuropathy in their feet. While most of these were expected, they were at times unprepared for certain symptoms.

> The side effects I've I had are quite sore feet at one stage when I was on the chemotherapy, which was difficulty walking. **Participant 7 (3 months)**

> Cos everybody expected when I stopped the chemo, especially me. I thought that was it (laughs), you know stop the chemo and that's fine. And, then I stopped the chemo, and I got ill (laughs). **Patient 6 (6 month)**

Four patients reported that during the trial their chemotherapy treatment had been changed or stopped due to pre-existing conditions, side-effects that they had experienced or that the treatment was not positively affecting their cancer outcomes. Two patients' experiences of these chemotherapy switches are described below. This demonstrates the complexities patients and clinicians may face when weighing up the side-effects of different chemotherapy regimens.

> I found the capecitabine taking those every day I think they were the hardest of the drugs that I was taking… I did notice with them the nausea and the sickness, and the fatigue was massive. When, they put me on [another chemotherapy drug] … I felt it was much gentler… unfortunate[ly] for me… having a blood clot… I think that was the worst thing… the blood clot was harder to recover from than the cancer (laughs)'. **Participant 4 (3 months)**

> The first chemo I was on, they had to change... I've got… Neuropathy… So, they changed it. And another one was because of my kidneys. They changed that to a different one right at the very beginning. **Participant 5 (3 months)**

Side-effects from radiotherapy

The experience of receiving radiotherapy was reported by most participants as being physically and psychologically arduous. Difficulty and pain swallowing experienced after radiotherapy were the main side-effects described by several participants.

> Because of what the radiotherapy does, it sort of burns all the inside and it's very difficult to swallow… but that was the worst thing to be perfectly honest with you, the thing is I would like to able to eat like I used to, but at the moment I can't but I am getting there… definitely tons better now. **Participant 2 (2- 3 months)**

> With the radiotherapy… I was completely and utterly flat out, nothing mattered at all... You can't win it at any point… you can't concentrate or want anything, you feel bad if there is no pain, nevertheless you feel dreadful. **Participant 1 (6 months)**

Recovery after chemoradiotherapy

After the completion of chemoradiotherapy, during the recovery period, participants experienced symptoms which ranged from mild to severe, having physical and psychological outcomes. Nausea, as well as fluctuations in appetite, weight and energy levels were reported by participants, often relating to pain and issues swallowing.

> I lost my appetite a bit, but … that's come back now, and … I am starting to regain weight… I still have problems digesting food … some foods just get stuck in my oesophagus, and that is still a little bit painful. **Participant 7 (3 months)**

Some participants recalled having to adapt to the fatigue caused by difficulty sleeping and pneumonia. Participants' symptoms tended to lessen over time, and when they had received support to reduce these symptoms from clinical services, they usually recalled noticeable improvements. Post-chemotherapy issues relating to bowel function included constipation and diarrhoea. Other symptoms were also reported including low immunity and hair loss.

> I had pneumonia… I started with the infection as soon as I finished the chemo… I was in hospital for a week. And, I had about four different courses of antibiotics and they just weren't working on the pneumonia. And I felt worse with that than I had been through all the treatment. And I was just starting to get better before we went away… within days I suddenly was much, much, much better. **Participants 6 (6 months)**

> I had trouble sleeping for quite some time and that has sorted itself out now and can sleep perfectly well now without any paracetamol at all, so night-time is good. **Participant 1 (2-3 months)**

It was not always possible to differentiate between the impact of chemotherapy or radiotherapy treatments, as participants described their symptoms more generally and did not necessarily attribute them to individual treatments.

Treatment impact over time

Participants reflected on their cancer treatment journey and how their symptoms had changed over time, including facing adversity throughout treatment regimens and gradual improvements.

> At the time during the treatment … I've felt really, really, really ill, worse than before I started the treatment… The treatment was tough… I have [had] a lot of symptoms, side-effects from it. But those have finished now, so obviously things are improving… when it finished, I was having problems… but each day I'm getting better. **Participant 5 (3 months)**

> I'm just feeling better every day and my eating is improving all the time. **Participant 6 (6 months)**

Information and support needs after treatment

Concerns were raised by several participants and their companions regarding what would happen post-treatment, as they felt that there was less information and support available than before and during their treatment. Participants expressed a need for further and more timely information and updates from healthcare professionals regarding potential side-effects, including recovery timescales post-treatment.

> We actually felt that we have huge information on side effects during treatment but virtually nothing on after [treatment]. **Companion of Participants 1 (2-3 months)**

> Patient: No interest at all in checking my general condition which could have changed because of the treatment …
>
> Companion: And you just hope that all the drugs are compatible…
>
> They all interact with each other and that is another hurdle. Who knows?...

Patient: It's thousands of, it's thousands of trials. How can you do it, interaction of drugs is a massive problem being tackled all the time. **Participant 1 (2-3 months).**

Participants described difficulties with eating and dietary needs and expressed the importance of being provided with relevant information from clinicians regarding how the disease or treatments impacted on these fundamental needs.

One thing that I asked all along was really about how much I could eat, we have been asking, haven't we? You sort of [know] it is going to get more difficult, is my throat going to be smaller, will it get bigger again, how much will I be able to eat? Will I be able to eat properly at the end and I think that all out questions have been like that.

Participant 3 (2-3 months)

Several participants described the high level of personal support from clinical and third sector services, including key workers, which made a significant impact on their trial and treatment experience. They described the support and information they received relating to their quality of life and practical needs.

I have phone calls from the clinical nurse [key worker] … sometimes just to ask how I am, he's helped to make appointments for me when I've had problems making them myself. And he's managed to make everything seamless from one thing to another, which I greatly appreciated, because I was a bit all over the place, especially at the beginning of diagnosis… if [clinical nurse] thought that maybe I wasn't getting something, that the Oncologist was saying to me… maybe sometimes I was lacking a

bit of understanding and he always made sure that I left that room, understanding everything. **Patient 6 (3 months)**

The medical staff have really been great, and ... I've got all the information … all I need to do is pick the phone up and I know I can speak to somebody with any questions … I have been in contact and … am on various forums with Macmillan, … which … my wife and I have accessed quite frequently … just to view other peoples' experiences, which has been good, because obviously whatever side effects you're having, there's always somebody else who's had them as well… it reinforces and puts you at ease really to see other people have gone … through the same thing. **Patient 7 (3 months)**

Patient outlook and quality of life after treatments

Psycho-social impact of treatments

In the first few months during and post-chemoradiotherapy patients described the psycho-social impact of treatment. This included disinterest or lack of energy to participate in previously enjoyed hobbies and social activities.

Things that I would have done, I am a cellist, I play cello and other things and no way completely uninterested, stopped, books and all I read stopped. **Participant 1 (2-3 months)**

Gradual improvements to quality of life

Participants explained how the treatment had impacted on their quality of life. Most participants experienced gradual improvements to their health and well-being. This related to regaining their capacity to participate in previous routines and social activities. However, they also felt that their physical health post-treatment had placed restrictions and strains on their everyday routines. Some felt they had relied heavily on their family for support with daily activities.

> My wife has done everything for me and is very, very protective… I do think it would have been lot tougher if I had been on my own. My daughter stepped in and did all the work… she moved heaven and earth to make sure that for the last three months she was available... There were days when I [said] "it's okay, let me drive" and getting back into that was *a biggish step but now I am back into driving.* **Participant 4 (6 months)**

Adaptation and normality

Regaining a sense of normality was important but complicated for some participants when re-adapting to life after treatment, as their daily lives had been significantly impacted by their experiences of cancer and treatment. Several participants explained that they struggled to readjust to life after treatment, due to the change in outlook that they needed to make, or the extra support that they had received on the trial, which was no longer available.

> I think there was a feeling of… as if you were left on your own. You get that initial feeling because the 12 weeks of treatment were so intense… we were in the hospital everyday, sometimes twice a day and then you know it's off you go then. It been

couple of months now rest, recuperate relax, get back to normal life and I found that quite a strange statement and I got to admit that's perhaps the hardest thing to do now was getting back to normal life**. Participant 4 (6 months)**

Positive outlook after treatment

Several participants described how they attempted to sustain a positive outlook about their survival prospects and their circumstances overall. Thus, being provided with adequate support and updated information aided their positive outlook.

Things improve on a daily basis and hopefully it will continue to improve. I don't like it (laughs)… a lot (laughs), yeah but that's fine you know, there will come a day when it will be fine and I will be able to go [out] again, so I will just wait for that day. **Participant 2 (3-6 months)**

I feel a lot better. Obviously, the time I was diagnosed it was a bit of a bolt out of the blue and I was left you know in big, big shock. So, the fact that they've now said to me that the cancer's gone, it's obviously a huge relief. **Participant 7 (6 months)**

Impact of the Covid-19 pandemic

Vulnerability and isolation

Some participants reflected on how the pandemic may have intensified the sense of isolation and stress that other patients felt during their treatment process, although these participants did not feel personally affected in this way.

> When you were sat in radiotherapy and chemo, some people probably needed somebody with them in chemo, I didn't… but there were people that were a lot sicker than I was I suppose. Pre- Covid you could have a friend with you to keep you company through the day. **Participant 8 (3 months)**

> When we were filling in the clinic surveys… isolation wouldn't have been isolation if it hadn't had been for Covid… Covid had an influence on everything… From times of clinics to staff levels… it was an influence on everything. **Participant 8 (3 months)**

The pandemic caused an increased sense of vulnerability and cautiousness amongst these patients. However, the comprehensive social restrictions put into place for infection control, and the vaccination programme at times allayed some of their fears and eased the sense that these participants missed out on their usual social activities.

> I haven't been out since the beginning of Covid… it's been isolation all the way… if everybody else wouldn't have been in isolation as well, I suppose it would've affected me more but because everybody else was in isolation. **Participant 8 (3 months)**

> I've read … which could have made me more vulnerable to Covid… to counter that … I had my two vaccines … quite quickly because… of the cancer I've had, so that most probably countered that bit … the stress of that … against catching the Covid. **Participant 7 (3 months)**

DISCUSSION

Main Findings

This qualitative study captured the experiences and perceptions of SCOPE2 trial participants, using longitudinal interviews. These interviews highlighted participants' practical, physical, and psychosocial needs at different time points. Participants described expected and unexpected side-effects from the radiotherapy and the chemotherapy schedules at different time points, although most of these symptoms lessened over time. Participants attempted to be positive about their survival prospects and applied coping strategies by readjusting their expectations and priorities, focusing on regaining a sense of 'normality'. The need for improved information and communication regarding the longer-term side-effects of chemoradiotherapy, aftercare, and cancer status was highlighted as necessary to improve overall patient experience and quality of life. (16)(17)

Comparison with the existing literature

Consistent with earlier qualitative studies, participants in this qualitative study experienced varying side-effects from the chemoradiotherapy treatments across the trial arms, which ranged from mild to severe. Shorter-term symptoms included pneumonia, fatigue, difficulty sleeping and pain swallowing, reflect symptoms reported more generally among oesophageal cancer patients (16). Gastrointestinal effects were also reported, including nausea, satiety and diarrhoea, poor appetite, and weight loss, reflecting side-effects after surgery reported in other studies (17)(18). Due to the low number of participants in this qualitative study, it was not possible to differentiate the impact that each treatment arm or PET scan had on the participants. However, the side-effects reported do reflect those expected for this group of participants, the number of cases relating to chemoradiotherapy

are reported in more detail in the SCOPE2 PET paper and will be available in the SCOPE2 trial findings. (19)

Participants' perceptions of their treatment and side-effects changed over time and they attempted to be positive about their survival prospects by readjusting their expectations and priorities, as reported in previous studies (20). Similar coping strategies and approaches to resilience and adaptation have been identified in studies that highlight the changing emotions that patients deal with when facing the uncertainties of life-threatening illnesses (21)(22). As reported in prior research findings, participants reflected on the importance of regaining a sense of 'normality', as their daily lives had been significantly disrupted by the cancer and its treatment, but for the most part were improving over a period of months. (23) (24).

Participants described varying levels of uncertainty and a lack of knowledge regarding potential longer-term side-effects from treatment. This reflects previous research findings illustrating the need to provide timely and appropriate patient communication and information, particularly relating to treatment aftercare, which can reduce anxiety and increase patients' well-being and their sense of agency (16,17,25). In contrast, best practice examples were described as key contacts organising appointments and providing signposting to appropriate information, (26) which reduced psychological and physical burdens on the participants during a time when they were acutely ill.

These findings illustrate how the Covid-19 pandemic had varying effects on participants when receiving cancer treatment. Some participants felt that due to social restrictions the impact on their social activities was less than it usually would have been pre-pandemic. Conversely, others felt a heightened sense of social isolation and reduced opportunities for

peer support, as previously reported in studies of patients with cancer during the pandemic (27,28).

Strengths and limitations compared with other studies.

This longitudinal qualitative research provided nuanced in-depth insights into participants' perceptions and experiences of the trial and impact of chemoradiotherapy before and during the Covid-19 pandemic. These insights are not comprehensively captured through other types of data collection (quantitative and clinical data) (29). Using longitudinal interviews has also informed the trial team of patients' ongoing information and support needs. However, recruitment to this qualitative study was slow and the relatively small numbers of participants recruited restricted data saturation. This particularly impacted the breadth of experiences explored across different trial arms and the ability to understand the additional impact of higher dose of radiotherapy on patients. These low numbers meant it was not possible to fully assess patient experience and perceptions of each dCRT arm of the trial. Recruitment to the qualitative study was delayed pre and post pandemic, as permissions to recruit to the qualitative element were granted separately to the main trial.

Although, the qualitative study was considered embedded in the overall trial, recruitment was not fully integrated, as trial and qualitative study participants were consented at different times. This increased the time, and resources required for qualitative recruitment. Additional barriers limiting recruitment included lack of available staff for recruitment, the health of participants and delays due to the Covid-19 pandemic. In contrast some quantitative (30)or combined qualitative and quantitative studies (31) which examined patients' experiences or quality of life after oesophageal cancer treatment recruited higher

numbers of participants. These were able to compare the broader range of patients' experiences of chemoradiotherapy. Nonetheless, these studies did not explore the depth and range of trial and treatment experiences through qualitative data collection.

Implications for policy makers and future research

OC clinical pathways need to provide opportunities for patients to discuss, revisit information and ask questions before, during and after their treatments, in order to enhance patient satisfaction with their trial, treatment and recovery experiences. Consistent signposting to charities and peer support could also enable patients to access relevant and timely support. Future trials and pathways should ensure ongoing access to support through the provision of a key contact for the patient. Sharing updates regarding the progress of the trial where possible, would also be useful for participants. A more integrated approach to qualitative studies embedded in trials including incorporating real-time reporting in future trials could provide improved opportunities for recruitment and patient experience.

CONCLUSION

Qualitative study participants of the SCOPE2 trial were generally positive about the impact of their treatments and recovery experiences, despite experiencing a range of side-effects, some of which were unexpected. Future trials and cancer services should consider patients' needs for ongoing information and support regarding treatment aftercare, longer-term side-effects, and cancer status to improve their overall health and wellbeing.

Contribution Statement

TC Chief Investigator responsible for overall trial design and oversight of study progress.

AN designed and oversaw qualitative evaluation.

ML oversaw the qualitative study.

DHH drafted the results and manuscript.

DH-H & ML collected and analysed qualitative data.

SB was the study manager and contributed to trial study design, qualitative recruitment and quantitative data.

LN contributed to trial study design, study management (including study documentation) and monitoring oversight.

MH contributed to the trial design.

TC is responsible for the overall content [as guarantor].

All authors contributed to revisions of the manuscript and approved the final version.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Data availability statement

The data that support the findings of this study are available on request from the corresponding author. Personal data are not publicly available due to privacy or ethical restrictions.

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Trial Registration

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Supplement 1

Consolidated criteria for reporting qualitative studies (COREQ): 32-item checklist

No	Item	Guide questions/description
Domain 1: Research team and reflexivity		
Personal Characteristics		
1.	Interviewer/facilitator	Which author/s conducted the interview or focus group? Dr Daniella Holland-Hart Dr Mirella Longo
2.	Credentials	What were the researcher's credentials? *E.g. PhD, MD* PhD
3.	Occupation	What was their occupation at the time of the study? Research Associate, Cardiff University
4.	Gender	Was the researcher male or female? Female
5.	Experience and training	What experience or training did the researcher have? All researchers hold extensive expertise in doing interviews. They all hold an updated GCP certificate and NVivo training and hold PhD's.
Relationship with participants		
6.	Relationship established	Was a relationship established prior to study commencement? No relationship but the researchers used their research experience and training to introduce the research study and mitigate the asymmetry of information between the two parties.

No	Item	Guide questions/description
7.	Participant knowledge of the interviewer	What did the participants know about the researcher? e.*g. personal goals, reasons for doing the research* Reasons for doing the research
8.	Interviewer characteristics	What characteristics were reported about the interviewer/facilitator? e.g. *Bias, assumptions, reasons and interests in the research topic* Research expertise
Domain 2: study design		
Theoretical framework		
9.	Methodological orientation and Theory	What methodological orientation was stated to underpin the study? *e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis* Thematic analysis, the conceptual thematic framework used in the study is described in the methodology section.
Participant selection		
10.	Sampling	How were participants selected? *e.g. purposive, convenience, consecutive, snowball* The sample were self-selecting.
11.	Method of approach	How were participants approached? e.*g. face-to-face, telephone, mail, email* Face to face through the research nurse. Then via phone from the researchers.
12.	Sample size	How many participants were in the study? 10
13.	Non-participation	How many people refused to participate or dropped out? Reasons? One patient was too unwell to participate in interviews after consenting.

No	Item	Guide questions/description
Setting		
14.	Setting of data collection	Where was the data collected? e.*g. home, clinic, workplace* At home or via telephone.
15.	Presence of non-participants	Was anyone else present besides the participants and researchers? Companions were present in some interviews.
16.	Description of sample	What are the important characteristics of the sample? *e.g. demographic data, date* Gender, age.
Data collection		
17.	Interview guide	Were questions, prompts, guides provided by the authors? Was it pilot tested? Interview schedules included prompts, which were tested by a senior qualitative researcher (AN).
18.	Repeat interviews	Were repeat interviews carried out? If yes, how many? No repeat interviews were carried out but follow up interviews were carried out.
19.	Audio/visual recording	Did the research use audio or visual recording to collect the data? All interviews were audio recorded.
20.	Field notes	Were field notes made during and/or after the interview or focus group? Field notes were not made during the interviews.
21.	Duration	What was the duration of the interviews or focus group? Mean average 44 minutes
22.	Data saturation	Was data saturation discussed? Yes, this was discussed within the team. However, we were unable to reach

No	Item	Guide questions/description
		saturation due to the limited number of interviews.
23.	Transcripts returned	Were transcripts returned to participants for comment and/or correction? No this was not done.
Domain 3: analysis and findings		
Data analysis		
24.	Number of data coders	How many data coders coded the data? 2 data coders (DHH) and (ML)
25.	Description of the coding tree	Did authors provide a description of the coding tree? A coding tree is available but not described in the paper. However, the main themes and sub-themes are outlined in Table 4.
26.	Derivation of themes	Were themes identified in advance or derived from the data? Derived from the data itself.
27.	Software	What software, if applicable, was used to manage the data? NVivo 12
28.	Participant checking	Did participants provide feedback on the findings? The patients did not comment but were offered a summary of findings.
Reporting		
29.	Quotations presented	Were participant quotations presented to illustrate the themes / findings? Was each quotation identified? e.*g. participant number* All main themes were illustrated by quotes. The patients are identified by a

No	Item	Guide questions/description
		number and at what stage the interview took place.
30.	Data and findings consistent	Was there consistency between the data presented and the findings? All main themes were illustrated by quotes, supplementary materials provide further evidence of these points and consistency.
31.	Clarity of major themes	Were major themes clearly presented in the findings? Major themes formed the basis of the presentation of the qualitative analysis, reflecting the purpose of the overall study (i.e. patient experience of the trial and treatments) and derived from the data itself.
32.	Clarity of minor themes	Is there a description of diverse cases or discussion of minor themes? Sub themes are also discussed, and examples of divergence between participants are outlined in the main text and additional quotations.

Supplement 2

Interview Guide

16.0 Embedded Qualitative Study Design

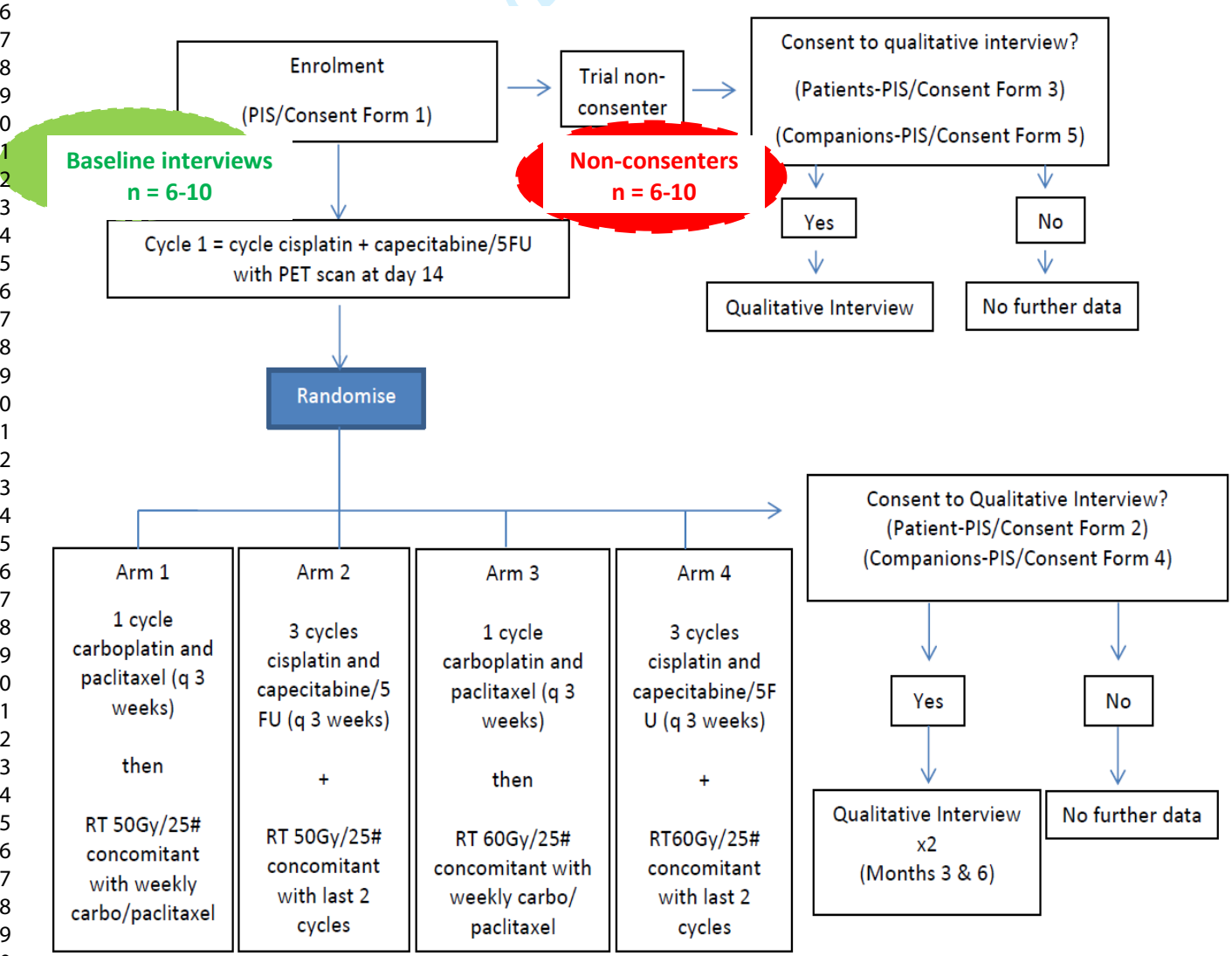
16.1 Rationale

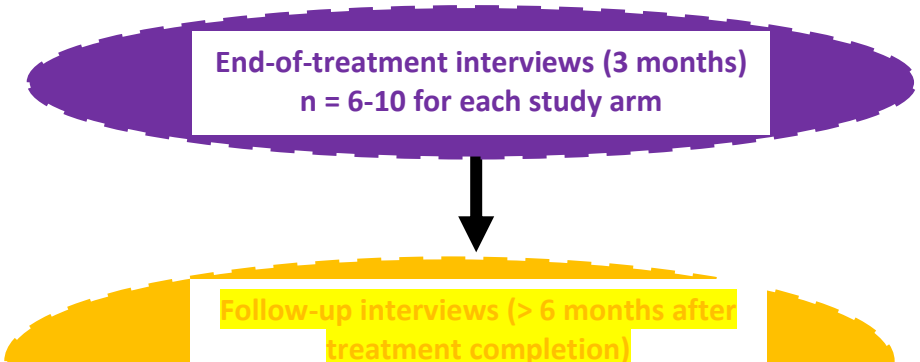
The qualitative component of the SCOPE 2 trial will explore patient experiences and perceptions of participating in a trial of escalated definitive chemoradiotherapy (dCRT) compared with standard dose, and of the two PET driven drug regimes.

16.2 Embedded qualitative study aims [AS PER PROTOCOL]

1. To assess patient experience and perceptions of each dCRT arm of the trial
2. To compare patient views across the dCRT arms of the trial
3. To consider how participants' views change over time spent on treatment
4. To examine the personal impact of treatment on patients' health and wellbeing
5. To understand patients' reasons for declining the trial

Qualitative interviews flowchart





BEFORE THE INTERVIEW

Rapport building

- Thank you for inviting me into your house

Introduction

- Thank you for agreeing to help me with this project – give a few details about the trial (e.g. name, centres, etc)
- I would also like to emphasise that only the study research team will see the information you give me.
- Your name will never be attached to any of them.
- As I mentioned I record the conversation to ease the analysis.
- However, in order for me to do this I need you to have your written consent
- Consenting the companion. As explained your …… can make any point or comment during the interview. However, again for us to be able to use the information given we need to consent ……. as well.
- Last but not least, if anything is not clear, please stop me at any time
- State the purpose of the interview

NON-CONSENTERS INTERVIEW GUIDE

Today we are going to talk about your experience of being invited to take to the SCOPE trial. The interview should take between 30 and 45 minutes. If you need a break at any time please let me know. Are you comfortable to carry on with the interview? (Reassure participants that this is not a test of knowledge – people remember different things)

Specific questions

1. When did you first hear about the trial?
    i. Who explained it to you?

2. What information were given to you?
    i. What did you think the aim of the trial was?
    ii. What was your understanding of the randomisation process?
    iii. Did you discuss the information given with others?
    iv. Did you feel you had enough time to think about the information given?

3. Can you tell me why you preferred not to participate in the trial?
    i. Did you feel that the trial was not what you expected?
    ii. Did you feel supported when making this decision?
    iii. Did you have any concern about turning the trial down?

4. Do you (or someone close to you) have any previous experience of being in a trial?

5. Do you (or someone close to you) have any experience of radiotherapy?
    i. Experience of chemotherapy?

6. Is there anything we could do to make it easier for patients to take part to a similar trial in future?

Concluding questions

7. I have been asking you many questions, is there anything you would like to ask me?

CONSENTERS BASELINE: INTERVIEW GUIDE

Today we are going to talk about how you have been feeling lately and how you feel about taking part in the trial. The interview should take between 30 and 45 minutes. If you need a break at any time please let me know. Are you comfortable to carry on with the interview?
(Reassure participants that this is not a test of knowledge – people remember different things)

Specific questions

1. When did you first hear about the trial?
    i. Who explained it to you?

2. What information did you receive?
    i. What did you think the aim of the trial was?
    ii. What was your understanding of the randomisation process?
        a. (Try to explore understanding of equipoise)
        b. (How they feel about uncertainty if raised)
    iii. Did you discuss the information given with others?
    iv. Did you feel you had enough time to think about the information given?

3. Can you tell me why you decided to participate in the trial?
    i. What were your main motives for joining
    ii. Did you feel supported when making this decision?

4. How are you feeling?

Concluding questions

5. I have been asking you many questions, is there anything you would like to ask me?

FOLLOW UP ARMS 1 TO 4 – TIME 1 (2-3 months): INTERVIEW GUIDE

Rapport building

- Thank you for inviting me again into your house

Introduction

- Thank you for wanting to help me again with the project.
- Similarly to last time I record the conversation to ease the analysis.
- However, I need you to give your written consent
- Consenting the companion. as explained your …… can make any point or comment during the interview. However, again for us to be able to use the information given we need to consent ……. as well.
- Last but not least, if anything is not clear, please stop me at any time

Today we are going to talk about how you have been feeling lately, your experience about the treatment you received and how you feel about taking part in the trial. The interview should take between 30 and 45 minutes. If you need a break at any time please let me know. Are you comfortable to carry on with the interview? (Reassure participants that this is not a test of knowledge – people remember different things)

Specific questions

Joining the trial

1. How have you found being part of a clinical trial so far?
   i. Is what you expected?
   ii. Anything particularly positive?
   iii. Anything negative or that could be improved?
2. Have you had any questions or concerns since you have been on the trial?
   i. Did you speak to somebody about these concerns?

Treatment allocation

3. Have you had all your treatment?
4. What treatment were you on?
5. Have you been given information on how the treatment is working for you on the current state of your illness?
   i. What was your reaction to this information?
   ii. What did you think of the way the information was given to you?
6. How long have you been on your treatment?

7. Is this the treatment that you preferred?
   i. With hindsight, would you have preferred a different treatment?

ii. How did you feel after your PET scan (*avoid this question if the patient was ineligible for pet scan – check with the RN*) (logistics, side effects)

Treatment experiences

8. How have you been feeling
   i. Symptoms
   ii. Psychologically
   iii. Coping (If there are psychological difficulties or coping difficulties, how have they been addressed? Has the participant talked to anyone? Who supports them?)
9. Are you experiencing any symptoms at the moment? How do you manage them (medications, complementary therapies)?
10. Have you been getting any side effects from the treatment you received?

Impact of treatment on quality of life

11. How has your treatment affected your daily life?
    i. What has it stopped you doing? (try to tease out aspects around the logistics of the treatment [e.g. time away from home] and side effects from drugs [side effects/fatigue])
    ii. How have these symptoms affected you family and social life?
12. How is your quality of life since starting the treatment?
13. Does your treatment affect your family/social life?
    i. Time away from home
    ii. Side effects/fatigue

Accessing other services

16. Have been accessing other services? (eg Macmillan or Marie Curie)
    iii. Is there any other kinds of support you feel would benefit you?
    iv. Would you know how to access it?

Concluding questions

17. I have been asking you many questions, is there anything you would like to ask me?

FOLLOW UP ARMS 1 TO 4 – TIME 2 (6 months): INTERVIEW GUIDE

Rapport building

- Thank you for inviting me again into your house

Introduction

- Thank you for wanting to help me again with the project.
- Similarly to last time I record the conversation to ease the analysis.
- However, I need you to give your written consent
- Consenting the companion. as explained your …… can make any point or comment during the interview. However, again for us to be able to use the information given we need to consent ……. as well.
- Last but not least, if anything is not clear, please stop me at any time

Today we are going to talk about how you have been feeling lately, how symptoms from treatment might have changed and how you feel about taking part in the trial. The interview should take between 30 and 45 minutes. If you need a break at any time please let me know. Are you comfortable to carry on with the interview? (Reassure participants that this is not a test of knowledge – people remember different things)

Specific questions

The trial follow up

1. What is your understanding of how long you will be in the trial and what happens next?
   i. Follow up at 9, 12, 16, 20, 24 months
   ii. 3, 4, 5 years after you first joined the trial
2. How do you feel about the health care support you have been getting since you joined the trail?
   i. Is this what you expected?

Post-treatment experiences

3. What treatment were you on?
4. How long were you on your treatment?
5. How have you been feeling
   i. Symptoms
   ii. Psychologically
   iii. Coping (If there are psychological difficulties or coping difficulties, how have they been addressed? Has the participant talked to anyone? Who supports them?)
6. Are you experiencing any symptoms at the moment? How do you manage them (medications, complementary therapies)?
7. Have you been getting any side effects from the treatment you received?

8. How did you feel about having a second PET scan? (*avoid this question if the patient was ineligible for pet scan – check with the RN*) (logistics, side effects)

Impact of treatment on quality of life

9. How has your treatment affected your daily life?
    i. What has it stopped you doing? (try to tease out aspects around the logistics of the treatment [e.g. time away from home] and side effects from drugs [side effects/fatigue])
    ii. How have these symptoms affected you family and social life?
10. How is your quality of life since starting the treatment?
11. Does your treatment affect your family/social life?
    i. Time away from home
    ii. Side effects/fatigue
    iii. Withdrawal
12. How would you say that any symptoms and side effects you've experienced changed over the course of your illness?
13. Do you feel better or worse now than you did at the time of the diagnosis
    i. Physically
    ii. Mentally
14. How have you learned to manage your illness?

Accessing other services

16. Have you been accessing other services? (eg Macmillan or Marie Curie)
    i. Is there any other kinds of support you feel would benefit you?
    ii. Would you know how to access it?

Concluding questions

17. I have been asking you many questions, is there anything you would like to ask me?

Supplement 3

Interview Schedule 2

16.0 Embedded Qualitative Study Design

16.1 Rationale

The qualitative component of the SCOPE 2 trial will explore patient experiences and perceptions of participating in a trial of escalated definitive chemoradiotherapy (dCRT) compared with standard dose, and of the two PET driven drug regimes.

16.2 Embedded qualitative study aims [AS PER PROTOCOL]

1. To assess patient experience and perceptions of each dCRT arm of the trial
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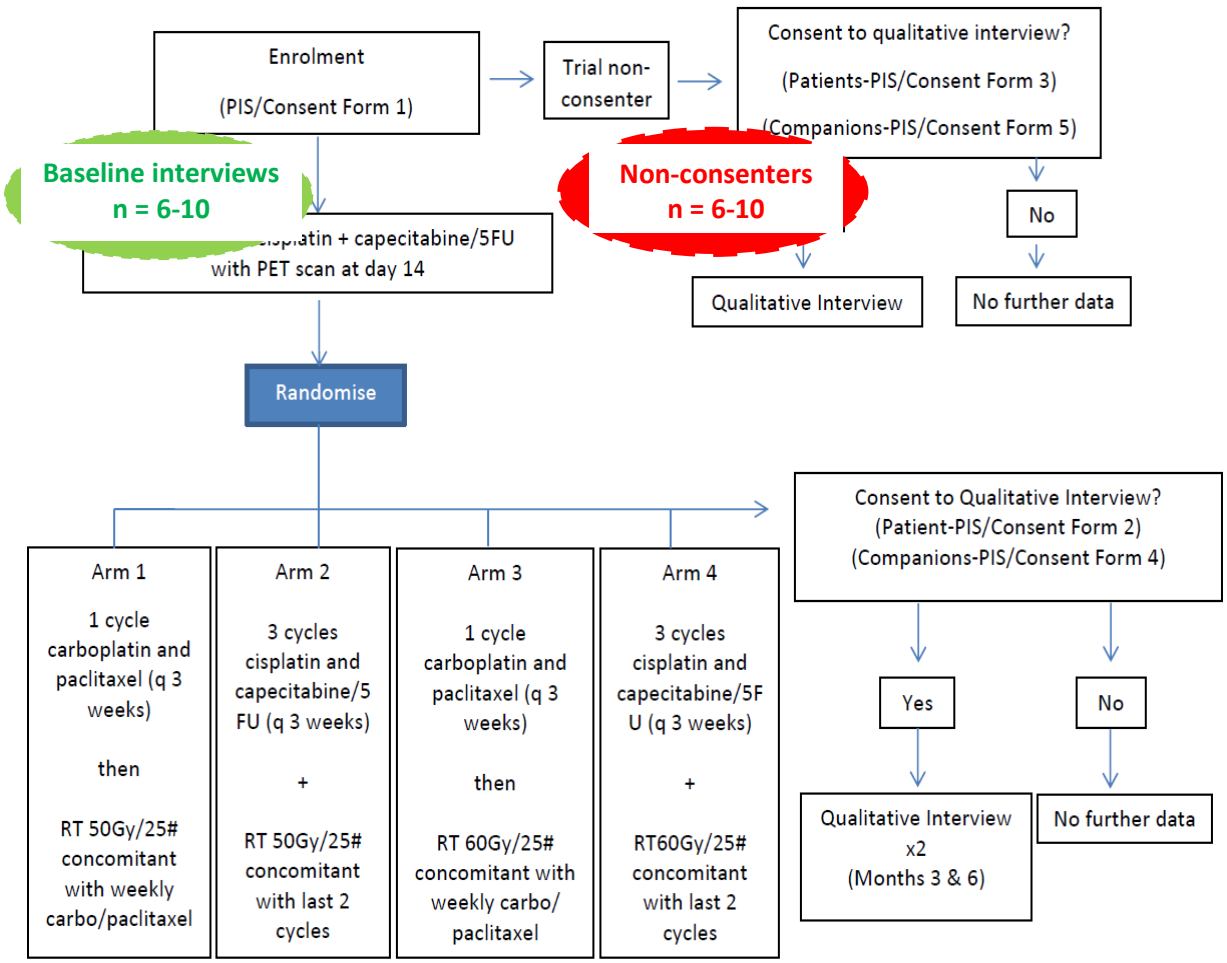
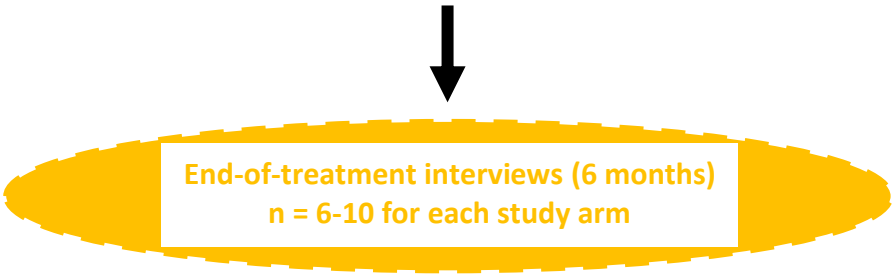
5. To understand patients' reasons for declining the trial

Qualitative interviews flowchart





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Specific questions

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    i. Who explained it to you?

2. What information were given to you?
    i. What did you think the aim of the trial was?
    ii. What was your understanding of the randomisation process?
    iii. Did you discuss the information given with others?
    iv. Did you feel you had enough time to think about the information given?

3. Can you tell me why you preferred not to participate in the trial?
    i. Did you feel that the trial was not what you expected?
    ii. Did you feel supported when making this decision?
    iii. Did you have any concern about turning the trial down?

4. Do you (or someone close to you) have any previous experience of being in a trial?

5. Do you (or someone close to you) have any experience of radiotherapy?
    i. Experience of chemotherapy?

6. Is there anything we could do to make it easier for patients to take part to a similar trial in future?

7. **Concluding questions**
8. I have been asking you many questions, is there anything you would like to ask me?

CONSENTERS BASELINE: INTERVIEW GUIDE

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1. When did you first hear about the trial?
    i. Who explained it to you?

2. What information did you receive?
    i. What did you think the aim of the trial was?
    ii. What was your understanding of the randomisation process?
        a. (Try to explore understanding of equipoise)
        b. (How they feel about uncertainty if raised)
        c. (understanding the different arms of the trial)
    iii. Did you discuss the information given with others?
    iv. Did you feel you had enough time to think about the information given?

3. Can you tell me why you decided to participate in the trial?
    i. What were your main motives for joining?
    ii. Did you feel supported when making this decision?

4. How are you feeling?

Concluding questions

5. I have been asking you many questions, is there anything you would like to ask me?

FOLLOW UP ARMS 1 TO 4 – TIME 1 (3 months): INTERVIEW GUIDE

Rapport building

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Joining the trial

1. How have you found being part of a clinical trial so far?
    i. Is what you expected?
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    iii. Anything negative or that could be improved?
2. Have you had any questions or concerns since you have been on the trial?
    i. Did you speak to somebody about these concerns?

Treatment allocation

3. Have you had all your treatment?
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5. Have you been given information on how the treatment is working for you on the current state of your illness?
    i. What was your reaction to this information?
    ii. What did you think of the way the information was given to you?
6. How long have you been on your treatment?
7. Is this the treatment that you preferred?
    i. With hindsight, would you have preferred a different treatment?

ii. How did you feel after your PET scan (*avoid this question if the patient was ineligible for pet scan – check with the RN*) (logistics, side effects)

Treatment experiences

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Impact of treatment on quality of life

11. How has your treatment affected your daily life?
    i. What has it stopped you doing? (try to tease out aspects around the logistics of the treatment [e.g. time away from home] and side effects from drugs [side effects/fatigue])
    ii. How have these symptoms affected you family and social life?
12. How is your quality of life since starting the treatment?
13. Does your treatment affect your family/social life?
    i. Time away from home
    ii. Side effects/fatigue
    iii. Withdrawal

Impact of Coronavirus

14. Do you feel that the coronavirus has had any impact on your treatment or recovery?

i. How has the coronavirus affected your quality of life?

ii. Has the coronavirus had an impact on your care or support?

Accessing other services

15. Have been accessing other services? (eg Macmillan or Marie Curie)
    i. Is there any other kinds of support you feel would benefit you?
    ii. Would you know how to access it?

Concluding questions

16. I have been asking you many questions, is there anything you would like to ask me?

FOLLOW UP ARMS 1 TO 4 – TIME 2 (6 months): INTERVIEW GUIDE

Rapport building

- Thank you for inviting me again into your house

Introduction

- Thank you for wanting to help me again with the project.
- Similarly to last time I record the conversation to ease the analysis.
- However, I need you to give your written consent
- Consenting the companion. as explained your …… can make any point or comment during the interview. However, again for us to be able to use the information given we need to consent ……. as well.
- Last but not least, if anything is not clear, please stop me at any time

Today we are going to talk about how you have been feeling lately, how symptoms from treatment might have changed and how you feel about taking part in the trial. The interview should take between 30 and 45 minutes. If you need a break at any time please let me know. Are you comfortable to carry on with the interview? (Reassure participants that this is not a test of knowledge – people remember different things)

Specific questions

The trial follow up

1. What is your understanding of how long you will be in the trial and what happens next?
    i. Follow up at 9, 12, 16, 20, 24 months
    ii. 3, 4, 5 years after you first joined the trial
2. How do you feel about the health care support you have been getting since you joined the trail?
    i. Is this what you expected?

Post-treatment experiences

3. What treatment were you on?
4. How long were you on your treatment?
5. How have you been feeling
    i. Symptoms
    ii. Psychologically
    iii. Coping (If there are psychological difficulties or coping difficulties, how have they been addressed? Has the participant talked to anyone? Who supports them?)
6. Are you experiencing any symptoms at the moment? How do you manage them (medications, complementary therapies)?
7. Have you been getting any side effects from the treatment you received?

8. How did you feel about having a second PET scan? (*avoid this question if the patient was ineligible for pet scan – check with the RN*) (logistics, side effects)

Impact of treatment on quality of life

9. How has your treatment affected your daily life?
    i. What has it stopped you doing? (try to tease out aspects around the logistics of the treatment [e.g. time away from home] and side effects from drugs [side effects/fatigue])
    ii. How have these symptoms affected you family and social life?
10. How is your quality of life since starting the treatment?
11. Does your treatment affect your family/social life?
    i. Time away from home
    ii. Side effects/fatigue
    iii. Withdrawal
12. How would you say that any symptoms and side effects you've experienced changed over the course of your illness?
13. Do you feel better or worse now than you did at the time of the diagnosis
    i. Physically
    ii. Mentally
14. How have you learned to manage your illness?

Impact of coronavirus

15. Do you feel that the coronavirus has had any impact on your treatment or recovery?
    i. How has the coronavirus affected your quality of life?
    ii. Has the virus had an impact on your care or support?

Accessing other services

16. Have you been accessing other services? (eg Macmillan or Marie Curie)
    i. Is there any other kinds of support you feel would benefit you?
    ii. Would you know how to access it?

Concluding questions

17. I have been asking you many questions, is there anything you would like to ask me?

Supplement 4: Illustrative Quotations

Key Themes	Illustrative Quotations
Experiences of treatment	
Impact of treatment	
Initial treatments and support provided by clinical teams earlier in the trial were described as having resulted in small improvements for some participants' cancer symptoms. These symptoms mainly related to difficulties eating.	*I know when I started, I had difficulty swallowing obviously with the oesophagus tumour and it was sort of every meal, every few mouthfuls was getting difficult and I did feel in about two weeks into the first cycle, I was pretty much able to swallow normally. So, something positive is happening'*. **Participant 4 (2-3 months)**
	I had a tube fitted in my arm yesterday, ready for the chemo on Friday, and I've got a feeding tube, so I don't have to worry about not getting enough nutrition in, so I think a lot of worries I had at the beginning have faded. **Participant 6 (Baseline)**
Side-effects from treatments	
Side-effects from chemotherapy Participants described common side-effects they experienced after receiving chemotherapy including muscular fatigue, pain and neuropathy in their feet, while most of which were expected some they were unexpected.	*The side effects I've I had are quite sore feet at one stage when I was on the chemotherapy, which was difficulty walking.* **Participant 7 (3 months)**
	Cos everybody expected when I stopped the chemo, especially me, I thought that was it (laughs), you know stop the chemo and that's fine. And, then I stopped the chemo and I got ill (laughs). **Patient 6 (6 months)**
	During the 1st cycle … the pain in my feet and little bit sort of pins and needles like that, I think that's the worst side effect that I have experienced... Tiredness, you know, just feel worn out… the other thing that I get is almost like fatigue in my thighs… I think one day where I felt sick which is just cleaning my teeth. **Participant 4 (Baseline)**
Four patients reported that during the trial their chemotherapy treatment had been changed or stopped due to pre-existing conditions, side-effects that they had experienced or that it was not making enough of a difference to their cancer	*I found the capecitabine taking those every day I think they were the hardest of the drugs that I was taking… I did notice with them the nausea and the sickness and the fatigue was massive. When, they put me on [another chemotherapy drug] … I felt it was much gentler… unfortunate[ly] for me… having a blood clot… I think that was the worst thing… the blood clot was harder to recover from than the cancer (laughs)'.* **Participant 4 (3 months)**

outcomes. One participant described the unforeseen development of thrombosis after switching the types of chemotherapy they received due the initial side-effects. This demonstrates the complexities some patients face when weighing up the side-effects of different chemotherapy regimens.	*Companion: The last week of September that he couldn't eat… and that's why they stopped the treatment too early… and that tails off then because he has a dose of steroids and it boosted his appetite and It boosted everything.* *Patient: There were huge difference because of steroids… that was before all the, the pneumonia came on… that was again the weeks following the treatment which I be… happens.* **Participant 1 (6 months)** *After they took the test at the end of just one cycle and they said it didn't made enough difference so it was being changed*. **Participant 3 (2-3 months)** *The first chemo I was on, they had to change... I've got… Neuropathy. So, they changed it. And, another one was because of my kidneys. They changed that to a different one right at the very beginning*. **Participant 5 (3 months)**
Side-effects from radiotherapy The experience of receiving radiotherapy was reported by most patients as being physically and psychologically arduous. Difficulty and pain swallowing experienced after radiotherapy were the main side-effects described by several patients.	*Because of what the radiotherapy does, it sort of burns all the inside and it's very difficult to swallow… but that was the worst thing to be perfectly honest with you, the thing is I would like to able to eat like I used to, but at the moment I can't but I am getting there… definitely turns better now.* **Participant 2 (2- 3 months)** *With the radiotherapy… I was completely and utterly flat out, nothing mattered at all... You can't win it at any point… you can't concentrate or want anything, you feel bad if there is no pain, nevertheless you feel dreadful.* **Participant 1 (6 months)** *Once radiotherapy started I could feel then that the inflamed and the tumour and the oesophagus, I could feel that it sort of was creeping back to where I was before and it just got a little harder to swallow but not to the extent that I couldn't eat.* **Participant 4 (6 months)** *It's worse right now but then we've only just finished radiotherapy, it's very tender right now, it's burning from inside out… the consultant did say... I've been trying to get on purées, semi solids... It's not how thin or thick it is it's the texture of it, whether it'll slide down or it won't slide down, so every now and again I experiment sending something down there. Sometimes I can do it but this particular week it's been difficult, but the consultant explained to me "I'm full up of chemo and I'm full up of radiotherapy and everything's pretty raw right now".* **Participant 8 (3 months)**

I just have a slight problem with swallowing sometimes but that's they say that's to do with the radiation but it didn't stop me eating what I want, I just have to make sure I chew it properly that's all. **Participant 9 (6 months)**

Recovery after chemoradiotherapy

After the completion of chemoradiotherapy, during the recovery period, participants experienced symptoms which ranged from mild to severe, having physical and psychological outcomes. Nausea, as well as fluctuations in appetite, weight and energy levels were reported by participants, often relating to pain and issues swallowing. Some participants recalled having to adapt to the fatigue caused by difficulty sleeping and pneumonia. Participants' symptoms tended to lessen over time, and when they had received support to reduce these symptoms they usually recalled noticeable improvements. It was not always possible to differentiate between the longer-term impact of chemotherapy or radiotherapy treatments, as participants described their symptoms more generally.

I lost my appetite a bit, but, … that's come back now, and … I am starting to regain weight… I still have problems digesting food … some foods just get stuck in my oesophagus, and that is still a little bit painful. **Participant 7 (3 months)**

I had pneumonia… I started with the infection as soon as I finished the chemo… I was in hospital for a week. And, I had about four different courses of antibiotics and they just weren't working on the pneumonia. And, I felt worse with that than I had been through all the treatment. I was just starting to get better before we went away… within days I suddenly was much, much, much better. **Participants 6 (6 months)**

I had trouble sleeping for quite some time and that sorted itself out now and can sleep perfectly well now without any paracetamol at all, so night-time is good. **Participant 1 (2-3 months)**

*The treatment make[s] you very tired… I have to rest a lot and whilst I think to myself I feel really good today lets go out. When I have out a couple of hours I have to come home, even now you know it tires me, but that's fine. Things improve on a daily basis and hopefully it will continue to improve***. Participant 2 (3-6 months)**

I had some constipation, I have to admit and that's been an issue throughout… I had to listen to my body and you know rather than fighting sleep, rather than thinking that you know I am going to battle this , sometimes you just got to shut your eyes and think you know what I will sleep all day, doesn't matter. **Participant 4 (2-3 months)**

The fatigue, the tiredness… did seem to last a little bit longer than I really anticipated… you know some days I didn't feel like lifting my head off the pillow… I think the fatigue was a biggest one for me. **Participant 4 (6 months)**

I'm getting stronger in myself as well, so. And, the treatment has gone and I'm getting taste back, so I can taste things better than I did. You know cos just drinking. Just drinking water, it wasn't very nice, but it's alright now. **Participant 5 (2-3 months)**

I had nausea, tiredness has been the biggest one for me… it's slowly improving, I'm not dropping off to sleep as I'm talking to people type of thing now, but that was happening, (chuckling)… I've started to eat again, tiredness is the main thing, but nothing that I can't cope with and was expected, they told me that I would be, my body's going to, gotta kind of repair itself a bit now. I'm still taking the anti-nausea medications, but I have reduced them… I've still got the RIG feeder tube, so, I'm trying to wean myself, at the moment, off it. So, I'm starting to try and take some of my medications orally, instead of through the tube. I'm on a lot less medication than I was. **Participant 6 (3 months)**

I was sleeping up to 17 hours a day … which is… I've spoke to the people down there and they say that's a natural side effect, but it happens. **Participant 7 (3 months)**

Treatment impact over time

Participants reflected on their cancer treatment journey and how their symptoms had changed over time, including facing adversity throughout treatment regimens gradual improvements.

At the time during the treatment … I've felt really, really, really ill, worse than before I started the treatment… The treatment was tough… I have [had] a lot of symptoms, side-effects from it. But those have finished now, so obviously things are improving… when it finished I was having problems… but each day I'm getting better. **Participant 5 (3 months)**

I'm just feeling better every day and my eating is improving all the time. **Participant 6 (6 months)**

I feel a lot better. Obviously the time I was diagnosed it was a bit of a bolt out of the blue and I was left you know in big, big shock. So, the fact that they've now said to me that the cancer's gone, it's obviously a huge relief. ***Participant*** **7 (6 months)**

In some instances, however, participants described the reality of the unexpected longer-term side-effects of the illness and treatment, emphasising the need for ongoing support and updates from healthcare professionals.

I was quite euphoric all the way through the treatment and it was after the treatment ended that I sort of thought it's all over now. The fatigue, the tiredness [will] all be going and it did seem to last a little bit longer than I really anticipated and unfortunately the wound with the blood clot still hasn't healed. **Participant 4 (6 months)**

Patient: No interest at all in checking my general condition which could have changed because of the treatment …

Companion: And you just hope that all the drugs are compatible. They all interact with each other and that is another hurdle. Who knows?...
Patient: It's thousands of, it's thousand of trials. How can you do it, interaction of drugs is a massive problem being tackled all the time. **Participant 1 (2-3 months)**

Information and support needs after treatment

Concerns were raised by several participants and their companions regarding what would happen post-treatment, as they felt that there was less information and support available than before and during their treatment. A need for further and more timely information and updates from healthcare professionals regarding potential longer-term side-effects including rare events such as blood clots and recovery timescales post-treatment was also expressed by participants.

We actually felt we have huge information on side effects during [treatment] but virtually nothing on after [treatment]. **Companion of Participants 1 (2-3 months)**

When it comes to this particular type of blood clot I had, there was nothing, no description there and I suppose if I could sort of say anything about the website- that's the one thing they missed because all the symptoms I read about were symptoms that were associated the side effects of the drugs as well. **Participant 4 (6 months)**

The fortnight before we draw the line for the end of treatment and to know things are likely to move on and likely tests and however… some sort of framework… As it is, we haven't got any date at all for anything beyond next Friday, week Friday, nothing at all… We didn't have a cohesive view on the whole thing presented by one person anyway, it was bits and pieces. **Participant 1 (2-3 months)**

Companion: Its general advice be kind to yourself for few months (coughs) and then you should begin to feel stronger or sleep more than you would have done so that your body recover. So the body has had fair hammering… It isn't just the 10 weeks when you take the chemotherapy challenge is it? It's much bigger picture. **Participant 1 (2-3 months)**

It's all been a bit strange because, I had to come off the initial chemotherapy drugs. It was sort of we will have to take you off the trial but still keep collecting the data from the trial and I understood that because… I think trials have to be very specific and if you stay outside the guidelines then it does blur the data… I don't know whether I will be monitored a little bit extra. I don't know whether I am assuming when I go back to check up in six months there would be the same questionnaires and the same sort of things. **Participant 4 (6 months)**

Participants described difficulties with eating and dietary needs, and expressed the

One thing that I asked all along was really about how much I could eat, we have been asking, haven't we? You sort of [know] it is going to get more difficult, is my throat going to be smaller, will it get bigger again,

importance of being provided with relevant information regarding how the disease or treatments impacted on these fundamental needs.	*how much will I be able to eat? Will I be able to eat properly at the end and I think that all out questions have been like that.* **Participant 3 (2-3 months)**
Several participants described a high level of personal support from clinical and third sector services, which made a significant impact on their trial experience. They described how they had received support relating to their quality of life and practical needs, which they may not have accessed from healthcare professionals.	*I have phone calls from the clinical nurse… sometimes just to ask how I am, he's helped to make appointments for me when I've had problems making them myself and he's managed to make everything seamless from one thing to another, which I greatly appreciated, because I was a bit all over the place, especially at the beginning of diagnosis… if [clinical nurse] thought that maybe I wasn't getting something, that the Oncologist was saying to me… maybe sometimes I was lacking a bit of understanding and he always made sure that I left that room, understanding everything.* **Patient 6 (3 months)**
	Age Connect, Age Concern one of those we have used their advice a few times. Just popped in and seen them… has been very, very good as a system for us. **Participant 4 (3 months)**
	The medical staff have really been great, and ... I've got all the information … all I need to do is pick the phone up and I know I can speak to somebody with any questions … have been in contact and … am on various forums with Macmillan, … which … my wife and I have accessed quite frequently … just to view other peoples' experiences, which has been good, because obviously whatever side effects you're having, there's always somebody else who's had them as well… it reinforces and puts you at ease really to see other people have gone … through the same thing. **Patient 7 (3 months)**
	Somebody did contact us from Macmillan right at the very, very start. He went through all sort of social things like… carers allowance and things like that and that's one of the things that I got to say that we were very, very grateful for… The information was fantastic and you know lots of the sites were really really good… I think I read along from the Macmillan website because that was quite sympathetic. **Participant 4 (2-3 months)**
Patient outlook and quality of life	
Psycho-social impact of treatments	
The psycho-social impact that some patients experienced in the first few months following treatment included disinterest or	*Things that I would have done, I am a cellist, I play cello and other things and no way completely uninterested, stopped, books and all I read stopped.* **Participant 1 (2-3 months)**

lack of energy to participate in hobbies and social activities that they had previously.	*I suppose it has affected my social life … I don't really [go out]… at the moment, I've only just started going out perhaps socially a little bit more.* **Patient 7 (3 months)** *In my previous life basically, I was able to do a bit… of online communicating with people not that I felt like chatting to them but you know, I could keep [up] with things… to be one by phoning them, or writing to them, or visiting.* **Participant 3 (2-3 months)**
Gradual improvements to quality of life Participants explained how the treatment had impacted on their quality of life overall. Their physical health post-treatment had placed restrictions and strains on their everyday routines. At times they felt they had relied heavily on their family for support with daily activities. Gradual improvements to participants' health and well-being related to readapting and regaining their capacity to participate in previous routines and social activities.	*My wife has done everything for me and is very, very protective… I think it would have been lot tougher if I had been on my own. My daughter stepped in and did all the … she moved heaven and earth to make sure that for the last three months she was available... There were days when I [said] "it's okay, let me drive" and getting back into that was a biggish step but now I'm back into driving.* **Participant 4 (6 months)** *I've seen a daily improvement, day on day something else seems to improve… I could eat things today that I couldn't eat yesterday. It's an ongoing thing but it's an onwards and upwards kind of feeling. Today I'm going to my granddaughter's birthday and tomorrow I'm going out with friends. I couldn't do that a couple of months ago… starting to get back to normal now.* **Participant 5 (3 months)** *I say we are completely together, and I have completely depended on (names wife)… I been thinking very much about this, see people on a walk, people who are old, and they have nobody at home and they have to go back to an empty house as well and that's terrible you know at the end of the day its absolutely awful and I have been much aware of this and seen this kind of and there are simply people who are by themselves… how would I have coped that it not been for the kind of relationship*. **Participant 1 (3 months)** *My middle daughter, the nurse, when I didn't know what I was doing at the very beginning, she came with me to the, to the clinics and to the meetings… and asked the questions that I didn't know what to ask or wasn't aware to ask at the time*. Participant **8 (3 months)** *It's been very tiring … my wife and I, we do like to do a little bit of walking and that. I obviously haven't been able to do anything like that.* **Participant 7 (3 months)**
Adaptation and normality	

Regaining a sense of normality was important but complicated for several participants when re-adapting to life after treatment, as their daily lives had been significantly impacted by their experiences of cancer and treatment. Some participants explained that they struggled to readjust to life after treatment, due to the change in outlook that they needed to make or the extra support that they had been provided with during their trial until that point but was no longer receiving.

I think there was a feeling of… as if you were left on your own. You get that initial feeling because the 12 weeks of treatment were so intense… we were in the hospital everyday, sometimes twice a day and then you know it's off you go then. It been couple of months now rest, recuperate relax, get back to normal life and I found that quite a strange statement and I got to admit that's perhaps the hardest thing to do now was getting back to normal life. **Participant 4 (6 months)**

The days and the nights are not the same at all and you don't see people and you miss all your normal, normal things that you do certain days and certain, lose all your fixed points (laughs). **Participant 1 (6 months)**

I have found that because we actually went in on Saturday night, the first time it was to a function, a dinner and I said "I am coming but I don't know how long I can stay" and we stayed until 12'oclock, had a really nice time and then the next day I went out again to a food… had a fabulous weekend it was really nice, to break the mould to being ill…. I probably paid for that because I had couple days where I have needed to rest a lot, you know, that's fine. **Participant 2 (3-6 months)**

I do think back fondly because you sort of make acquaintances with people… I saw the same people 5 weeks, every day of the week. We got to know each other, we got to chat, we got to talk about our cancer, we got to talk about our treatments and how tired we were. You know we got to sympathise and carers got a chance to talk to carers and have laugh and have a little fun and have a giggle and what you have been doing today, bit of gardening you know those sort of things and roaring with laughter sometimes so that's, that's how I have handled it. **Participant 4 (6 months)**

Well you got to keep cheerful. It's not… been easy. It's been bit of a struggle getting back to normality but… we getting there…. It been couple of months now rest, recuperate relax, get back to normal life and I found that quite a strange statement and I got to admit that's perhaps the hardest to do now was getting back to normal life… I am sort of getting to the point where I am starting to feel better my wife is noticing that I am feeling better … I do a little bit of help around the house and do little things… So that's the thing now getting back to normality. **Participant 4 (6 months)**

I am getting back to normality then. **Participant 7 (3 months)**

I'll tell you one thing that I don't know whether you come across this a lot, but when I went to see the consultant he told me that the cancer had gone I expected to feel quite elated, but I didn't… if anything I felt sort of a bit down and I don't know why… And, my wife felt the same as well. **Participant 7 (6 months)**

Physically, I probably feel better, I feel good, no problems… I am getting back to normal, I am really where I was before the treatment. My social life and my family life, yes, it's back to where it was, it's normal, quite happy it didn't make any different after the treatment. **Participant 7 (6 months)**

Positive outlook after treatment

Several participants described how they attempted to sustain a positive outlook about their survival prospects and their circumstances overall, as a coping mechanism. Thus, being provided with adequate support and information aided their positive outlook.

Things improve on a daily basis and hopefully it will continue to improve. I don't like it (laughs)… yeah a lot (laughs), yeah but that's fine you know, there will come a day when I will be fine and I will be able to go [out] again, so I will just wait for that day. **Participant 2 (3-6 months)**

Mentally… I have got no problems at all, never had, also with treatment I didn't have any difficulties that way, I knew what was happening, I was aware of it, and all it was about just waiting for the outcome. **Participant 9 (6 months)**

We are not doom mongers… I don't particularly think it will [be] good, it will [be] bad. It will be as it is. I really don't think I am bothered in that sort of sense at all what's going to happen. It's just a treatment. **Participant 1 (2-3 months)**

I… try to keep healthy, try to keep active you know and I also try to have a very positive outlook ... I think that's the huge thing during the situation is to be positive, to be hopeful. I constantly say to people I have not got the time to worry, I haven't got the energy to worry. I need all my energy now to look after myself to get better. Its pointless panicking, its pointless crying, its pointless breaking down and saying what if and why and I think a big part was accepting that, yes I got cancer, yes I going to have to go through the treatment… I think a lot of the stories about the treatment were horrendous. I haven't felt that as yet. **Participant 4 (2-3 months)**

I feel a lot better. Obviously the time I was diagnosed it was a bit of a bolt out of the blue and I was left you know in big, big shock. So, the fact that they've now said to me that the cancer's gone, it's obviously a huge relief. **Participant 7 (6 months)**

Impact of COVID-19 pandemic

Vulnerability and isolation

Some participants reflected on how the pandemic may have intensified the sense of isolation and stress that other patients felt during their treatment process, although these participants did not feel personally affected in this way.	*When you were sat in radiotherapy and chemo, some people probably needed somebody with them in chemo, I didn't… but there were people that were a lot sicker than I was I suppose pre- Covid you could have a friend with you to keep you company through the day*. **Participant 8 (3 months)** *It's not nice sometimes when you've got to go through things on your own, where you like having your partner sitting outside the door, but I don't think it's affected my treatment.* **Participant 6 (3 months)** *When we were filling in the clinic surveys… isolation wouldn't have been isolation if it hadn't have been for Covid… Covid had an influence on everything… From times of clinic, to staff levels to… it was an influence on everything.* **Participant 8 (3 months)**
The pandemic caused an increased sense of vulnerability and cautiousness amongst cancer patients. However, the comprehensive social restrictions put into place for infection control, and the vaccination programme at times, eased the sense that some of these participants missed out on their usual social activities.	*I haven't been out since the beginning of Covid… it's been isolation the way… if everybody else wouldn't have been in isolation as well, I suppose it would've affected me more, but because everybody else was in isolation… I don't suppose it bothered me that much, no, I was quite comfy that everybody else was stuck in as well*. **Participant 8 (3 months)** *Everybody's been really cautious around me; you know any family members that were coming here were doing lateral flow tests before. And, I still wear a mask wherever I go… we went away on holiday other people weren't wearing masks, when they were going to the bar or the restaurants, but I was. There is a bit of anxiety, but I'm double vaccinated. I still go to shops and stuff, but I do get a bit of a rumbly tummy if I'm around people and they've not got masks on.* **Participant 6 (6 months)** *I've read … which could have made me more vulnerable to Covid, to counter that … I had my two vaccines … quite quickly because… of the cancer I've had, so that most probably countered that bit … the stress of that … against catching the Covid.* **Participant 7 (3 months)** *You've gotta wear masks and things like that… So, obviously you couldn't go out as much… Whilst you're going through treatment I didn't wanna go anywhere anyway, so the… Coronavirus didn't affect me, very, very little.* **Participant 7 (6 months)**
Potential Improvements Sharing information among peers Opportunities for participants and their caregivers to share information regarding	*I think there should be opportunities where people that have been through [cancer treatment]… share maybe positive experiences, can also point people in the direction you know? ... I think there is an*

their experiences of cancer and their treatment pathway through peer support networks were suggested as a means of improving patient knowledge.

Follow up information

Follow up information regarding the participants' current cancer status, as well as results from the trial, were desired by a participant, who felt that they were unsure about their personal outcomes or how this related to the wider trial.

opportunity there maybe a support network of people's needs, need to be arranged. **Participant 4 (6 months)**

Did they tell me it was a 70/60 chance… they said to me they can burn it away… if it's not burnt away why not, you know what I mean? I think it should be followed up and I suppose my question to follow onto that would be, would we, the participants be able to see the outcome of your survey? **Participant 8 (3 months)**