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Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2020-047813
Article Type:	Original research
Date Submitted by the Author:	11-Dec-2020
Complete List of Authors:	Sawyer, Chelsea; The Christie NHS Foundation Trust, CPRC Preston, Laurie; The Christie NHS Foundation Trust, Christie Patient Centred Research Taylor, Sally; The Christie NHS Foundation Trust, Christie Patient Centred Research Davies, Michelle; The Christie Hospital NHS Trust, The Experimental Cancer Medicine Team, Carter, Louise; The Christie NHS Foundation Trust, The Experimental Cancer Medicine Team; The University of Manchester Division of Cancer Sciences Kreb, Matthew; The Christie NHS Foundation Trust, The Experimental Cancer Medicine Team; The University of Manchester Division of Cancer Sciences Cook, Natalie; The Christie NHS Foundation Trust, The Experimental Cancer Medicine Team, ; The University of Manchester Division of Cancer Sciences Graham, Donna; The Christie Hospital NHS Trust, The Experimental Cancer Medicine Team; The University of Manchester Division of Cancer Sciences Thistlewaite, Fiona; The Christie Hospital NHS Trust, The Experimental Cancer Medicine Team; The University of Manchester Division of Cancer Sciences Yorke, Janelle ; The Christie NHS Foundation Trust, Christie Patient Centred Research (CPCR); University of Manchester , Division of Nursing, Midwifery and Social Work; School of Health Sciences
Keywords:	Adult oncology < ONCOLOGY, QUALITATIVE RESEARCH, Clinical trials < THERAPEUTICS

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Patients' experiences of early phase experimental medicine cancer trials

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Word count: 4450

Abstract

Objectives: The study aimed to explore patients' experiences of Experimental Cancer Medicine (ECM) clinical trials.

Design: The study's design was qualitative. Two focus groups with patients were undertaken followed by semi-structured interviews, to explore patients' experiences of ECM clinical trials. Interviews and focus groups were audio recorded and transcribed verbatim. Data were analysed using thematic analysis.

Setting: A regional cancer centre (tertiary care) in North-West England.

Participants: Twelve patients (aged 52-89) who consented to participate in an early phase ECM trial participated in one of the two focus groups. An additional twenty-two patients (aged 42-83) who consented to participate in an early phase trial were interviewed.

Primary outcome measure: Patients experiences of an ECM trial.

Results: Four main themes were identified from the analysis. The main themes were around decision-making, information needs, experience of trial participation, and impact of trial participation.

Conclusion: The results from this study improve our understanding of patients experience on experimental cancer trials and can be used to inform clinical practice in this area.

Strengths and Limitations

- Participants demographic varied with regards to phase of trial, duration on trial, age range, and disease group to capture a range of experiences
- A limitation is the cross-sectional nature of the study, experiences and perspectives may change throughout the trial process.

- The study was limited as participants were recruited from one comprehensive cancer centre, patients' experiences may vary across hospitals.

INTRODUCTION

Experimental cancer trials (or early phase clinical trials) play an important role in the progression and advancement of cancer treatments. It is estimated in the United Kingdom (UK) that one in five cancer patients participate in clinical trials.[1] Early phase clinical trials (defined as Phase I and non-randomised phase II) are designed to assess the pharmacodynamics, pharmacokinetics and safety of novel drugs.[2] The drug dose is gradually increased Phase I trials, to explore safety and best dose. In phase II trials the efficacy of the drug is evaluated, side effects and safety are also investigated. Early phase clinical research primarily focuses on the physical outcomes of experimental therapies including appropriate drug dosing, treatment toxicities, survival, and response rate.[2]. Within the protocol and trial design limited attention is afforded to patient experience, consequently, little is understood about the personal impact of trial participation.[3]

Understanding the patient experience is of particular importance in relation to early phase trials, where significant adverse events associated with treatment toxicity may outweigh any possible therapeutic benefit.[4] Undesirable side effects are an important factor in shaping patients' experiences of trial involvement, influencing their psychological wellbeing and sense of hope, and in some instances increased participants' fear of death.[5] Furthermore, patients may not fully understand the burden and demands of participation in clinical trials, and the impact trial participation could have on their Quality of Life (QoL) and that of their loved ones.[3]

Despite the various physical, emotional and practical challenges, patients have generally reported positive experiences of trial participation and feel an increased sense of 'control' over their illness.[5] Moore also suggested that trial participation reflects a coping

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3 strategy against hopelessness.[6] When standard treatment is ineffective, clinical trials are
4 perceived by some to offer a 'second chance' at finding a cure.[3] Early phase trials can be
5 perceived by others to be a "last ditch effort" for patients who are otherwise considered to
6 have exhausted all other treatment options.[4] Cox also found that participants derived
7 comfort from being closely monitored by clinicians due to the belief that they were in 'expert'
8 hands, and in providing a sense of purpose through helping others.[3] However, patients
9 often misunderstand trial information, their understanding and the meanings that patients
10 ascribe to their participation will determine how they make sense of their experiences
11 throughout the trial process.[7]
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23 Patient experience is considered to be an integral component of excellent
24 healthcare.[8] As outlined in the NHS Outcomes Framework, a deeper understanding of
25 patient perceptions of trial involvement will drive quality improvement and aid learning.[8] Yet
26 there is limited understanding into patients' experiences of participating in early phase
27 clinical trials. Therefore, this study aimed to explore the experience of patients who
28 consented to participate in a Phase I or II experimental cancer medicine trial.
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36 **METHOD:**

37 **Study Design**

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42 In this qualitative study, semi-structured interviews and focus groups were used to explore
43 patients' experiences of Experimental Cancer Medicine (ECM) trials. Participants were
44 recruited from a regional cancer centre in North-west England. The inclusion criteria for the
45 study were (a) any cancer type, and (b) anyone who has been screened for a observational
46 trial or a phase I-II experimental cancer medicine trial. Participants were excluded if they
47 were unable to provide informed consent, or comprehend written English.
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55 Potential participants were approached by the research team, who provided written
56 study information and answered any questions. Informed signed consent was obtained.
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Face to face interviews were conducted at either the patient's home or in a quiet hospital room, depending on the patient's preference.

Two focus groups were conducted face to face in a quiet hospital room. The interviews and focus groups were audio recorded and lasted from 14 to 62 minutes and 48 to 108 minutes, respectively. Ethical approval was gained from the south central-Oxford b Research Ethics Committee (reference number 18/SC/0299) and the local NHS Trust.

Sample

A total of 34 patients participated in an interview or a focus group. Participants' demographics are presented in Table 1. Twenty-two patients participated in a semi-structured interview and the cancer disease groups included breast, lung, lymphoma, colon, and stomach. Twelve participants in total participated in one of the two focus groups and the cancer disease groups included lung, lymphoma, leukaemia, renal, and larynx (head and neck).

Insert Table 1. here Participants demographic information

Table 1. Participants' demographic information

	Interviews (n = 22)	Focus groups (n =12)
Age range (years (Median))	42 – 83 (65.5)	52-89 (68.5)
Gender (female %)	59%	8%
Ethnicity %		
White British	95%	100%
Chinese	5%	
Type of trial n (%)		
Not eligible for the trial (Screen fails)	2 (9%)	-
Observational	2 (9%)	-

Phase I	9 (41%)	7(67%)
Phase II	9 (41%)	5 (33%)

Data analysis

The interviews were analysed using an inductive thematic approach.[9] An initial transcript was read by two authors (J.Y, C.S) to explore patterns/themes in the data. Two reviewers then coded an additional three transcripts and compared these to assess for inter-rater reliability (86%). Remaining transcripts were subsequently coded by one researcher (CS). Themes and interpretations of the data were discussed in regular meetings (J.Y, C.S). Data were presented as four overarching themes: (a) Decision-making, (b) Information needs, (c) Experience of trial participation, and (d) Impact of trial participation. Quotes from the interviews are presented as participant's ID, gender (M=male, F=female) and age (in years). Quotes from the focus groups are presented as FG and number (1 or 2).

Patient and Public Involvement:

Patients reviewed and provided feedback on all study documents including participant information sheets, informed consent sheet, and interview schedule. Once the interviews were analysed the main themes were discussed with the study team and patient representatives. The final study results will be disseminated via a letter with summary of the study to participants who stated they would like to receive the summary.

RESULTS

Decision-making

Patient preference regarding involvement in decision-making varied. Some patients highlighted the importance of including family and friends in their decisions, whereas other

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3 patients felt the decision as to whether to participate in a trial was only theirs to make. Due to
4 the difficulties understanding the information, the uncertainties around trials, and patient
5 perception that the doctors are the experts, some patients relied on the doctors to make the
6 best decision for them.
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12 *"It was mine [decision]. It's got to be, it's my life."*(25M83)
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15 *"I think the consultants made the decision about what was most suitable."*(28F72)
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18 A few patients perceived the clinical trial as their only option and for those who were
19 ineligible for the trial, this view lead to feelings of despair and uncertainty about their options.
20 Conversely the majority of the patients felt the clinical trial provided them with another
21 treatment option. This was particularly important for patients who did not want the alternative
22 treatment options.
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29 *"I had no other choice, so at the end of the day, that's the one."*(25M83)
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32 The clinical trial also provided the majority of patients with hope. For some it was a
33 potential chance for a cure, stopping the progression of the cancer, and/or extending their
34 life. While others hoped their participation would help others with cancer in the future.
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40 *"There's that hope there that the...a chance of a cure."*(19M56)
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43 **Information needs**

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45 Patients wanted enough information about their choices to make the best decision regarding
46 their treatment. Patients also highlighted the need for more simplified information, as the
47 information they received regarding trials was scientific and on occasions difficult to
48 understand.
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54 *"doctors know all the technical terms, but we don't, most of us; and it has to be said in*
55 *plain English"*(22F52)
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3 Patients were divided on whether they had received enough information about the
4 possible side effects of the trial prior to participation, with a number of patients reporting that
5 they were not fully informed. Patients recognised however that it might not always be
6 possible to provide this information, as the purpose of clinical trial are to identify side effects
7 produced by the trial treatment. One patient felt the risk of permanent side effects had not
8 been fully explained to them, and prior knowledge of this risk, would have affected their
9 decision to participate in the trial.
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19 *"I don't remember anybody sitting down and saying, before you go on this, your thyroid*
20 *could do this, that and the other, and it will be permanent"(23F68)*
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24 *"Well I think the list of possible side effects is they just think of everything they can*
25 *think of that might go wrong and list them all down" (FG2)*
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29 During the trial, patients wanted updated information regarding i) their response to the
30 treatment, ii) alternative options to the trial, iii) the success of the overall trial to date, and iv)
31 the experiences of other patients on the trial. This information helped them to re-evaluate
32 their trial involvement and make decisions about future participation.
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38 *"I want him to say to me, now look here, if this doesn't work it's chemo."(21F70)*
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41 A few patients who felt they had been given false hope and had been misled about the
42 personal benefit they would gain from the trial. These patients believed this false hope
43 reduced their ability to cope with updates regarding no or negative response to the trial.
44 These patients felt information about possible outcomes of the trial should not focus on
45 potential benefits but should also highlight the risks and possibilities the trial may not work,
46 even if the trial has previously had some positive results.
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54 *"if they hadn't built my expectation, then the crash wouldn't have been as*
55 *hard"(03M42)*
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3 Patients were informed on whom to contact if they required medical support. However,
4 many were unaware of the psychological support available to them and could not recall
5 doctors discussing psychological support options. Some patients who knew support was
6 available highlighted that the psychological support was not always accessible to patients
7 and/or their family due to length of treatments and distance travelling to the hospital. The
8 majority of patients also did not know if there was any psychological/financial/practical
9 support available for family members.
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19 “you do feel that there's a void like, you know, where do I get that information [about
20 support].”(FG2)
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23 **Experience of trial participation**

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26 Many patients perceived themselves as a guinea pig with regards to side effects. Despite
27 this perception, the majority of patients reported receiving personalised care and some
28 participants discussed how the trial team were able to rearrange their appointments to fit in
29 around their priorities. However there were a few patients who felt they were treated
30 impersonally.
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38 *“the clinical trials team were I felt tailoring their treatment of me.”(24F56)*
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41 *“it didn't feel personal; it felt as though I was being treated as a number that was*
42 *insignificant.”(22F52)*
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46 One of the main concerns for patients was disclosing side effects from the clinical trial,
47 for fear of being taken off the trial, especially among those who felt the trial was their only
48 treatment option. Some patients who did disclose side effects even reported “down playing”
49 side effects and/or regretting disclosing side effects due to being taken off the trial.
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3 *“is the most frightening thing because you say, at that point in time when you come off*
4 *that point when you've been given, this is your one hope to live and somebody says,*
5 *I'm just going to take it away from you, and that's the end of the matter.” (FG2)*
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10 One patient who was taken off the trial admitted they would be reluctant to disclose
11 side effects if they participated in future trials. Other patients discussed the internal conflict of
12 the fear of being taken off the trial and the risk to themselves if they did not disclose side
13 effects. A few patients highlighted the fact that by not disclosing side effects they may be
14 compromising the trial and patients own safety.
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21 *“and I made the mistake of telling them about some of the side effects” (FG2)*
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24 *“if you don't tell them about it, then you're compromising not only the trial but you're*
25 *compromising yourself more importantly.”(FG2)*
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29 Patients felt they needed more information from the research team about what would
30 happen if they experienced side effects. They felt patients needed to be aware that
31 experiencing side effects does not always result in withdrawal from the trial, and instead the
32 dosage may be reduced.
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39 *“if they[trial team] said to you that if you were to disclose the side-effects you're having,*
40 *that they would be more likely to change your treatment levels or do something about*
41 *it, other than say on or off because it's the fear of the on or off is the most frightening*
42 *thing”.(FG2)*
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48 **Impact of trial participation**

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51 Trial participation affected many aspects of a participant's life including their QoL, their free
52 time, their finances, and their family. Patients highlighted the need to fit their life around the
53 trials schedule (due to the frequency and long duration of trial days, and travelling to the
54 hospital). Patients frequently stated once the trial had finished they could *get their “life back.”*
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3 *"It's an impact on your life having to come in every two weeks, especially the thing I*
4 *was on initially was an all-day effort"* (FG2)
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8 The impact on QoL was mixed. Some patients believed their QoL had improved, for
9 example they were once again able to perform activities that they had been unable to due to
10 ill health. In contrast other patients were unable to partake in regular activities or trips away,
11 due to side effects or their frequent hospital visits, with some of these visits requiring
12 inpatient admission.
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19 *"I was in and out like a yo yo And I didn't realise it was the trial"*(14M66)
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23 *"Our life has changed absolutely beyond recognition. I had a good job and we were*
24 *very active, cycled everywhere and went diving on holiday and all of those things which we*
25 *can't do now"*(24F56)
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30 Patients discussed the burden of clinical trials on their time, due to frequency and
31 duration of hospital visits. Some patients reported requiring the next day to recover and rest,
32 so perceived they had "lost" another day due to the trial. However, patients reported some
33 benefits to their frequent hospital visits. This included seeing experienced doctors and
34 additional monitoring, care, and support they perceived they would not receive with standard
35 treatment. Patients reported a lot of waiting around, which was tiring but understandable.
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45 *"the frequency of the visits is good and bad, as I say It's travelling every week but*
46 *having that line of contact and support weekly is great."* (24F56)
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50 An unanticipated impact of the trial was on patients and their significant others
51 holidays and trips away. This was due to the trials schedule preventing them from going
52 away for their preferred duration. Patients also perceived their participation in the trial
53 affected patients' ability to get travel insurance. There were also concerns around what
54 would happen if the patient became ill during their travels and if the treatment they received
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3 from other hospitals could react with trial treatment or affect trial participation. Limitation to
4 travel was especially difficult for patients who were unable to see their family who lived
5 abroad.
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10 Patients felt their participation on a clinical trial was a shared experience with their
11 families and discussed the psychological impact of trial participation on their family and
12 friends. Some patients felt their spouses were “trapped” or they were a “burden” to their
13 family. While others mentioned their family/friends had to change their usual activities due to
14 their participation in the trial. Patients highlighted the need for support for their family/friends.
15 Many patients felt it was crucial that clinical trial teams ask family/friends about the impact of
16 the trials on them as well.
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26 *“It’s a really valid question to ask around carers and family members and how are they*
27 *coping”*(26F48)
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30 *“it’s difficult for my daughter because she had her studies and she came with me*
31 *every time”*(29M55)
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36 Some patients described the financial burden of participating in a trial, due to travel
37 costs, as well as food and drinks needed during visits. These patients were not aware of any
38 financial aids available.
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43 *“It costs you a lot of money”*(07F61)
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46 Patients also mentioned during the screening process they experience anxiety and
47 depression around not knowing if they were eligible for the trial. Patients also mentioned
48 they feared their trial space may go to another patient whilst waiting for their results, as they
49 were aware the trials had limited spaces. One patient even said they felt rushed to make a
50 decision.
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57 *“Depressed. it got me down, the waiting”*(28F72)
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3 *“So I’m on the waiting list. They may pick somebody else. I don’t know.” (25M83)*
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6 **DISCUSSION**

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9 The study explored the experience of patients who were screened and/or recruited onto an
10 ECM clinical trial. Overall the majority of patients had a positive experience and perceived
11 the care they received as patient-centred. To aid decision-making regarding initial and
12 continued participation patients identified several areas which could be improved (a) the
13 simplification of trial information (b) more information on side effects, (c) regular updates on
14 their response to the treatment, and (d) to be informed of alternative options. Patients also
15 needed more information about support available for themselves and their family members.
16 Patients admitted to being reluctant to inform clinical trial teams about side effects they were
17 experiencing.
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29 Patients found the information about the trials too scientific and difficult to understand,
30 which is consistent with previous studies.[7, 10-11] Patients also wanted more information
31 about the risk of side effects but also mentioned how daunting the long list of side effects
32 could be. However, patients seemed to focus on the personal benefit they hoped they would
33 get from the trial rather than the potential side effects. Previous studies have shown patients
34 often have unrealistic expectations about the benefit they will receive and their reduced
35 susceptibility to side effects when compared with other patients.[12-17] In order to make the
36 information easier to read and ensure patients fully understand what they are consenting to
37 and the potential risks, Donovan has recommended interviews with patients reviewing study
38 documentation to identify any aspects that are unclear or could be misinterpreted.[18]
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51 Misinterpretation of the trial information provided could lead to ‘false hope’ (the patient
52 hopes the treatment results in a cure, improvement of health, or prolongation of life).[19].
53 False hope may have also been caused by patients overestimating the personal benefit of
54 clinical trials (therapeutic misconceptions) or by the clinical trial team emphasising the
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3 benefits of being on a trial (regular appointments, great care, extra attention to their health,
4 and potential benefit for future patients).[12, 17, 19] These patients with 'false hope'
5 perceived their ability to cope with bad news had been reduced and feelings of frustration
6 and disappointment were amplified and more destructive.[19] This also may call into
7 question whether the patient gave fully informed consent. Early phase dose escalation trials
8 are not designed to provide personal medical benefit to patients of the trial,[14] yet this is
9 often a reason for participation, therefore the unlikelihood of personal benefit may need to be
10 emphasised more clearly to patient.[13-14,20-25] From the current evidence,[14, 21-22] it
11 seems that the hope to obtain medical benefit is not indicative of compromised informed
12 consent. However, when introducing patients to trials and providing them with possible
13 treatment options there is a need for equipoise (the assumption that there is not one 'better'
14 treatment option).[18, 26-27] Any inkling of preferential treatment combined with the patient's
15 belief that doctors and nurses act in the patient's best interest, could lead to patients feeling
16 they have been given false hope.[3,18]

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34 A few patients reported feeling rushed to make a decision; these patients had anxieties
35 that if they did not decide quickly they may lose the trial to another patient. It is crucial that
36 patients are given the time and information they require, to make a fully informed decision
37 about trial participation. The patient's anxieties may have been caused by the patient's
38 therapeutic misconceptions or unrealistic expectations that the trial will benefit them
39 combined with the knowledge that early phase trials recruit small numbers of patients across
40 multiple sites.[12, 22] The clinical trial teams may need to consider these factors when
41 discussing trial participation. In addition the wording used to inform patients they are
42 "eligible" may also affect patient's decision-making regarding trial participant. Previous
43 studies have found patients reported feeling "lucky" or "honoured" they were eligible for a
44 trial, as it gave them another chance for a cure.[26, 28] Therefore it was important to also
45 capture their experiences of being screened and failing to meet the eligibility criteria for a
46 clinical trials. [3, 4] Those who were ineligible felt disappointed and as if they were out of

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3 options. Brown et al. found patients suggested instead of “eligible” the phrase “the trial is
4 suitable for you” could be used, as the phrase was perceived to objectify the study and
5 highlight there may be other treatment options which are also suitable for the patient. In
6 addition the use of “unsuitable” may minimise the disappointment felt by those ineligible for
7 the study.[26]
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14 To aid decision making regarding continued participation in early phase clinical trials,
15 patients desired regular updates about their response to trial treatment. Patients also desired
16 information about other patients’ experiences of side effects while on the trial and response
17 to the trial and more detailed feedback about the trial progress (i.e. recruitment and
18 retention). Previous studies also found patients desired feedback and regular updates on the
19 trials results and patients frequently share information with each other about side effects and
20 their experience on the trial.[24, 29-30] Providing information about other patients’
21 experiences may be feasible depending on the information received from the trial sponsor.
22 However, it is important to ensure the information is presented in a way that does not lead to
23 false hope emphasising that there are no guaranteed benefits or side effects, and that
24 patients have different reactions to treatment.
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38 For the majority of early phase trials the main aim is to investigate the safe dosage
39 range and side effects experienced by patients.[3] Therefore to ensure patients safety and
40 validity of the trial, it is crucial patients are honest about the side effects and severity of side
41 effects they are experiencing.[12] Yet many patients admitted holding back information about
42 side effects due to fear of being taken off the trial.
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49 The disclosure of side effects is likely influenced by the patients beliefs.[12, 28]
50 Previous studies have found trial patients believed that the higher the dose the more
51 effective the trial treatment is and that side effects were caused by effective treatment.[31-
52 32]. In order to reduce fear and address any misconceptions detailed information regarding
53 dose level and effectiveness, and the possible outcomes if they were to disclose side effect,
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3 such as dose reduction) could be incorporated into a question prompt list (is a list comprised
4 of standard questions, which prompt discussion between patient and doctor).[13, 34]
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6 However, further research is required to see if providing this information would reduce
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8 under-reporting of side effects.
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12 Another possible option to improve accuracy of reporting side effects is the integration
13 of electronic Patient Reported Outcomes (ePROs) in clinical trials. Patients often delay
14 reporting side effect which can lead to their effect being minimised [16, 33-34]. The
15 integration of ePROs enables regular monitoring of patients side effects and can improve the
16 accuracy and timing of reporting side effects.[36-37] EPROs aid real time data collection,
17 which can be used to notify their clinical trial team of adverse events, allowing for earlier
18 clinical decisions. In addition relevant medical advice, tailored to the patients response, can
19 be provided.[38] Therefore, enhancing the patients quality of care and communication with
20 their clinical trial team.[39]
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32 Participation in clinical trials led to a reduced QoL for some patients. However, some of
33 these patients were not aware their poor health was due to treatment toxicity from the trial
34 and attributed it to their cancer instead. Some of these patients may have limited life
35 expectancy [3] and the quality of that time left may be more important than staying on the
36 trial. Therefore, clinical trial teams should have on-going discussions throughout the trial
37 about the patient's trial response, the risks and benefit of trial continuation, and other
38 treatment options including palliative care. These discussion may enable patients to make
39 fully informed choices and find a balance between trial participation and QoL.[3, 40]
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50 As well as impacting the patient's QoL, research has shown trial patients can
51 experience undesirable side effects, which can have a negative impact on patient's
52 psychological wellbeing.[5] Yet the majority of patients felt they did not need
53 emotional/psychological support. Despite this perception, patients experienced psychological
54 distress (anxiety and/or depression) at various points throughout the trial (initial screening to
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3 determine if patients were eligible or awaiting test results). Previous research has also
4 shown patients impacted either physically or psychologically may benefit from specialist
5 palliative care.[41] However, due to the conflicting beliefs (that palliative care is for end of life
6 whereas the trial provides hope for another treatment option) patients were less likely to
7 access specialist palliative care.[41] The clinical trial teams may need to provide more
8 information and education about the supports available to patients and the potential benefit
9 of specialist palliative care alongside trial treatment. [41]
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19 Trial participation can require both the patient and their families' time, physical and
20 emotional energy, and some parts of their lives to be put on hold.[40] Due to this patients felt
21 that it was important that their family had psychological, financial, and/ or practical support.
22 Family and friends acting in a caregiver role (this includes management of medications and/
23 or appointment schedules, providing emotional support and/ or physical care, and managing
24 finances) commonly experience burden and depression.[42] This perception of caregivers life
25 being on hold was also found in patients with advanced cancer, but was only perceived by
26 patients when the caregiver was their child.[43] In addition caregivers of trial patients
27 experience greater distress and anxiety than population norms of caregivers of cancer
28 patients.[44] If anxiety and depression are untreated it can lead to both poor physical and
29 mental health, as well as reduced QoL for carers and potentially patients as well.[42] Despite
30 this, very few patients knew if there was any support available to their family and friends,
31 other than the medical support provided by the clinical trials team. The clinical trial team
32 should provide information about various support service available to both the patient and
33 their family throughout the trial. However, there is minimal literature on the most effective
34 support for carers of cancer patients and further research is required to identify the support
35 needs of carers.[42]
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55 **Limitations**

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3 One of the studies limitations is the cross-sectional nature of the study which may limit the
4 data about their experiences and perspectives throughout the trial process. Future studies
5 could use a longitudinal design targeting people at the various stages (initial introduction to
6 the trial, screening, consenting, experience of first treatment, on-going experience on the
7 trial, and, withdrawing from the trial). Secondly the study was limited in the samples ethnic
8 diversity and therefore non-representative of the area where the data was collected. Finally
9 the study recruited participants from a single site comprehensive cancer centre, patients'
10 experiences may vary across hospitals.
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21 **Conclusion**

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23 Overall the study has improved our understanding of patients' experiences of being
24 screened and/or recruited onto a clinical trial. Our findings found patients required the
25 simplification of trial information and required more information about side effects, support,
26 their response to trial treatment and trial progress. Due to trial burden and impact on patients
27 QoL on-going discussions are required to help patients find the balance between QoL and
28 trial participation.
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37 **Contributors:** J.Y and S.T developed the study design. J.Y has supervised the study. C.S
38 and JY analysed the materials. CS and LP wrote the manuscript. J.Y, S.T, L.C, N.C, M.K,
39 D.G, F.T, and M.D, have given substantial input throughout the development and writing of
40 the paper. J.T (patient representative) was involved with the study design and discussion of
41 main themes.
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49 **Funding:** The study was funded by Manchester Experimental Cancer Medicine Centres
50 (ECMC) and The Christie CRF Charity, there is no grant number for this award. The study
51 was supported by the NIHR Manchester Biomedical Research Centre.
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56 **Conflicts of Interest:** The authors declare that they have no conflict of interest.
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3 **Ethics approval:** Ethical approval was gained from the appropriate Research Ethics
4 Committee (reference number 18/SC/0299) and the local NHS Trust.
5
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8 **Data sharing statement:** The interview transcripts are available to show proof of the paper.
9
10 However, they would only be available for legal purposes. They are confidential and can only
11 be given access to in case of legal Requirements
12
13

14
15 **Acknowledgements:** Patients, Carer's, the Christie Experimental Cancer Medicine Team.
16 We would also like to thank Elaine Blowers, Rana Lee, Grant Punnett, and Sarah Bellhouse
17 for their help with the study. We would also like to thank J.T for all their help with the study.
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For peer review only

BMJ Open

Oncology patients' experiences in experimental medicine cancer trials: a qualitative study

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2020-047813.R1
Article Type:	Original research
Date Submitted by the Author:	24-Jun-2021
Complete List of Authors:	Sawyer, Chelsea; The Christie NHS Foundation Trust, CPRC Preston, Laurie; The Christie NHS Foundation Trust, Christie Patient Centred Research Taylor, Sally; The Christie NHS Foundation Trust Christie Patient Centred Research, Christie Patient Centred Research Davies, Michelle; The Christie Hospital NHS Trust, The Experimental Cancer Medicine Team, Carter, Louise; The Christie NHS Foundation Trust, The Experimental Cancer Medicine Team; The University of Manchester Division of Cancer Sciences Krebs, Matthew; The Christie NHS Foundation Trust, The Experimental Cancer Medicine Team, Manchester; The University of Manchester Faculty of Biology Medicine and Health, Division of Cancer Sciences Cook, Natalie; The Christie NHS Foundation Trust, The Experimental Cancer Medicine Team, ; The University of Manchester Division of Cancer Sciences Graham, Donna; The Christie Hospital NHS Trust, The Experimental Cancer Medicine Team; The University of Manchester Division of Cancer Sciences Thistlewaite, Fiona; The Christie Hospital NHS Trust, The Experimental Cancer Medicine Team; The University of Manchester Division of Cancer Sciences Yorke, Janelle ; The Christie NHS Foundation Trust Christie Patient Centred Research, Christie Patient Centred Research (CPCR); The University of Manchester, Division of Nursing, Midwifery and Social Work; School of Health Sciences
Primary Subject Heading:	Oncology
Secondary Subject Heading:	Qualitative research
Keywords:	Adult oncology < ONCOLOGY, QUALITATIVE RESEARCH, Clinical trials < THERAPEUTICS

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3 1 **Oncology patients' experiences in experimental medicine cancer trials: a qualitative**
4 2 **study**
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22 **Abstract**

23 **Objectives:** The study aimed to explore patients' experiences of early phase Experimental
24 Cancer Medicine (ECM) clinical trials.

25 **Design:** The study's design was qualitative. Two focus groups with patients were
26 undertaken followed by semi-structured interviews, to explore patients' experiences of ECM
27 clinical trials. Interviews and focus groups were audio-recorded and transcribed verbatim.
28 Data were analysed using thematic analysis.

29 **Setting:** A regional cancer centre (tertiary care) in North-West England.

30 **Participants:** Twelve patients (aged 52-89) participated in one of the two focus groups and
31 twenty-two patients (aged 42-83) participated in interviews.

32 **Primary outcome measure:** Patients' experiences of an ECM trial.

33 **Results:** Four main themes were identified from the analysis: decision-making, information
34 needs, the experience of trial participation, and impact of trial participation. Subthemes are
35 presented in the manuscript.

36 **Conclusion:** To make fully informed decisions about trial participation, patients required the
37 simplification of trial information and wanted more information about side effects, their
38 response to trial treatment, and the overall trial progress throughout the trial. Patients
39 highlighted the need for improvement for the support provided to their family and friends.

41 **Strengths and Limitations**

- 42 • The study explored the perspectives of a diverse group of patients approached to
43 participate in early phase clinical trials, allowing the study to capture an abundance of
44 experiences. Aspects of diversity included age range, duration on trial, disease

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3 45 group, and phase of the trial. Patients who had been ineligible or withdrawn from the
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5 46 trial were also included.
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8 47 • The study generated comprehensive and detailed insights as interviews were
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10 48 conducted to build on experiences highlighted in focus groups, and interviews were
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12 49 conducted until data saturation.
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15 50 • A limitation is the cross-sectional nature of the study, experiences and perspectives
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17 51 may change throughout the trial process.
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20 52 • Participants were recruited from one comprehensive cancer centre, patients'
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22 53 experiences may vary across hospitals.
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56 INTRODUCTION

57 Experimental cancer trials (or early phase clinical trials) play an important role in progressing
58 and advancing cancer treatments. It is estimated in the United Kingdom (UK) one in five
59 cancer patients participate in clinical trials.¹ Early phase clinical trials (defined as Phase I
60 and non-randomised phase II) are designed to assess the safety of novel drugs,
61 pharmacodynamics, and pharmacokinetics.² The drug doses is gradually increased Phase I
62 trials, to explore safety and the best dose. In phase II trials the efficacy of the drug is
63 evaluated, side effects and safety are also investigated. Early phase clinical research
64 primarily focuses on physical outcomes of experimental therapies, including appropriate drug
65 dosing, treatment toxicities, survival, and response rate.² Within the protocol and trial design,
66 limited attention is afforded to patient experience, consequently, little is understood about the
67 personal impact of trial participation.³

68 Understanding patient experience is of particular importance concerning early phase
69 trials, where significant adverse events associated with treatment toxicity may outweigh
70 possible therapeutic benefit.⁴ Undesirable side effects are an important factor in shaping
71 patients' experiences of trial involvement, influencing their psychological wellbeing and
72 sense of hope, and in some instances increased participants' fear of death.⁵ Furthermore,
73 patients may not fully understand the burden and demands of participation in clinical trials,
74 and the impact trial participation could have on their and their loved one's quality of life.³

75 Despite the various physical, emotional and practical challenges, patients generally
76 report positive experiences of trial participation and feel an increased sense of "control" over
77 their illness.⁵ Moore suggested trial participation reflects a coping strategy against
78 hopelessness.⁶ When standard treatment is ineffective, clinical trials are perceived by some
79 to offer a 'second chance' at finding a cure.³ Early phase trials can be perceived by others to
80 be a "last-ditch effort" for patients who are otherwise considered to have exhausted all other
81 treatment options.⁴ Cox also found participants derived comfort from being closely monitored

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3 82 by clinicians due to the belief they were in 'expert' hands, and in providing a sense of
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5 83 purpose through helping others.³ However, patients often misunderstand trial information,
6
7 84 their understanding and the meanings patients ascribe to their participation will determine
8
9 85 how they make sense of their experiences throughout the trial process.⁷
10
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12 86 Patient experience is considered to be an integral component of excellent healthcare.⁸ As
13
14 87 outlined in the NHS Outcomes Framework, a deeper understanding of patient perceptions of
15
16 88 trial involvement will drive quality improvement and aid learning.⁸ Yet there is limited
17
18 89 understanding of patients' experiences of participating in early phase clinical trials. Due to
19
20 90 the aims of early phase trials and the uncertainties around drug side effects and safety, the
21
22 91 present study aimed to explore the experiences of participants in early phase ECM clinical
23
24 92 trials.
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28 93 **METHOD:**

29 30 31 94 **Study Design**

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34 95 In this qualitative study, focus groups were conducted first to explore patients' experiences
35
36 96 of ECM trials and capture main themes/experiences, which were explored in more depth in
37
38 97 semi-structured interviews.⁹ The same topic guide was used for focus groups and interviews
39
40 98 (Appendix 1). Questions captured patients' experiences of trial introduction and participation
41
42 99 and their decision-making process regarding participating in the trial they were offered.
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45 100 **Sample/data collection**

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47
48 101 Participants were recruited from a regional cancer centre in North-west England. The
49
50 102 inclusion criteria for the study were (a) any cancer type, and (b) anyone who has been
51
52 103 screened for an observational trial or a phase I-II ECM trial. Participants were excluded if
53
54 104 they were unable to provide informed consent, or comprehend written English.
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3 105 The clinical team identified potential participants, who were approached by the
4
5 106 research team, who explained the study and provided written information. Participants were
6
7 107 given the opportunity to ask any questions about study participation or the information
8
9 108 provided. Written informed signed consent was obtained. Twenty-one face-to-face interviews
10
11 109 were conducted in a quiet hospital room and one face-to-face interview was conducted at
12
13
14 110 the patient's home, determined by the patient's preference.

15
16 111 Both focus groups were conducted face-to-face in a quiet hospital room. The
17
18 112 interviews and focus groups were audio-recorded and lasted from 14 to 62 minutes and 48
19
20 113 to 108 minutes, respectively. Ethical approval was gained from South central-Oxford b
21
22 114 Research Ethics Committee (reference number 18/SC/0299) and the local NHS Trust.

23
24
25
26 115 Figure 1. Present the study's recruitment process. Participant demographics are presented
27
28 116 in Table 1.

29
30
31 117 *Insert Figure 1. here Study flow diagram*

32
33
34 118 *Insert Table 1. here Participants' demographic information*

35
36
37 119 **Table 1. Participants' demographic information**

	Interviews (n = 22)	Focus groups (n =12)
Age range (years (Median))	42 – 83 (65.5)	52-79 (68.5)
Gender (female %)	59%	8%
Ethnicity %		
White British	95%	100%
Chinese	5%	
Marital status (%)		
Single	4.55%	16.67%
Married/domestic partner	90.91%	66.67%
Widowed	4.55%	8.33%

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2			
3	Divorced	-	8.33%
4			
5	Employment status (%)		
6			
7	Self-employed	-	8.33%
8			
9	Retired	75.00%	83.33%
10			
11	Unable to work	18.75%	8.33%
12			
13	Homemaker	6.25%	-
14			
15	Performance status (%)		
16			
17	0	52.94%	45.45%
18			
19	1	47.06%	54.55%
20			
21	Type of trial n (%)		
22			
23	Patients who are considered	2 (9%)	-
24	for the trial and then deemed		
25	ineligible (are often referred to		
26	as 'screen fail')		
27			
28	Observational	2 (9%)	-
29			
30	Phase I	9 (41%)	7(67%)
31			
32	Phase II	9 (41%)	5 (33%)
33			
34	Time on trial (<1 year, %)	54.55%	50%
35			
36	Disease group		
37			
38	Breast	31.82%	-
39			
40	Colorectal	13.64%	16.67%
41			
42	Head & Neck	-	8.33%
43			
44	Haematological	9.09%	-
45			
46	Lung	22.73%	16.67%
47			
48	Leukemia		8.33%
49			
50	Lymphoma	18.18%	41.67%
51			
52	Penile	4.55%	-
53			
54	Renal	-	8.33%
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3 121 **Data analysis**
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6 122 The interviews and focus groups were analysed by hand using an inductive thematic
7
8 123 approach.¹⁰ The six-phase guidelines of Braun and Clarke were used to analyse the data,
9
10 124 the first step was familiarisation with the data.¹⁰ Two authors (J.Y, C.S) explored themes in
11
12 125 the data from an initial transcript and produced a document outlining key themes and
13
14 126 findings. Two reviewers then coded an additional three transcripts and compared these to
15
16 127 determine inter-rater reliability (86%). One researcher (CS) subsequently coded the
17
18 128 remaining transcripts. Themes and interpretations of the data were discussed in regular
19
20 129 meetings (J.Y, C.S).
21
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24 130 **Patient and Public Involvement:**
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27 131 The patient representative is a patient with secondary breast cancer, who has participated in
28
29 132 an early phase clinical trial. They reviewed and provided feedback on all study documents
30
31 133 including participant information sheets, informed consent form, and interview schedule.
32
33 134 Once the interviews were analysed the main themes were discussed with the study team
34
35 135 and patient representative, who all provided feedback. A letter providing a summary of the
36
37 136 study's results will be sent to all participants who stated they would like to receive the
38
39 137 summary.
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43 139 **Reflexivity:**
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46 140 Interviews were conducted sensitively by five researchers (J.Y, C.S, R.L, S.B, D.C) who
47
48 141 were not part of the patients' clinical team and all have experience in interviewing people
49
50 142 with cancer or regarding sensitive topics (self-harm). The analysis was discussed with the
51
52 143 research team (J.Y, C.S, L.C, M.D). All members of the research team have relevant
53
54 144 research or clinical experience. Researchers conducted balanced interviews and focus
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56 145 groups, and reminded patients the research team was not involved in the clinical trial.
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3 146 **RESULTS**
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5 147 We identified four main themes: decision-making, information needs, the experience of trial
6 participation, and impact of trial participation. The subthemes are described below with
7 148 supporting quotations provided in table 2.
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12 150 *Insert table 2 here*
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151 **Table 2 Presents the themes and their sub-themes with supporting quotations.**

1. Decision-making	
1.1 Decision maker	<p><i>"It was mine [decision]. It's got to be, it's my life."</i>(25M83)</p> <p><i>"I think the consultants made the decision about what was most suitable."</i>(28F72)</p> <p><i>"The whole family read it, all my children, my husband. We discussed it, come back and said yes."</i> (07F61)</p>
1.2 No other option	<i>"I had no other choice, so at the end of the day, that's the one."</i> (25M83)
1.3 Hope	<i>"There's that hope there that the...a chance of a cure."</i> (19M56)
2. Information needs	
2.1 Volume & simplicity of information	<p><i>"doctors know all the technical terms, but we don't, most of us; and it has to be said in plain English"</i>(22F52)</p> <p><i>"I don't remember anybody saying, before you go on this, your thyroid could do this, and it will be permanent"</i>(23F68)</p>
2.2 Side effects	<i>"Well I think the list of possible side effects is they just think of everything they can think of that might go wrong and list them all down"</i> (FG2)
2.3 Updates throughout treatment	<i>"I want him to say to me, now look here, if this doesn't work it's chemo."</i> (21F70)
2.4 Provision of False hope	<i>"if they hadn't built my expectation, then the crash wouldn't have been as hard"</i> (03M42)
2.5 Support available	<i>"you do feel that there's a void like, you know, where do I get that information [about support]."</i> (FG2)
3. Experience of trial	
3.1 Patient centred	<p><i>"the clinical trials team were I felt tailoring their treatment of me."</i>(24F56)</p> <p><i>"it didn't feel personal; it felt as though I was being treated as a number that was insignificant."</i>(22F52)</p> <p><i>"is the most frightening thing, at that point in time when you come off that point when you've been given, this is your one hope to live and somebody says, I'm just going to take it away from you, and that's the end of the matter."</i> (FG2)</p> <p><i>"and I made the mistake of telling them about some of the side effects"</i> (FG2)</p>
3.2 Disclosing side effects	<p><i>"if you don't tell them [side effects], then you're compromising not only the trial but you're compromising yourself more importantly."</i>(FG2)</p> <p><i>"if they [trial team] said to you that if you were to disclose the side-effects you're having, that they would be more likely to change your treatment levels or do something about it, other than say on or off because it's the fear of the on or off is the most frightening thing"</i>.(FG2)</p>
4. Impact of trial participation	
4.1 Quality of Life (QoL)	<p><i>"It's an impact on your life having to come in every two weeks, especially the thing I was on initially was an all-day effort"</i> (FG2)</p> <p><i>"I was in and out like a yo yo And I didn't realise it was the trial"</i>(14M66)</p> <p><i>"Our life has changed absolutely beyond recognition. I had a good job and we were very active, cycled everywhere and went diving on holiday and all of those things which we can't do now"</i>(24F56)</p>

4.2 Time	“the frequency of the visits is good and bad, as I say It’s travelling every week but having that line of contact and support weekly is great.” (24F56)
4.3. Family	“It’s a really valid question to ask around carers and family members and how are they coping”(26F48)
4.4 Financial	“it’s difficult for my daughter because she had her studies and she came with me every time”(29M55)
4.5 Psychological impact	“It costs you a lot of money”(07F61)
	“Depressed. it got me down, the waiting”(28F72)
	“So I’m on the waiting list. They may pick somebody else. I don’t know.” (25M83)

152 Quotes from the interviews are presented as participant’s ID, gender (M=male, F=female), and age (in years). Quotes from the focus groups
 153 are presented as FG and number (1 or 2).

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3 154 **Decision-making**
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6 155 *Decision-makers*
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9 156 Patient preference regarding involvement in decision-making varied. Some patients
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11 157 highlighted the importance of including family and friends in their decisions, whereas others
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13 158 felt it was only their decision to make. Due to difficulties understanding the information,
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15 159 uncertainties around trials, and patients' perception of doctor's expertise, some patients
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17 160 relied on the doctors to make the best decision for them.
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20 161 *No other option*
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23 162 A few patients perceived clinical trials as their only option and for those who were
24
25 163 ineligible for the trial, this view led to feelings of despair and uncertainty about their options.
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27 164 Conversely, the majority of patients felt clinical trials provided them with another treatment
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29 165 option. This was particularly important for patients who did not want the alternative treatment
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31 166 options.
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34 167 *Hope*
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36
37 168 Clinical trials provided the majority of patients with hope. For some it was a potential
38
39 169 chance for a cure, stopping the progression of their cancer, and/or extending their life. While
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41 170 others hoped their participation would help others with cancer in the future.
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45 171 **Information needs**
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48 172 *Wealth/volume and simplicity of information*
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51 173 Patients wanted enough information about their choices to make the best decision regarding
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53 174 their treatment. Patients highlighted the need for more simplified information, as the
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55 175 information they received regarding trials was scientific and sometimes difficult to
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57 176 understand.
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3 177 *Side effects*
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6 178 Patients were divided on whether they had received enough information about possible side
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8 179 effects of the trial before participation, with some patients reporting they were not fully
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10 180 informed. Patients recognised it might not always be possible to provide this information, as
11
12 181 the purpose of clinical trials is to identify side effects. One patient felt the risk of permanent
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14 182 side effects had not been fully explained to them, and prior knowledge of this risk would
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16 183 have affected their decision to participate.
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19 184 *Updates throughout treatment*
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22 185 During the trial, patients wanted updated information regarding i) their response to the
23
24 186 treatment, ii) alternative options to the trial, iii) the success of the overall trial to date, and iv)
25
26 187 the experiences of other patients on the trial. This information helped them to re-evaluate
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28 188 their trial involvement and make decisions about future participation.
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31 189 *Provision of False hope*
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34 190 A few patients felt they received false hope and were misled about potential personal
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36 191 benefit from trial participation. These patients believed this false hope reduced their ability to
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38 192 cope with updates regarding no or negative response to the trial. These patients felt
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40 193 information about possible outcomes of the trial should not focus on potential benefits but
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42 194 highlight the risks and possibilities the trial may not work, even if the trial has previously had
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44 195 some positive results.
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48 196 Patients who were ineligible for the trial (screen fail) recalled how upsetting it was to be
49
50 197 told they were ineligible. One patient even stated it felt like a “death sentence”.
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53 198 *Support available*
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56 199 Patients were informed of whom to contact if they required medical support. However,
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58 200 many were unaware of the psychological support available and could not recall doctors
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3 201 discussing psychological support options. Some patients who knew support was available
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5 202 highlighted the psychological support was not always accessible to patients and/or their
6
7 203 families due to the length of treatments and distance travelling to the hospital. The majority
8
9 204 of patients did not know if there was any psychological/financial/practical support available
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11 205 for family members.
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14 206 **Experience of trial participation**

17 207 *Patient-centred*

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20 208 Many patients perceived themselves as a guinea pig concerning side effects. Despite this
21
22 209 perception, the majority of patients reported receiving personalised care and some
23
24 210 discussed the flexibility to fit appointments around their priorities. However, a few patients
25
26 211 felt their treatment was impersonal.
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29 212 *Disclosing side effects*

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32 213 *The* main concern for patients was disclosing side effects from the clinical trial, for fear
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34 214 of being taken off the trial, especially among those who felt the trial was their only treatment
35
36 215 option. Some patients who disclosed side effects even reported “downplaying” side effects
37
38 216 and/or regretting disclosing side effects due to being taken off the trial.
39
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41
42 217 One patient who was taken off the trial admitted they would be reluctant to disclose
43
44 218 side effects in future trials. Other patients discussed the internal conflict between the fear of
45
46 219 being taken off the trial and the risk to themselves if they did not disclose side effects. Some
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48 220 patients were aware by not disclosing side effects they are compromising the trial and the
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50 221 patient's safety.
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53 222 Patients felt they needed more information from the research team about what would
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55 223 happen if they experienced side effects. They felt patients needed to be aware experiencing
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224 side effects does not always result in withdrawal from the trial, and instead, the dosage may
225 be reduced.

226 **Impact of trial participation**

227 *Quality of Life*

228 Trial participation affected many aspects of a participant's life including QoL, free time,
229 finances, and their family. Patients highlighted the need to fit their life around the trial
230 schedule (due to the frequency and long duration of trial days, and travelling to the hospital).
231 Patients frequently stated once the trial had finished they could *get their "life back."*

232 The impact on QoL was mixed. Some patients believed their QoL had improved, for
233 example, they were once again able to perform activities they had been unable to due to ill
234 health. In contrast, other patients were unable to partake in regular activities or trips away,
235 due to side effects or their frequent hospital visits, which on occasion required inpatient
236 admission.

237 *Time*

238 Patients discussed the burden of clinical trials on their time, due to the frequency and
239 duration of hospital visits. Some patients reported requiring the next day to recover and rest,
240 perceiving they had "lost" another day due to the trial. However, some benefits to frequent
241 hospital visits were reported. This included seeing experienced doctors and additional
242 monitoring, care, and support they perceived they would not receive with standard treatment.
243 Patients reported a lot of waiting around, which was tiring but understandable. Some
244 patients were frustrated when they were not informed of delays to their treatment.

245 An unanticipated impact of the trial was on patients and their significant others'
246 holidays and trips away. This was due to the trial schedule preventing them from going away
247 for their preferred duration. Patients perceived their participation in the trial affected patients'

1
2
3 248 ability to get travel insurance. There were concerns around what would happen if the patient
4
5 249 became ill during their travels and if the treatment they received from other hospitals could
6
7 250 react with trial treatment or affect trial participation. Limitation to travel was especially difficult
8
9 251 for patients who were unable to see their family who lived abroad.

252 *Family*

253 Patients felt their participation in a clinical trial was a shared experience with their
254 families and discussed the psychological impact of trial participation on their family and
255 friends. Some patients felt their spouses were “trapped” or they were a “burden” to their
256 family. While others mentioned their family/friends had to change their usual activities due to
257 their participation in the trial. Patients highlighted the need for support for their family/friends.
258 Many patients felt it was crucial that clinical trial teams ask family/friends about the impact of
259 the trials on them as well.

260 *Financial*

261 Some patients described the financial burden of participating in trials, due to travel
262 costs, as well as food and drinks needed during visits. These patients were not aware of any
263 financial aids available.

264 *Psychological impact*

265 Patients mentioned experiencing anxiety and depression, during the screening
266 process, due to uncertainties around their trial eligibility. Patients feared “their” trial space
267 could be allocated to another whilst awaiting their results, due to their knowledge of limited
268 trial spaces. One patient even felt “rushed” to make a decision.

269 **DISCUSSION**

270 Overall, the majority of patients had a positive experience and received patient-centred care.
271 To aid decision-making regarding initial and continued participation, patients identified

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3 272 several areas of improvement (a) the simplification of trial information (b) more information
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5 273 on side effects, (c) regular updates on their response to the treatment, and (d) to be
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7 274 informed of alternative options. Patients needed more information about support available for
8
9 275 themselves and their family members. Patients admitted to being reluctant to inform clinical
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11 276 trial teams about side effects experienced.

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14 277 Patients found the trial information too scientific and difficult to understand, which is
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16 278 consistent with previous studies.^{7 11 12} Patients wanted more information about the risk of
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18 279 side effects but mentioned the long list of side effects could be daunting. However, patients
19
20 280 often focused on the anticipated personal benefit they would get from the trial rather than
21
22 281 potential side effects. Previous studies reported patients often have unrealistic expectations
23
24 282 about their potential benefit and reduced susceptibility to side effects when compared with
25
26 283 other patients.^{6 13-17} To improve comprehension of information, ensure patients provide fully
27
28 284 informed consent, and understand the potential risks, Donovan recommends interviewing
29
30 285 patients while reviewing study documentation to identify any aspects that are unclear or
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32 286 could be misinterpreted.¹⁸

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36 287 Misinterpretation of the trial information provided could have led to 'false hope' (the
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38 288 patient hopes the treatment results in a cure, improvement of health, or prolongation of
39
40 289 life).¹⁹ For example, patients overestimation of personal benefit (therapeutic misconceptions)
41
42 290 or if the clinical team emphasised the benefits of being on trials (regular appointments, great
43
44 291 care, extra attention to their health, and potential benefit for future patients).^{13 17 19} False
45
46 292 hope was perceived to reduce the patient's ability to cope with bad news, and lead to
47
48 293 feelings of frustration and disappointment being amplified and more destructive.¹⁹ This calls
49
50 294 into question whether the patient gave fully informed consent. Early phase dose-escalation
51
52 295 trials may not lead to personal medical benefit to patients of the trial, yet this is often a
53
54 296 reason for participation.¹⁵ The unlikelihood of personal benefit needs to be emphasised more
55
56 297 clearly to the patients.^{14 15 20-25} From the current evidence, it seems the hope to obtain

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3 298 medical benefit is not indicative of compromised informed consent.^{15 21 22} However, when
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5 299 introducing patients to trials and providing them with possible treatment options there is a
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7 300 need for equipoise (the assumption there is not one 'better' treatment option).^{18 26 27} Any
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9 301 inkling of preferential treatment combined with the patient's belief that doctors and nurses
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11 302 act in the patient's best interest, could lead to patients feeling they have been given false
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13 303 hope.^{3 18}

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17 304 A few patients reported feeling rushed to make a decision; these patients had anxieties
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19 305 that if they did not decide quickly they may lose the trial to another patient. It is crucial
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21 306 patients are given the time and information they require, to make a fully informed decision
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23 307 about trial participation. The patient's anxieties may be due to their therapeutic
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25 308 misconceptions or unrealistic expectations about the benefit, combined with their knowledge
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27 309 of small recruitment numbers across multiple sites.^{13 22} Clinical trial teams should consider
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29 310 these factors when discussing trial participation. In addition, the wording used to inform
30
31 311 patients they are "eligible" could affect patient's decision-making regarding trial participation.
32
33 312 Patients frequently report feeling "lucky" or "honoured" they were eligible for the trial, as it
34
35 313 gave them another chance for a cure.^{26 28} Therefore it was important to capture patients'
36
37 314 experiences who were ineligible for clinical trials.^{3 4} Those who were ineligible felt
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39 315 disappointed and were out of treatment options. Brown et al. found patients suggested the
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41 316 phrase "the trial is suitable for you" could be used instead of "eligible", as the phrase was
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43 317 perceived to objectify the study and highlight the possibility of other treatment options. In
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45 318 addition the use of "unsuitable" may minimise the disappointment felt by those ineligible for
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47 319 the study.²⁶

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51 320 To aid decision-making regarding continued participation in early phase clinical trials,
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53 321 patients desired regular updates about their response to trial treatment. Patients desired
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55 322 information about other patients' experiences of side effects while on the trial and response
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57 323 to the trial and more detailed feedback about the trial progress (i.e. recruitment and
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3 324 retention). This is in line with previous studies, which also found patients frequently shared
4
5 325 information with each other about side effects and their experience on the trial.^{24 29 30}
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7 326 Providing information about other patients' experiences will depend on the information
8
9 327 received from the trial sponsor. However, it is crucial information is presented in a way that
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11 328 does not lead to false hope emphasising there are no guaranteed benefits or side effects,
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14 329 and patients have different reactions to treatment.

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16
17 330 The main aim of the majority of early phase trials is to investigate the safe dosage
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19 331 range and side effects experienced by patients.³ Therefore to ensure patients' safety and
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21 332 validity of the trial, it is crucial patients are honest about the side effects and severity of side
22
23 333 effects they are experiencing.¹³ Yet many patients admitted holding back information about
24
25 334 side effects due to fear of being taken off the trial.

26
27 335 The disclosure of side effects is likely influenced by patients' beliefs.^{13 28} Previous
28
29 336 studies found trial patients believed higher doses were more effective and side effects were
30
31 337 caused by effective treatment.^{31 32} To reduce fear and address any misconceptions
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33 338 (regarding dose level and effectiveness, and withdrawal of trial if they disclose the trial),
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35 339 these misconceptions could be incorporated into a question prompt list (a list comprised of
36
37 340 standard questions to prompt discussion between patient and doctor) highlighting dose
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39 341 reduction as an option if side effects are disclosed.^{14 33} However, further research is required
40
41 342 to see if providing this information would reduce the under-reporting of side effects.

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45 343 Another possible option to improve the accuracy of reporting side effects is the
46
47 344 integration of electronic Patient Reported Outcomes (ePROs) in clinical trials. Patients often
48
49 345 delay reporting side-effect leading to their effect being minimised.^{16 33 34} The integration of
50
51 346 ePROs enables regular monitoring of patients' side effects and can improve the accuracy
52
53 347 and timing of reporting side effects.^{35 36} EPROs aid real-time data collection, which can be
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55 348 used to notify their clinical trial team of adverse events, allowing for earlier clinical decisions,
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3 349 and provide relevant medical advice, tailored to patients' responses.³⁷ Therefore, enhancing
4
5 350 the patients' quality of care and communication with their clinical team.³⁵
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8 351 Participation in clinical trials led to a reduced quality of life for some patients and not all
9
10 352 were aware their poor health was due to treatment toxicity and attributed it to their cancer
11
12 353 instead. Some of these patients may have a limited life expectancy and their quality of time
13
14 354 left may be more important than staying on the trial.³ Therefore, clinical trial teams should
15
16 355 have ongoing discussions throughout the trial about the patient's trial response, risks and
17
18 356 benefits of trial continuation, and other treatment options including palliative care. These
19
20 357 discussions will enable patients to make fully informed choices and find a balance between
21
22 358 trial participation and quality of life.^{3 38}
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26 359 As well as impacting patient's quality of life, patients can experience undesirable side
27
28 360 effects, which can have a negative impact on patient's psychological wellbeing.⁵ Yet the
29
30 361 majority of patients felt they did not need emotional/psychological support. Despite this
31
32 362 perception, patients experienced psychological distress (anxiety and/or depression) at
33
34 363 various points throughout the trial (initial screening to determine if patients were eligible or
35
36 364 awaiting test results). Patients, who are physically or psychologically impacted, may benefit
37
38 365 from specialist palliative care.³⁹ However, due to the conflicting beliefs (palliative care is for
39
40 366 end of life whereas the trial provides hope for another treatment option) patients were less
41
42 367 likely to access specialist palliative care.³⁹ The clinical trial teams may need to provide more
43
44 368 information and education about the supports available to patients and the potential benefit
45
46 369 of specialist palliative care alongside trial treatment.³⁹
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50 370 Trial participation can require both the patient and their families' time, physical and
51
52 371 emotional energy, and some parts of their lives to be put on hold.⁴⁰ Therefore, patients felt it
53
54 372 was important their family had psychological, financial, and/or practical support.
55
56 373 Family/friends acting in a caregiver role (including managing medications, appointment
57
58 374 schedules, finances, and/or providing emotional support and/or physical care) commonly
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3 375 experience burden and depression.⁴¹ Patients with advanced cancer also perceived their
4
5 376 caregivers' lives were on hold when the caregiver was their child.⁴¹ Additionally, caregivers
6
7 377 of trial patients experience greater distress and anxiety when compared with the population
8
9 378 norms of caregivers of cancer patients.⁴² Untreated anxiety and depression can lead to poor
10
11 379 physical and mental health, as well as reduced quality of life for carers and potentially
12
13 380 patients as well.⁴¹ Despite this, very few patients knew if there was any support available to
14
15 381 their family and friends, other than the medical support provided by the clinical trials team.
16
17 382 The clinical trial team should provide information about various support services available to
18
19 383 patients and their families throughout the trial. However, there is minimal literature on the
20
21 384 most effective support for carers of cancer patients and further research is required to
22
23 385 identify the support needs of carers.^{41 42}
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25
26

27 386 **Limitations**

28
29
30 387 One limitation is the cross-sectional nature of the study, as experiences and perspectives
31
32 388 may vary throughout the trial. Future studies should use a longitudinal design targeting
33
34 389 people at various stages throughout the trial. A second limitation is the study's sample. All
35
36 390 participants are from a single comprehensive cancer centre, patients' experiences may vary
37
38 391 across hospitals and clinical trial units. However, the study has a large sample size and
39
40 392 heterogeneous population in terms of cancer diagnosis, duration of trial participation, and
41
42 393 stage of the clinical trial (only two patients interviewed were "screen fails", but it was still
43
44 394 important to capture their experiences). The ethnic diversity of the sample was limited and
45
46 395 therefore not representative of the area where the data was collected. However, recruitment
47
48 396 levels for clinical trials are lower for ethnic minority groups. The majority of trial patients are
49
50 397 white British, therefore the sample used was representative of people who usually participate
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52 398 in clinical trials.^{43 44}
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400 **Conclusion**

401 Patients require the simplification of trial information and want more information regarding
402 side effects, available support, their response to trial treatment, and overall trial progress
403 throughout the trial, to make fully informed decisions about ongoing trial participation. Due to
404 the trial burden, ongoing discussions are required to help patients find the balance between
405 quality of life and trial participation. Patients were unaware of the support available for their
406 family and wanted more support for their family.

407 **Contributors:** J.Y and S.T developed the study design. J.Y has supervised the study. C.S
408 and JY analysed the materials. CS and LP wrote the manuscript. J.Y, S.T, L.C, N.C, M.K,
409 D.G, F.T, and M.D, have given substantial input throughout the development and writing of
410 the paper. J.T (patient representative) was involved with the study design and discussion of
411 main themes.

412 **Funding:** The study was funded by Manchester Experimental Cancer Medicine Centres
413 (ECMC) and The Christie CRF Charity, the grant number for this award is A01008. The study
414 was supported by the NIHR Manchester Biomedical Research Centre.

415 **Conflicts of Interest:** The authors declare that they have no conflict of interest.

416 **Ethics approval:** Ethical approval was gained from the appropriate Research Ethics
417 Committee (reference number 18/SC/0299) and the local NHS Trust.

418 **Data sharing statement:** The interview transcripts are available to show proof of the paper.
419 However, they would only be available for legal purposes. They are confidential and can only
420 be given access to in case of legal Requirements

421 **Acknowledgements:** Patients, Carer's, the Christie Experimental Cancer Medicine Team.
422 We would also like to thank Elaine Blowers, Rana Lee, Grant Punnett, and Sarah Bellhouse
423 for their help with the study. We would also like to thank J.T for all their help with the study.

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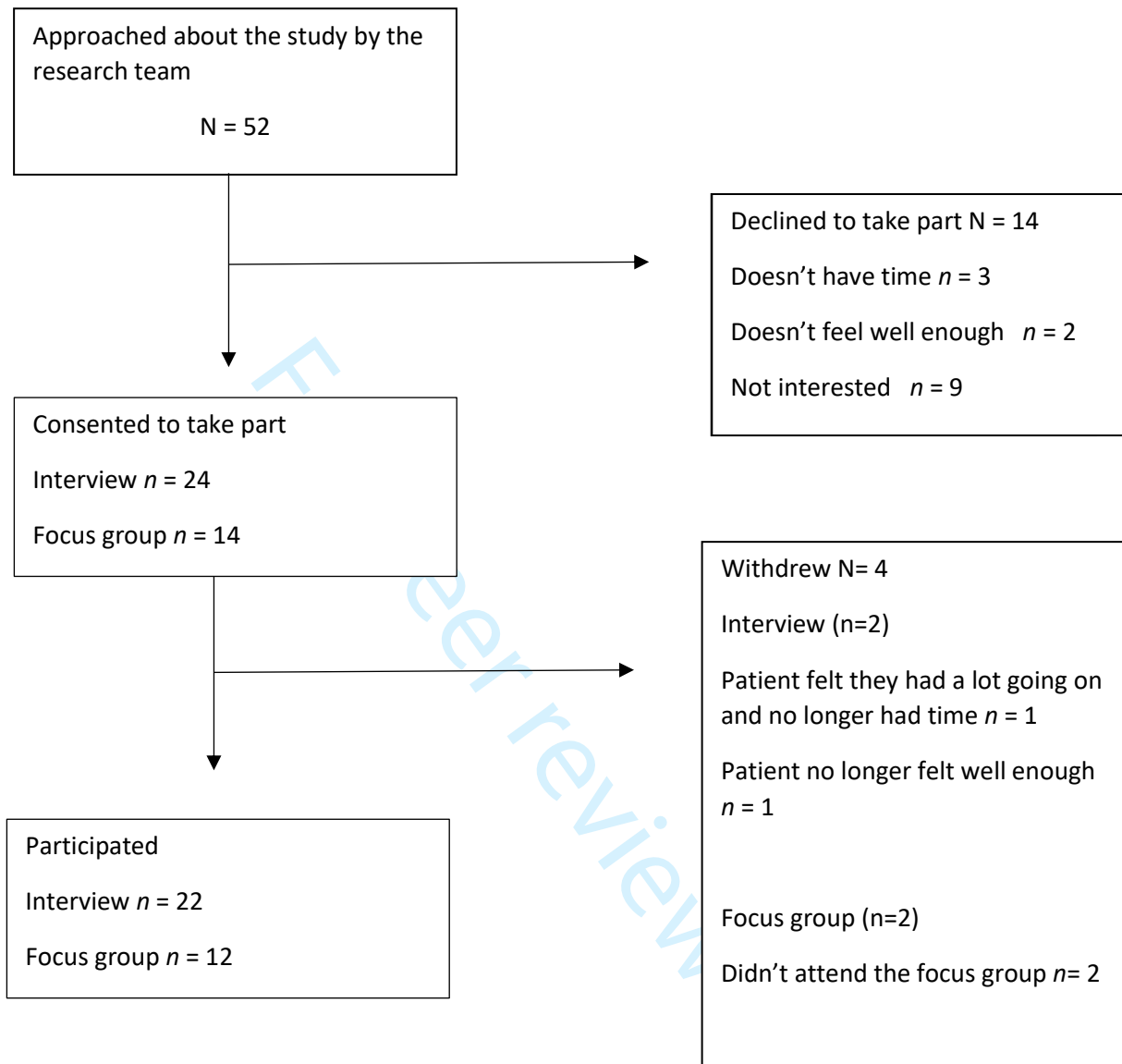
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Figure 1. Study flow diagram



Questions

Pre Trial

1. At diagnosis, how were you informed about your illness?
 - Was there anything that could have been done differently?
2. What was your understanding of the treatment?
 - Was there a discussion about different options for treatment?
 - Was there a discussion about if the treatment didn't work, how was that approached?
3. How were you involved in decisions about your treatment?
4. How did you feel after your first meeting with the doctors at the Christie?
 - Was this for a trial or standard of care?
 - Were you seen by different teams for trial and non-trial visits?
 - If so how were the visits different?
5. How was the subject of a clinical trial approached?
 - At what point was this done?
 - Was the timing appropriate for you?
6. Was there a discussion about side effects and management?
 - How was this approached?
 - What advice and information was given?
 - Did this change your decision making and how?
7. Was there a discussion about supportive care?
 - When did this take place?
 - What was discussed?
 - How did this make you feel?
 - Would you like this to have been approached differently or at a different time?
 - How did this information impact your decision making going onto a trial?
8. Were your family and friends involved if you wanted them to be?
9. Was there anything you would have like to be prioritised more?

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2
3 10. When you were told that a trial was the next option, how were you supported?
4
5 - How was the care pathway explained to you?
6
7 - Was it consistent across all members of staff?
8
9 - Was the pathway updated to suit your needs? Can you give an example?
10
11 - What could have been done differently?
12
13
14 11. What was your impression of communication between your clinical team?
15
16 - Was everyone you spoke to aware of your care path?
17
18 12. Was everything explained to you in a way that you understood, how was this done?
19
20 13. Were you given time to ask questions?
21
22 - How did you feel about asking questions?
23
24 14. Did you know who to contact if you had questions or needed support?
25
26 - How were you told about this?
27
28 - Who were you told to contact?
29
30 - What information were you given about when and why to contact?
31
32
33 15. Going onto a clinical trial, what were your expectations?
34
35 - What did you expect from the treatment?
36
37 - What did you expect from your doctors and nurses?
38
39 - Were these expectations met?
40
41 16. Did the care you receive feel personal?
42
43 - What was/could have been done to make it feel personal?
44
45
46 17. Was there anything that detracted from your care?
47
48 18. How were the visits organised?
49
50 - Did they run on time?
51
52 - What were some problems you encountered?
53
54 - Were you waiting for long periods of time?
55
56 - If so were you kept informed?
57
58 - Do you think this would have been different if you weren't on a trial and how?
59
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3 19. In a questionnaire – what questions would allow you to get your experience across?
4

5 - What would you like to be/have been asked?
6

7 20. What would you like to see change?
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9 21. Based on your experience, would you go onto another trial in the future and why?
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11 22. *Do you worry about your carers?*
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13 *What support do you think they need?*
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For peer review only

BMJ Open

Oncology patients' experiences in experimental medicine cancer trials: a qualitative study

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2020-047813.R2
Article Type:	Original research
Date Submitted by the Author:	10-Aug-2021
Complete List of Authors:	Sawyer, Chelsea; The Christie NHS Foundation Trust, CPRC Preston, Laurie; The Christie NHS Foundation Trust, Christie Patient Centred Research Taylor, Sally; The Christie NHS Foundation Trust Christie Patient Centred Research, Christie Patient Centred Research Davies, Michelle; The Christie Hospital NHS Trust, The Experimental Cancer Medicine Team, Carter, Louise; The Christie NHS Foundation Trust, The Experimental Cancer Medicine Team; The University of Manchester Division of Cancer Sciences Krebs, Matthew; The Christie NHS Foundation Trust, The Experimental Cancer Medicine Team, Manchester; The University of Manchester Faculty of Biology Medicine and Health, Division of Cancer Sciences Cook, Natalie; The Christie NHS Foundation Trust, The Experimental Cancer Medicine Team, ; The University of Manchester Division of Cancer Sciences Graham, Donna; The Christie Hospital NHS Trust, The Experimental Cancer Medicine Team; The University of Manchester Division of Cancer Sciences Thistlewaite, Fiona; The Christie Hospital NHS Trust, The Experimental Cancer Medicine Team; The University of Manchester Division of Cancer Sciences Yorke, Janelle ; The Christie NHS Foundation Trust Christie Patient Centred Research, Christie Patient Centred Research (CPCR); The University of Manchester, Division of Nursing, Midwifery and Social Work; School of Health Sciences
Primary Subject Heading:	Oncology
Secondary Subject Heading:	Qualitative research
Keywords:	Adult oncology < ONCOLOGY, QUALITATIVE RESEARCH, Clinical trials < THERAPEUTICS



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3 **1 Oncology patients' experiences in experimental medicine cancer trials: a qualitative**
4 **2 study**
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22 **Abstract**

23 **Objectives:** The study aimed to explore patients' experiences of early phase Experimental
24 Cancer Medicine (ECM) clinical trials.

25 **Design:** The study's design was qualitative. Two focus groups with patients were
26 undertaken followed by semi-structured interviews, to explore patients' experiences of ECM
27 clinical trials. Interviews and focus groups were audio-recorded and transcribed verbatim.
28 Data were analysed using thematic analysis.

29 **Setting:** A regional cancer centre (tertiary care) in North-West England.

30 **Participants:** Twelve patients (aged 52-89) participated in one of the two focus groups and
31 twenty-two patients (aged 42-83) participated in interviews.

32 **Primary outcome measure:** Patients' experiences of an ECM trial.

33 **Results:** Four main themes were identified from the analysis: decision-making, information
34 needs, the experience of trial participation, and impact of trial participation. Subthemes are
35 presented in the manuscript.

36 **Conclusion:** To make fully informed decisions about trial participation, patients required the
37 simplification of trial information and wanted more information about side effects, their
38 response to trial treatment, and the overall trial progress throughout the trial. Patients
39 highlighted the need for improvement for the support provided to their family and friends.

41 **Strengths and Limitations**

- 42 • The study explored the perspectives of a diverse group of patients approached to
43 participate in early phase clinical trials, allowing the study to capture an abundance of
44 experiences. Aspects of diversity included age range, duration on trial, disease

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3 45 group, and phase of the trial. Patients who had been ineligible or withdrawn from the
4
5 46 trial were also included.
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8 47 • The study generated comprehensive and detailed insights as interviews were
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10 48 conducted to build on experiences highlighted in focus groups, and interviews were
11
12 49 conducted until data saturation.
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15 50 • A limitation is the cross-sectional nature of the study, experiences and perspectives
16
17 51 may change throughout the trial process.
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20 52 • Participants were recruited from one comprehensive cancer centre, patients'
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22 53 experiences may vary across hospitals.
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56 INTRODUCTION

57 Experimental cancer trials (or early phase clinical trials) play an important role in progressing
58 and advancing cancer treatments. It is estimated in the United Kingdom one in five cancer
59 patients participate in clinical trials.¹ Early phase clinical trials (Phase I and non-randomised
60 phase II) are designed to assess the safety of novel drugs, pharmacodynamics, and
61 pharmacokinetics.² Drug doses are gradually increased Phase I trials, to explore safety and
62 optimum dose. In phase II trials, drug efficacy, side effects, and safety are also investigated.
63 Early phase clinical research primarily focuses on physical outcomes, including appropriate
64 drug dosing, treatment toxicities, survival, and response rate.² Limited attention is afforded to
65 patient experience, consequently, little is understood about the personal impact of trial
66 participation.³

67 Understanding patient experience is particularly important in early phase trials, where
68 significant adverse events associated with treatment toxicity may outweigh possible
69 therapeutic benefit.⁴ Undesirable side effects are an important factor in shaping patients'
70 experiences of trial involvement, influencing their psychological wellbeing, sense of hope,
71 and potentially increasing fear of death.⁵ Furthermore, patients may not fully understand the
72 burden and demands of participation in clinical trials, and the impact trial participation could
73 have on their and their loved one's quality of life.³

74 Despite the various physical, emotional and practical challenges, patients generally
75 report positive experiences of trial participation and feel an increased sense of "control" over
76 their illness.⁵ Moore suggested trial participation reflects a coping strategy against
77 hopelessness.⁶ When standard treatment is ineffective, clinical trials are perceived by some
78 to offer a 'second chance' at finding a cure.³ Early phase trials can be perceived by others to
79 be a "last-ditch effort" for patients who are otherwise considered to have exhausted all other
80 treatment options.⁴ Cox also found participants derived comfort from being closely monitored
81 by clinicians due to the belief they were in 'expert' hands, and in providing a sense of

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3 82 purpose through helping others.³ However, patients often misunderstand trial information,
4
5 83 their understanding and the meanings patients ascribe to their participation will determine
6
7 84 how they make sense of their experiences throughout the trial process.⁷
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9

10 85 Patient experience is considered to be an integral component of excellent healthcare.⁸ As
11
12 86 outlined in the NHS Outcomes Framework, a deeper understanding of patient perceptions of
13
14 87 trial involvement will drive quality improvement and aid learning.⁸ Yet there is limited
15
16 88 understanding of patients' experiences of participating in early phase clinical trials. Due to
17
18 89 the aims of early phase trials and the uncertainties around drug side effects and safety, the
19
20 90 present study aimed to explore the experiences of participants in ECM clinical trials.
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22

23 24 91 **METHOD:**

25 26 27 92 **Study Design**

28
29
30 93 In this qualitative study, focus groups and semi-structured interviews were used. Focus
31
32 94 groups were conducted first to explore patients' experiences of ECM trials allowing patients
33
34 95 to discuss similarities and differences in their experiences. The main themes/experiences
35
36 96 from the focus groups were explored in more depth in semi-structured interviews.⁹ The same
37
38 97 topic guide was used for focus groups and interviews (Appendix 1). Questions captured
39
40 98 patients' experiences of trial introduction and participation and their decision-making process
41
42 99 regarding participating in the trial they were offered. For those on observational trial studies,
43
44 100 the interviews focused on their experiences of trial introduction and decision-making
45
46 101 process.
47
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49 102 **Sample/data collection**

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51
52 103 Participants were recruited from a regional cancer centre in North-west England. The
53
54 104 inclusion criteria for the study were (a) any cancer type, and (b) anyone who has been
55
56 105 screened for an observational or phase I-II ECM trial. Participants were excluded if they
57
58 106 were unable to provide informed consent, or comprehend written English.
59
60

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2
3 107 After identification by the clinical team, potential participants were approached by the
4
5 108 research team, who explained the study and provided written information. Participants were
6
7 109 given the opportunity to ask questions about study participation or the information provided.
8
9 110 Written informed signed consent was obtained. Twenty-one face-to-face interviews were
10
11 111 conducted in a quiet hospital room and one face-to-face interview was conducted at the
12
13 112 patient's home, determined by the patient's preference.
14
15

16 113 Both focus groups were conducted face-to-face in a quiet hospital room. The
17
18 114 interviews and focus groups were audio-recorded and lasted from 14 to 62 minutes and 48
19
20 115 to 108 minutes, respectively. Ethical approval was gained from South central-Oxford b
21
22 116 Research Ethics Committee (reference number 18/SC/0299) and the local NHS Trust.
23
24

25
26 117 Figure 1. Present the study's recruitment process. Participant demographics are presented
27
28 118 in Table 1.
29

30
31 119 *Insert Figure 1. here Study flow diagram*
32

33
34 120 *Insert Table 1. here Participants' demographic information*
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36
37 121 **Table 1. Participants' demographic information**
38

	Interviews (n = 22)	Focus groups (n =12)
Age range (years (Median))	42 – 83 (65.5)	52-79 (68.5)
Gender (female %)	59%	8%
Ethnicity %		
White British	95%	100%
Chinese	5%	
Marital status (%)		
Single	4.55%	16.67%
Married/domestic partner	90.91%	66.67%
Widowed	4.55%	8.33%

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2			
3	Divorced	-	8.33%
4			
5	Employment status (%)		
6			
7	Self-employed	-	8.33%
8			
9	Retired	75.00%	83.33%
10			
11	Unable to work	18.75%	8.33%
12			
13	Homemaker	6.25%	-
14			
15	Performance status (%)		
16			
17	0	52.94%	45.45%
18			
19	1	47.06%	54.55%
20			
21	Type of trial n (%)		
22			
23	Patients who are considered	2 (9%)	-
24	for the trial and then deemed		
25	ineligible (are often referred to		
26	as 'screen fail')		
27			
28	Observational	2 (9%)	-
29			
30	Phase I	9 (41%)	7(67%)
31			
32	Phase II	9 (41%)	5 (33%)
33			
34	Time on trial (<1 year, %)	54.55%	50%
35			
36	Disease group		
37			
38	Breast	31.82%	-
39			
40	Colorectal	13.64%	16.67%
41			
42	Head & Neck	-	8.33%
43			
44	Haematological	9.09%	-
45			
46	Lung	22.73%	16.67%
47			
48	Leukemia		8.33%
49			
50	Lymphoma	18.18%	41.67%
51			
52	Penile	4.55%	-
53			
54	Renal	-	8.33%
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123 **Data analysis**

124 Interviews and focus groups were analysed by hand using an inductive thematic approach.¹⁰

125 The six-phase guidelines of Braun and Clarke were used.¹⁰ After familiarisation with the

126 data, two authors (J.Y, C.S) coded an initial transcript and produced a coding document.

127 After creating the coding document, themes were developed and discussed. Any

128 disagreements regarding codes and themes were discussed between the authors until a

129 consensus was agreed. The codes and themes were then refined to improve clarity. Two

130 reviewers then coded an additional three transcripts and compared these to determine inter-

131 rater reliability (86%). One researcher (CS) subsequently coded the remaining transcripts.

132 Themes and interpretations of the data were discussed in regular meetings (J.Y, C.S).

133 **Patient and Public Involvement:**

134 The patient representative is a patient with secondary breast cancer, who has participated in

135 an early phase clinical trial. They reviewed study documents (participant information sheets,

136 informed consent form, interview schedule) and provided feedback. After analysis, the main

137 themes were discussed with the study team and patient representative, who all provided

138 feedback. A summary of study results will be sent to all participants who requested it.

139

140 **Reflexivity:**

141 Interviews were conducted sensitively by five researchers (J.Y, C.S, R.L, S.B, D.C) who

142 were not part of the patients' clinical team and all have experience in interviewing people

143 with cancer or regarding sensitive topics (self-harm). The data analysis was primarily

144 conducted by one researcher (C.S) who took an inductive approach and was unfamiliar with

145 the relevant literature at that time. They had no previous experience working in clinical trials,

146 or any personal experiences with clinical trials. This allowed the researcher to analyse the

147 data without looking for preconceived themes or experiences. The analysis was then

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3 148 discussed with the research team (J.Y, C.S, L.C, M.D), to minimise any biases which may
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5 149 have occurred. All members of the research team have relevant research or clinical
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7 150 experience. Researchers conducted balanced interviews and focus groups, and reminded
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9 151 patients the research team was not involved in the clinical trial.
10

11 12 152 **RESULTS**

13
14 153 We identified four main themes: decision-making, information needs, experience of trial
15
16 154 participation, impact of trial participation. The subthemes are described below with
17
18 155 supporting quotations provided in Table 2. All themes were mentioned in both the interviews
19
20 156 and focus groups. However, false hope was more prominent in the interviews. All patients
21
22 157 mentioned fear around disclosing side effects, patients in the focus group emphasised the
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24 158 impact of not disclosing side effects and discussed how to try and encourage patients to
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26 159 disclose side effects.
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30 160 *Insert table 2 here*
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161 **Table 2 Presents the themes and their sub-themes with supporting quotations.**

1. Decision-making	
1.1 Decision maker	<p><i>"It was mine [decision]. It's got to be, it's my life."</i>(25M83)</p> <p><i>"I think the consultants made the decision about what was most suitable"</i>(28F72)</p> <p><i>"The whole family read it, all my children, my husband. We discussed it and they all come back and said yes."</i> (07F61)</p>
1.2 No other option	<i>"I had no other choice, so at the end of the day, that's the one."</i> (25M83)
1.3 Hope	<i>"There's that hope there that the...a chance of a cure."</i> (19M56)
2. Information needs	
2.1 Volume & simplicity of information	<i>"doctors know all the technical terms, but we don't, most of us; and it has to be said in plain English"</i> (22F52)
2.2 Side effects	<p><i>"I don't remember anybody saying, before you go on this, your thyroid could do this, and it will be permanent"</i>(23F68)</p> <p><i>"Well I think the list of possible side effects is they just think of everything they can think of that might go wrong and list them all down"</i> (FG2)</p>
2.3 Updates throughout treatment	<i>"I want him to say to me, now look here, if this doesn't work it's chemo."</i> (21F70)
2.4 Provision of False hope	<i>"if they hadn't built my expectation, then the crash wouldn't have been as hard"</i> (03M42)
2.5 Support available	<i>"you do feel that there's a void like, you know, where do I get that information [about support]."</i> (FG2)
3. Experience of trial	
3.1 Patient centred	<p><i>"the clinical trials team were I felt tailoring their treatment of me."</i>(24F56)</p> <p><i>"it didn't feel personal; it felt as though I was being treated as a number that was insignificant."</i>(22F52)</p>
3.2 Disclosing side effects	<p><i>"is the most frightening thing, at that point in time when you come off the point when you've been given, this is your one hope to live and somebody says, I'm just going to take it away from you, and that's the end of the matter."</i> (FG2)</p> <p><i>"and I made the mistake of telling them about some of the side effects"</i> (FG2)</p> <p><i>"if you don't tell them [side effects], then you're compromising not only the trial but you're compromising yourself more importantly."</i>(FG2)</p> <p><i>"if they [trial team] said to you that if you were to disclose the side-effect you're having, that they would be more likely to change your treatment levels or do something about it, other than say on or off because it's the fear of the on or off is the most frightening thing".</i>(FG2)</p>

4. Impact of trial participation

4.1 Quality of Life (QoL)

“It’s an impact on your life having to come in every two weeks, especially the thing I was on initially was an all-day effort” (FG2)

“I was in and out like a yo yo And I didn’t realise it was the trial”(14M66)

“Our life has changed absolutely beyond recognition. I had a good job and we were very active, cycled everywhere and went diving on holiday and all of those things which we can’t do now“(24F56)

4.2 Time

“the frequency of the visits is good and bad, as I say It’s travelling every week but having that line of contact and support weekly is great.” (24F56)

4.3. Family

“It’s a really valid question to ask around carers and family members and how are they coping”(26F48)

“it’s difficult for my daughter because she had her studies and she came with me every time”(29M55)

4.4 Financial

“It costs you a lot of money”(07F61)

4.5 Psychological impact

“Depressed. it got me down, the waiting”(28F72)

“So I’m on the waiting list. They may pick somebody else. I don’t know.”(25M83)

162 Quotes from the interviews are presented as participant’s ID, gender (M=male, F=female), and age (in years). Quotes from the focus groups
163 are presented as FG and number (1 or 2).

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3 164 **Decision-making**
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6 165 *Decision-makers*
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9 166 Patient preference regarding involvement in decision-making varied. Some patients
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11 167 highlighted the importance of including family and friends in their decisions, whereas others
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13 168 felt it was only their decision to make. Due to difficulties understanding the information,
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15 169 uncertainties around trials, and patients' perception of doctor's expertise, some patients
16
17 170 relied on the doctors to make the best decision for them.
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20 171 *No other option*
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23 172 A few patients perceived clinical trials as their only option and for those who were
24
25 173 ineligible for the trial, this view led to feelings of despair and uncertainty about their options.
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27 174 Conversely, the majority of patients felt clinical trials provided them with another treatment
28
29 175 option. This was particularly important for patients who did not want the alternative treatment
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31 176 options.
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34 177 *Hope*
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37 178 Clinical trials provided the majority of patients with hope. For some it was a potential
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39 179 chance for a cure, stopping the progression of their cancer, and/or extending their life. While
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41 180 others hoped their participation would help others with cancer in the future.
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45 181 **Information needs**
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48 182 *Wealth/volume and simplicity of information*
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51 183 Patients wanted enough information about their choices to make the best decision regarding
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53 184 treatment. Patients highlighted the need for more simplified trial information, as the
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55 185 information they received was scientific and sometimes difficult to understand.
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58 186 *Side effects*
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3 187 Patients were divided on whether they had received enough information about possible side
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5 188 effects of the trial before participation, with some patients reporting they were not fully
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7 189 informed. Patients recognised it might possible difficult to provide this information, as the
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9 190 purpose of clinical trials is to identify side effects. One patient felt the risk of permanent side
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11 191 effects had not been fully explained, and prior knowledge of this risk would have affected
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13 192 their decision to participate.

16 193 *Updates throughout treatment*

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19 194 During the trial, patients wanted updated information regarding i) their response to treatment,
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21 195 ii) alternative treatment options, iii) the success of the overall trial to date, and iv) the
22
23 196 experiences of other patients on the trial. This information helped them to re-evaluate their
24
25 197 trial involvement and make decisions about future participation.

28 198 *Provision of False hope*

30
31 199 A few patients felt they received false hope and were misled about potential personal
32
33 200 benefit from trial participation. These patients believed this false hope reduced their ability to
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35 201 cope with a negative response to treatment. These patients felt information about possible
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37 202 outcomes of the trial should highlight the risks and the possibility the trial may not work,
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39 203 rather than focusing on potential benefits.

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43 204 Patients who were ineligible for the trial (screen fail) recalled how upsetting it was to be
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45 205 told they were ineligible. One patient even stated it felt like a “death sentence”.

47 206 *Support available*

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51 207 Patients were informed of whom to contact if they required medical support. However,
52
53 208 many were unaware of the psychological support available and could not recall doctors
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55 209 discussing psychological support options. Some patients who were aware of psychological
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57 210 support, highlighted difficulties access the support due to the length of treatments and
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3 211 distance travelling to the hospital. The majority of patients did not know if there was any
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5 212 psychological/financial/practical support available for family members.
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8 213 **Experience of trial participation**

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10 214 *Patient-centred*

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14 215 Many patients perceived themselves as a guinea pig concerning side effects and some felt
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16 216 their treatment was impersonal. The majority of patients however, reported receiving
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18 217 personalised care and some discussed the flexibility to fit appointments around their
19
20 218 priorities.
21

22 219 *Disclosing side effects*

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26 220 Patients, especially those who saw the trial as their only treatment option, were
27
28 221 concerned about disclosing side effects in case it impacted trial participation. Some patients
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30 222 who disclosed side effects even reported “downplaying” side effects and/or regretting
31
32 223 disclosing side effects due to withdrawal from the trial.
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34
35 224 This theme was discussed in great detail in the second focus group, with one patient
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37 225 who was taken off the trial admitted they would be reluctant to disclose side effects in future
38
39 226 trials. Other patients discussed the internal conflict between the fear of withdrawal from the
40
41 227 trial and the risk to themselves if they did not disclose side effects. Some patients were
42
43 228 aware by not disclosing side effects they are compromising the trial and the patient's safety.
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47 229 Patients in the focus group felt they needed more information from the clinical team
48
49 230 about what would happen if they experienced side effects. Particularly emphasising that
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51 231 experiencing side effects does not always result in withdrawal from the trial, instead, the
52
53 232 dosage may be reduced.
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55 233 **Impact of trial participation**

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3 234 *Quality of Life*
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6 235 Trial participation affected many aspects of a participant's life including QoL, free time,
7
8 236 finances, and their family. Patients highlighted the need to fit their life around the trial
9
10 237 schedule (due to the frequency and long duration of trial days, and travelling to the hospital).
11
12 238 Patients frequently stated once the trial had finished they could *get their "life back."*
13
14

15 239 The impact on QoL was mixed. Some patients believed their QoL had improved, for
16
17 240 example, they were able to perform activities they had been unable to due to ill health. In
18
19 241 contrast, other patients were unable to partake in regular activities or trips away, due to side
20
21 242 effects or frequent hospital visits, which on occasion required inpatient admission.
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23

24 243 *Time*
25
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27 244 Patients discussed the burden of clinical trials on their time, due to the frequency and
28
29 245 duration of hospital visits. Some patients reported requiring the next day to recover and rest,
30
31 246 perceiving they had "lost" another day due to the trial. However, some benefits to frequent
32
33 247 hospital visits were reported including seeing experienced doctors and additional monitoring,
34
35 248 care, and support they perceived they would not receive with standard treatment. Patients
36
37 249 reported a lot of waiting around, which was tiring but understandable. Some patients were
38
39 250 frustrated when they were not informed of delays to their treatment.
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41
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43 251 An unanticipated impact of the trial was on holidays and trips away. Trial schedules
44
45 252 often prevented patients from going away for their preferred duration. Travel insurance was
46
47 253 also often difficult to obtain. There were concerns around what would happen if the patient
48
49 254 became ill on holiday and if the treatment they received from other hospitals could react with
50
51 255 trial treatment or affect trial participation. Limitation to travel was especially difficult for
52
53 256 patients who were unable to see their family who lived abroad.
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56 257 *Family*
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3 258 Patients felt their participation in a clinical trial was a shared experience with their
4
5 259 families and discussed the psychological impact of trial participation on their family and
6
7 260 friends. Some patients felt their spouses were “trapped” or they were a “burden” to their
8
9 261 family. While others mentioned their family/friends had to change their usual activities due to
10
11 262 their participation in the trial. Patients highlighted the need for support for their family/friends.
12
13 263 Many patients felt it was crucial that clinical trial teams ask family/friends about the impact of
14
15 264 the trials on them as well.

18 19 265 *Financial*

20
21 266 Some patients described the financial burden of participating in trials, due to travel
22
23 267 costs, as well as food and drinks needed during visits. These patients were not aware of any
24
25 268 financial aids available.

27 28 29 269 *Psychological impact*

30
31 270 Patients mentioned experiencing anxiety and depression, during the screening
32
33 271 process, due to uncertainties around their trial eligibility. Patients feared “their” trial space
34
35 272 could be allocated to another whilst awaiting their results, due to their knowledge of limited
36
37 273 trial spaces. One patient even felt “rushed” to make a decision.

40 41 274 **DISCUSSION**

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43
44 275 Overall, the majority of patients had a positive experience and received patient-centred care.
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46 276 To aid decision-making regarding initial and continued participation, patients identified
47
48 277 several areas of improvement (a) simplification of trial information (b) more information on
49
50 278 side effects, (c) regular updates on response to treatment, and (d) information about
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52 279 alternative options. Patients needed more information about support available for
53
54 280 themselves and their family members. Patients admitted to being reluctant to inform clinical
55
56 281 trial teams about side effects experienced.

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3 282 Patients found trial information too scientific and difficult to understand, which is
4
5 283 consistent with previous studies.^{7 11 12} Patients wanted more information about the risk of
6
7 284 side effects but mentioned the long list of side effects could be daunting. However, patients
8
9 285 often focused on the anticipated personal benefit they would get from the trial rather than
10
11 286 potential side effects. Previous studies reported patients often have unrealistic expectations
12
13 287 about their potential benefit and reduced susceptibility to side effects when compared with
14
15 288 other patients.^{6 13-17} To improve comprehension of information, ensure patients provide fully
16
17 289 informed consent, and understand the potential risks. Donovan recommends interviewing
18
19 290 patients while reviewing study documentation to identify any aspects that are unclear or
20
21 291 could be misinterpreted.¹⁸

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24
25 292 Misinterpretation of trial information could have led to 'false hope' (the patient hopes
26
27 293 the treatment results in a cure, improvement of health, or prolongation of life).¹⁹ For example,
28
29 294 patients overestimating personal benefit (therapeutic misconceptions) or if the clinical team
30
31 295 emphasised the benefits of being on trials (regular appointments, great care, extra attention
32
33 296 to their health, and potential benefit for future patients).^{13 17 19} False hope was perceived to
34
35 297 reduce the patient's ability to cope with bad news, and lead to feelings of frustration and
36
37 298 disappointment being amplified and more destructive.¹⁹ This calls into question whether the
38
39 299 patient gave fully informed consent. Early phase dose-escalation trials may not lead to
40
41 300 personal medical benefit to patients of the trial, yet this is often a reason for participation.¹⁵
42
43 301 The unlikelihood of personal benefit needs to be emphasised more clearly to the patients.¹⁴
44
45 302 ^{15 20-25} From the current evidence, it seems the hope to obtain medical benefit is not
46
47 303 indicative of compromised informed consent.^{15 21 22} However, when introducing patients to
48
49 304 trials and providing them with possible treatment options there is a need for equipoise (the
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51 305 assumption there is not one 'better' treatment option).^{18 26 27} Any inkling of preferential
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53 306 treatment combined with the patient's belief that doctors and nurses act in the patient's best
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55 307 interest, could lead to patients feeling they have been given false hope.^{3 18}

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3 308 A few patients reported feeling rushed to make a decision; these patients had anxieties
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5 309 that if they did not decide quickly they may lose the trial to another patient. It is crucial
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7 310 patients are given the time and information they require, to make a fully informed decision
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9 311 about trial participation. The patient's anxieties may be due to their therapeutic
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11 312 misconceptions or unrealistic expectations about the benefit, combined with their knowledge
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13 313 of small recruitment numbers across multiple sites.^{13 22} Clinical trial teams should consider
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15 314 these factors when discussing trial participation. In addition, the wording used to inform
16
17 315 patients they are "eligible" could affect patient's decision-making regarding trial participation.
18
19 316 Patients frequently report feeling "lucky" or "honoured" they were eligible for the trial, as it
20
21 317 gave them another chance for a cure.^{26 28} Therefore it was important to capture patients'
22
23 318 experiences who were ineligible for clinical trials.^{3 4} Those who were ineligible felt
24
25 319 disappointed and were out of treatment options. Brown et al. found patients suggested the
26
27 320 phrase "the trial is suitable for you" could be used instead of "eligible", as the phrase was
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29 321 perceived to objectify the study and highlight the possibility of other treatment options. In
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31 322 addition the use of "unsuitable" may minimise the disappointment felt by those ineligible for
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33 323 the study.²⁶

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37 324 To aid decision-making regarding continued participation in early phase clinical trials,
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39 325 patients desired regular updates about their response to trial treatment. Patients desired
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41 326 information about other patients' experiences of side effects while on the trial and response
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43 327 to the trial and more detailed feedback about the trial progress (i.e. recruitment and
44
45 328 retention). This is in line with previous studies, which also found patients frequently shared
46
47 329 information with each other about side effects and their experience on the trial.^{24 29 30}
48
49 330 Providing information about other patients' experiences will depend on the information
50
51 331 received from the trial sponsor. However, it is crucial information is presented in a way that
52
53 332 does not lead to false hope emphasising there are no guaranteed benefits or side effects,
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55 333 and patients have different reactions to treatment.
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3 334 The main aim of the majority of early phase trials is to investigate the safe dosage
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5 335 range and side effects experienced by patients.³ Therefore to ensure patients' safety and
6
7 336 validity of the trial, it is crucial patients are honest about side effects and their severity.¹³ Yet
8
9 337 many patients admitted holding back information about side effects due to fear of being
10
11 338 taken off the trial.

12
13 339 The disclosure of side effects is likely influenced by patients' beliefs.^{13 28} Previous
14
15 340 studies found trial patients believed higher doses were more effective and side effects were
16
17 341 caused by effective treatment.^{31 32} To reduce fear and address any misconceptions
18
19 342 (regarding dose level and effectiveness, and withdrawal of trial if they disclose the trial),
20
21 343 these misconceptions could be incorporated into a question prompt list (a list comprised of
22
23 344 standard questions to prompt discussion between patient and doctor) highlighting dose
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25 345 reduction as an option if side effects are disclosed.^{14 33} However, further research is required
26
27 346 to see if providing this information would reduce the under-reporting of side effects.

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31 347 Another possible option to improve the accuracy of reporting side effects is the
32
33 348 integration of electronic Patient Reported Outcomes (ePROs) in clinical trials. Patients often
34
35 349 delay reporting side-effects leading to their effect being minimised.^{16 33 34} The integration of
36
37 350 ePROs enables regular monitoring of patients' side effects and can improve the accuracy
38
39 351 and timing of reporting side effects.^{35 36} EPROs aid real-time data collection, which can be
40
41 352 used to notify their clinical trial team of adverse events, allowing for earlier clinical decisions,
42
43 353 and provide relevant medical advice, tailored to patients' responses.³⁷ Therefore, enhancing
44
45 354 the patients' quality of care and communication with their clinical team.³⁵

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49 355 Participation in clinical trials led to a reduced QoL for some patients and not all were
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51 356 aware their poor health was due to treatment toxicity and attributed it to their cancer instead.
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53 357 Some of these patients may have a limited life expectancy and their quality of time left may
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55 358 be more important than staying on the trial.³ Therefore, clinical trial teams should have
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57 359 ongoing discussions throughout the trial about the patient's trial response, risks and benefits

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3 360 of trial continuation, and other treatment options including palliative care. These discussions
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5 361 will enable patients to make fully informed choices and find a balance between trial
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7 362 participation and QoL.^{3 38}
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9

10 363 As well as impacting patient's QoL, patients can experience undesirable side effects,
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12 364 which can have a negative impact on patient's psychological wellbeing.⁵ Yet the majority of
13
14 365 patients felt they did not need emotional/psychological support. Despite this perception,
15
16 366 patients experienced psychological distress (anxiety and/or depression) at various points
17
18 367 throughout the trial (initial screening to determine if patients were eligible or awaiting test
19
20 368 results). Patients, who are physically or psychologically impacted, may benefit from
21
22 369 specialist palliative care.³⁹ However, due to the conflicting beliefs (palliative care is for end of
23
24 370 life whereas the trial provides hope for another treatment option) patients were less likely to
25
26 371 access specialist palliative care.³⁹ The clinical trial teams may need to provide more
27
28 372 information and education about the supports available to patients and the potential benefit
29
30 373 of specialist palliative care alongside trial treatment.³⁹
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34 374 Trial participation can require both the patient and their families' time, physical and
35
36 375 emotional energy, and some parts of their lives to be put on hold.⁴⁰ Therefore, patients felt it
37
38 376 was important their family had psychological, financial, and/or practical support.
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40 377 Family/friends acting in a caregiver role (including managing medications, appointment
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42 378 schedules, finances, and/or providing emotional support and/or physical care) commonly
43
44 379 experience burden and depression.⁴¹ Patients with advanced cancer also perceived their
45
46 380 caregivers' lives were on hold when the caregiver was their child.⁴¹ Additionally, caregivers
47
48 381 of trial patients experience greater distress and anxiety when compared with the population
49
50 382 norms of caregivers of cancer patients.⁴² Untreated anxiety and depression can lead to poor
51
52 383 physical and mental health, as well as reduced QoL for carers and potentially patients as
53
54 384 well.⁴¹ Despite this, very few patients knew if there was any support available to their family
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56 385 and friends, other than the medical support provided by the clinical trials team. The clinical
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3 386 trial team should provide information about various support services available to patients and
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5 387 their families throughout the trial. However, there is minimal literature on the most effective
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7 388 support for carers of cancer patients and further research is required to identify the support
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9 389 needs of carers.^{41 42}
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11 12 390 **Limitations**

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14
15 391 One limitation is the cross-sectional nature of the study, as experiences and perspectives
16
17 392 may vary throughout the trial. Future studies should use a longitudinal design targeting
18
19 393 people at various stages throughout the trial. A second limitation is the study's sample. All
20
21 394 participants are from a single comprehensive cancer centre, patients' experiences may vary
22
23 395 across hospitals and clinical trial units. However, the study has a large sample size and
24
25 396 heterogeneous population in terms of cancer diagnosis, duration of trial participation, and
26
27 397 stage of the clinical trial (only two patients interviewed were "screen fails", but it was still
28
29 398 important to capture their experiences). The ethnic diversity of the sample was limited and
30
31 399 therefore not representative of the area where the data was collected. However, recruitment
32
33 400 levels for clinical trials are lower for ethnic minority groups. The majority of trial patients are
34
35 401 white British, therefore the sample used was representative of people who usually participate
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37 402 in clinical trials.^{43 44}
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42 43 44 404 **Conclusion**

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46
47 405 Patients require the simplification of trial information and want more information regarding
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49 406 side effects, available support, their response to trial treatment, and overall trial progress
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51 407 throughout the trial, to make fully informed decisions about ongoing trial participation. Due to
52
53 408 the trial burden, ongoing discussions are required to help patients find the balance between
54
55 409 quality of life and trial participation. Patients were unaware of the support available for their
56
57 410 family and wanted more support for their family.
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2
3 411 **Contributors:** J.Y and S.T developed the study design. J.Y has supervised the study. C.S
4
5 412 and JY analysed the materials. CS and LP wrote the manuscript. J.Y, S.T, L.C, N.C, M.K,
6
7 413 D.G, F.T, and M.D, have given substantial input throughout the development and writing of
8
9 414 the paper. J.T (patient representative) was involved with the study design and discussion of
10
11 415 main themes.

12
13
14 416 **Funding:** The study was funded by Manchester Experimental Cancer Medicine Centres
15
16 417 (ECMC) and The Christie CRF Charity, the grant number for this award is A01008. The
17
18 418 study was supported by the NIHR Manchester Biomedical Research Centre.

19
20
21 419 **Conflicts of Interest:** The authors declare that they have no conflict of interest.

22
23
24 420 **Ethics approval:** Ethical approval was gained from the appropriate Research Ethics
25
26 421 Committee (reference number 18/SC/0299) and the local NHS Trust.

27
28
29 422 **Data sharing statement:** The interview transcripts are available to show proof of the paper.
30
31 423 However, they would only be available for legal purposes. They are confidential and can only
32
33 424 be given access to in case of legal Requirements

34
35
36 425 **Acknowledgements:** Patients, Carer's, the Christie Experimental Cancer Medicine Team.
37
38 426 We would also like to thank Elaine Blowers, Rana Lee, Grant Punnett, and Sarah Bellhouse
39
40 427 for their help with the study. We would also like to thank J.T for all their help with the study.

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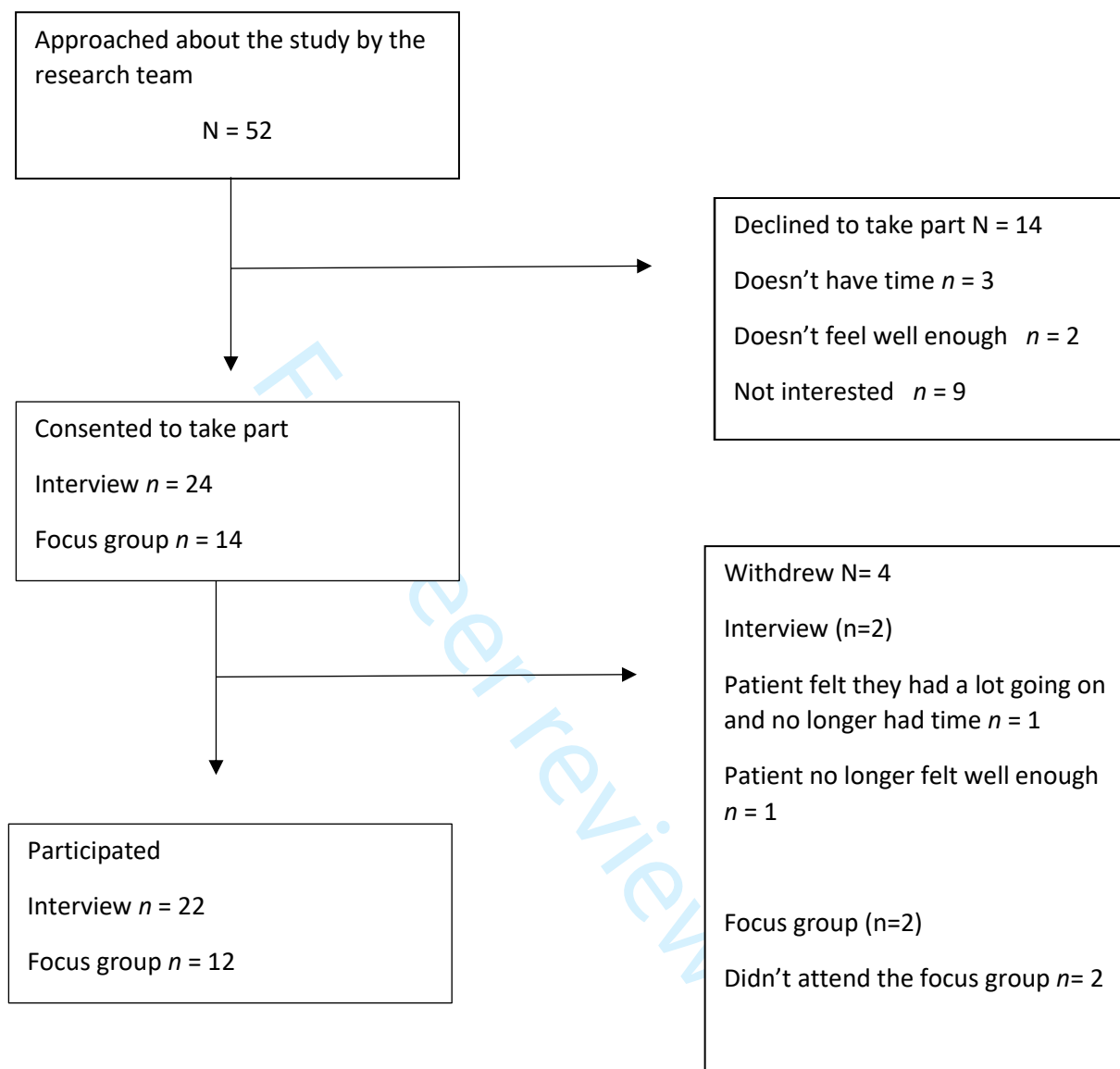
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559 **Figure Captions**

560 Figure 1. Study flow diagram

Figure 1. Study flow diagram



Questions

Pre Trial

1. At diagnosis, how were you informed about your illness?
 - Was there anything that could have been done differently?
2. What was your understanding of the treatment?
 - Was there a discussion about different options for treatment?
 - Was there a discussion about if the treatment didn't work, how was that approached?
3. How were you involved in decisions about your treatment?
4. How did you feel after your first meeting with the doctors at the Christie?
 - Was this for a trial or standard of care?
 - Were you seen by different teams for trial and non-trial visits?
 - If so how were the visits different?
5. How was the subject of a clinical trial approached?
 - At what point was this done?
 - Was the timing appropriate for you?
6. Was there a discussion about side effects and management?
 - How was this approached?
 - What advice and information was given?
 - Did this change your decision making and how?
7. Was there a discussion about supportive care?
 - When did this take place?
 - What was discussed?
 - How did this make you feel?
 - Would you like this to have been approached differently or at a different time?
 - How did this information impact your decision making going onto a trial?
8. Were your family and friends involved if you wanted them to be?
9. Was there anything you would have like to be prioritised more?

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2
3 10. When you were told that a trial was the next option, how were you supported?
4
5 - How was the care pathway explained to you?
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7 - Was it consistent across all members of staff?
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9 - Was the pathway updated to suit your needs? Can you give an example?
10
11 - What could have been done differently?
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14 11. What was your impression of communication between your clinical team?
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16 - Was everyone you spoke to aware of your care path?
17
18 12. Was everything explained to you in a way that you understood, how was this done?
19
20 13. Were you given time to ask questions?
21
22 - How did you feel about asking questions?
23
24 14. Did you know who to contact if you had questions or needed support?
25
26 - How were you told about this?
27
28 - Who were you told to contact?
29
30 - What information were you given about when and why to contact?
31
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33 15. Going onto a clinical trial, what were your expectations?
34
35 - What did you expect from the treatment?
36
37 - What did you expect from your doctors and nurses?
38
39 - Were these expectations met?
40
41 16. Did the care you receive feel personal?
42
43 - What was/could have been done to make it feel personal?
44
45
46 17. Was there anything that detracted from your care?
47
48 18. How were the visits organised?
49
50 - Did they run on time?
51
52 - What were some problems you encountered?
53
54 - Were you waiting for long periods of time?
55
56 - If so were you kept informed?
57
58 - Do you think this would have been different if you weren't on a trial and how?
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3 19. In a questionnaire – what questions would allow you to get your experience across?
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5 - What would you like to be/have been asked?
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7 20. What would you like to see change?
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9 21. Based on your experience, would you go onto another trial in the future and why?
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11 22. *Do you worry about your carers?*
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13 *What support do you think they need?*
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Standards for Reporting Qualitative Research (SRQR)*

<http://www.equator-network.org/reporting-guidelines/srqr/>

Page/line no(s).

Title and abstract

<p>Title - Concise description of the nature and topic of the study Identifying the study as qualitative or indicating the approach (e.g., ethnography, grounded theory) or data collection methods (e.g., interview, focus group) is recommended</p>	1/ 1-2
<p>Abstract - Summary of key elements of the study using the abstract format of the intended publication; typically includes background, purpose, methods, results, and conclusions</p>	2/ 22-39

Introduction

<p>Problem formulation - Description and significance of the problem/phenomenon studied; review of relevant theory and empirical work; problem statement</p>	5/ 67-89
<p>Purpose or research question - Purpose of the study and specific objectives or questions</p>	5/ 88-90

Methods

<p>Qualitative approach and research paradigm - Qualitative approach (e.g., ethnography, grounded theory, case study, phenomenology, narrative research) and guiding theory if appropriate; identifying the research paradigm (e.g., postpositivist, constructivist/ interpretivist) is also recommended; rationale**</p>	8/ 124-125
<p>Researcher characteristics and reflexivity - Researchers' characteristics that may influence the research, including personal attributes, qualifications/experience, relationship with participants, assumptions, and/or presuppositions; potential or actual interaction between researchers' characteristics and the research questions, approach, methods, results, and/or transferability</p>	8-9/141-151
<p>Context - Setting/site and salient contextual factors; rationale**</p>	5/ 103
<p>Sampling strategy - How and why research participants, documents, or events were selected; criteria for deciding when no further sampling was necessary (e.g., sampling saturation); rationale**</p>	5/ 103-106
<p>Ethical issues pertaining to human subjects - Documentation of approval by an appropriate ethics review board and participant consent, or explanation for lack thereof; other confidentiality and data security issues</p>	6/ 115-116
<p>Data collection methods - Types of data collected; details of data collection procedures including (as appropriate) start and stop dates of data collection and analysis, iterative process, triangulation of sources/methods, and modification of procedures in response to evolving study findings; rationale**</p>	6/ 107-116

Data collection instruments and technologies - Description of instruments (e.g., interview guides, questionnaires) and devices (e.g., audio recorders) used for data collection; if/how the instrument(s) changed over the course of the study	5/95-96 & 6/114
Units of study - Number and relevant characteristics of participants, documents, or events included in the study; level of participation (could be reported in results)	Table 1
Data processing - Methods for processing data prior to and during analysis, including transcription, data entry, data management and security, verification of data integrity, data coding, and anonymization/de-identification of excerpts	8/128-132
Data analysis - Process by which inferences, themes, etc., were identified and developed, including the researchers involved in data analysis; usually references a specific paradigm or approach; rationale**	8/ 124-134
Techniques to enhance trustworthiness - Techniques to enhance trustworthiness and credibility of data analysis (e.g., member checking, audit trail, triangulation); rationale**	7/ 129-132 7/136-138

Results/findings

Synthesis and interpretation - Main findings (e.g., interpretations, inferences, and themes); might include development of a theory or model, or integration with prior research or theory	9/ 153-159
Links to empirical data - Evidence (e.g., quotes, field notes, text excerpts, photographs) to substantiate analytic findings	Page 10-11

Discussion

Integration with prior work, implications, transferability, and contribution(s) to the field - Short summary of main findings; explanation of how findings and conclusions connect to, support, elaborate on, or challenge conclusions of earlier scholarship; discussion of scope of application/generalizability; identification of unique contribution(s) to scholarship in a discipline or field	16-17/ 275-281
Limitations - Trustworthiness and limitations of findings	21/ 390-402

Other

Conflicts of interest - Potential sources of influence or perceived influence on study conduct and conclusions; how these were managed	22/ 419
Funding - Sources of funding and other support; role of funders in data collection, interpretation, and reporting	22/ 416-418

*The authors created the SRQR by searching the literature to identify guidelines, reporting standards, and critical appraisal criteria for qualitative research; reviewing the reference lists of retrieved sources; and contacting experts to gain feedback. The SRQR aims to improve the transparency of all aspects of qualitative research by providing clear standards for reporting qualitative research.

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**The rationale should briefly discuss the justification for choosing that theory, approach, method, or technique rather than other options available, the assumptions and limitations implicit in those choices, and how those choices influence study conclusions and transferability. As appropriate, the rationale for several items might be discussed together.

Reference:

O'Brien BC, Harris IB, Beckman TJ, Reed DA, Cook DA. **Standards for reporting qualitative research: a synthesis of recommendations.** *Academic Medicine*, Vol. 89, No. 9 / Sept 2014
DOI: 10.1097/ACM.0000000000000388

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