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REVIEW

Deciding to Enrol in a Cancer Trial: A Systematic Review of Qualitative Studies

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Bianca Viljoen[1–3]
Suzanne K Chambers[1,2,4–7]
Jeff Dunn[1,2,4,5]
Nicholas Ralph[1,3–5]
Sonja March[1,8]

[1]Centre for Health Research, Institute for Resilient Regions, University of Southern Queensland, Springfield, Brisbane, Australia; [2]Cancer Council Queensland, Brisbane, Australia; [3]School of Nursing & Midwifery, University of Southern Queensland, Toowoomba, Australia; [4]Faculty of Health, University of Technology Sydney, Sydney, Australia; [5]Australian and New Zealand Urogenital and Prostate Cancer (ANZUP) Trials Group, Sydney, NSW, Australia; [6]Prostate Cancer Foundation of Australia, Sydney, NSW, Australia; [7]Exercise Medicine Research Institute, Edith Cowan University, Perth, WA, Australia; [8]School of Psychology and Counselling, University of Southern Queensland, Springfield, Brisbane, Australia

Background: Clinical trials are essential for the advancement of cancer treatments; however, participation by patients is suboptimal. Currently, there is a lack of synthesized qualitative review evidence on the patient experience of trial entry from which to further develop decision support. The aim of this review is to synthesise literature reporting experiences of participants when deciding to enrol in a cancer clinical trial in order to inform practice.

Methods: A systematic review and meta-synthesis of qualitative studies were conducted to describe the experiences of adult cancer patients who decided to enrol in a clinical trial of an anti-cancer treatment.

Results: Forty studies met eligibility criteria for inclusion. Three themes were identified representing the overarching domains of experience when deciding to enrol in a cancer trial: 1) need for trial information; (2) trepidation towards participation; and (3) justifying the decision. The process of deciding to enrol in a clinical trial is one marked by uncertainty, emotional distress and driven by the search for a cure.

Conclusion: Findings from this review show that decision support modelled by shared decision-making and the quality of a shared decision needs to be accompanied by tailored or personalised psychosocial and supportive care. Although the decision process bears similarities to theoretical processes outlined in decision-making frameworks, there are a lack of supportive interventions for cancer patients that are adapted to the clinical trial context. Theory-based interventions are urgently required to support the specific needs of patients deciding whether to participate in cancer trials.

Keywords: advanced cancer, qualitative, guideline development, consolidated framework for implementation research

Introduction

Clinical trials play a central role in the advancement of medical care, ensuring effectiveness and safety in new health-care interventions and treatments.[1] In oncology, cancer treatments are evaluated on a pathway of development, testing and implementation, relying on results from clinical trials to substantiate their therapeutic efficacy.[2] Despite more than 2300 clinical trials initiated across the globe in 2016 alone,[3] consistent estimates suggest fewer than one in twenty adults with cancer enrol in a trial.[2] Although as many as 70% of individuals diagnosed with cancer are willing to participate in trials[4] barriers to participation have persisted over the last twenty years.[5] Hence, there appears to be a gap between the numbers of individuals willing to enrol in a clinical trial and the percentage of those who actually participate. Barriers to participant recruitment and retention in oncology

Correspondence: Nicholas Ralph
Institute for Resilient Regions, University of Southern Queensland, Springfield, Brisbane, QLD 4350, Australia
Email nicholas.ralph@usq.edu.au

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trials are well reported and include, but are not limited to, treatment uncertainty;[6] financial barriers;[7] logistical concerns such as protocol stringency;[8] and a lack of resources for patients and clinicians to support clinical trial enrolment and retention.[7] Findings from a systematic review of barriers to participant recruitment report similar challenges persisting in studies published from 1995 to 2012.[9]

One approach to addressing these barriers has been the development and application of decisions aids in the clinical trial setting. A Cochrane review of decision aids in this context outlined the application of informational-based decisional tools targeting outcomes such as decisional regret, knowledge, conflict, anxiety, trial participation and attrition.[10] The review found only low-level evidence for effectiveness of these decision aids, and further noted that process outcomes, such as decisional involvement, values and risk expectations, were not considered. In addition, a deeper consideration of more patient-centred outcomes for such studies was proposed. In this regard, the decision to enrol in a clinical trial of a cancer treatment is influenced by a range of extrinsic and intrinsic factors with the process both complex, personal and potentially significant given it can have life-altering consequences.[11] Studies report that for individuals with cancer, these factors can include, but are not limited to, increased hope about disease prognosis;[12,13] the chance to compare interventions;[14] enhanced therapeutic relationships with specialist clinicians;[12] relief from the financial burden of care in some cases;[14] and improved overall survival.[15] Additionally, making the decision to participate in a clinical trial is particularly difficult where proposed treatments are new or novel and information about their safety, efficacy or effectiveness is lacking when compared to conventional treatments.[9]

Despite the need to understand the context in which trial participation is made and how to support individuals with cancer, there is a lack of synthesized review evidence on both the patient experience of deciding to enrol in a clinical trial and how best to support them. To date, a review by Gregerson et al[16] on clinical trial decision making in advanced cancer with a focus on end of life decisions is the only review that examines experiences of patients in this area. To our knowledge, there is no review-based evidence reporting the experiences and subsequent supportive care and decision needs of cancer patients deciding to enrol in a clinical trial. Accordingly, we undertook a systematic review of qualitative studies describing the experiences of adult cancer patients deciding to enrol in a clinical trial of an anti-cancer treatment.

Methods

The aim of this review was to synthesise literature reporting experiences of participants deciding to enrol in a clinical trial of anti-cancer treatment. For the purposes of this study, active cancer treatment includes the provision of anti-cancer therapy to patients with active cancer. For example, chemotherapy, immunotherapy, radiotherapy and surgery. This study will systematically review all aspects of participant enrolment in active anti-cancer treatment trials. The study proposes to develop and exhaustive qualitative understanding of the experience leading up to consenting to a clinical trial in order to identify the individual factors, barriers and enablers that may influence the decision to enrol in a clinical trial of an anti-cancer treatment.

Search Strategy

A comprehensive search strategy sought all eligible qualitative studies from the following electronic databases: PubMed, Cumulative Index to Nursing and Allied Health Literature (CINAHL), PsycINFO, Scopus and ProQuest Theses & Dissertations. No date restriction was applied. The search strategy for each database or platform consists of both Medical Subject Headings (MeSH) and free-text words (as appropriate) (see Table 1).

Eligibility Criteria

We included studies that reported the experiences of patients deciding to enrol in clinical trial of anti-cancer treatment. For this reason, qualitative studies on the experiences of this cohort were included. Studies were included if they were peer-reviewed, published in English and included adult human patients only. Dissertations and theses were also included; however none were identified. Full-text articles were also included. Studies were excluded if they were nested and reported quantitative data only. We also excluded nested studies within cancer-related interventions that were not for anti-cancer treatment. Grey literature was not included in the review (eg, government or professional organisation documents) (see Table 2 for the inclusion and exclusion criteria).

Study Selection

Succeeding the search, all identified citations were gathered and uploaded into EndNote database (EndNote X8.1)

Table 1 Search Strategy

Database	Search Strategy
PUBMED	((((((randomized controlled trial[Title]) OR clinical trial[Title]) OR trial[Title]) OR randomized trial[Title]) AND Humans[Mesh] AND English[lang])) AND (((“cancer”[Title]) AND (((((((((motivation[Title]) OR recruit[Title) OR decision[Title]) OR attitude[Title]) OR “focus group”[Title]) OR “qualitative”[Title]) OR participant[Title]) OR enrol [Title]) OR reason)) (1285)
CINAHL	TI Cancer AND TI (motivation OR recruit OR decision OR attitude OR “focus group” OR “qualitative” OR participant OR enrol OR reason) AND TI (“randomized controlled trial” OR “randomised controlled trial” OR “clinical trial” OR “trial” OR “randomized trial”) (622)
PsycInfo	(S1 AND S2 AND S3) S1 TI (cancer) S2 TI(motivation or recruit or decision or attitude or “focus group” or “qualitative” or participant or enrol or reason) S3 TI(“randomized controlled trial” or “randomised controlled trial” or “clinical trial” or “trial” or “randomized trial”) (161)
Scopus	(TITLE (cancer) AND TITLE (motivation OR recruit OR decision OR attitude OR “focus group” OR “qualitative” OR participant OR enrol OR reason) AND TITLE (“randomized controlled trial” OR “randomised controlled trial” OR “clinical trial” OR “trial” OR “randomized trial”)) AND (LIMIT-TO (LANGUAGE, “English”)) (910)
ProQuest Theses & Dissertations	(ti(randomised controlled trial) OR ti(randomized controlled trial) OR ti(clinical trial) OR (trial) OR (randomised trial)) AND (ti(cancer)) AND (ti(attitude) OR ti(motivation) OR ti(reason) OR ti(decision) OR ti(enrol) OR ti(focus group) OR ti(qualitative) OR ti(recruit) OR ti(participant)) (351)

Table 2 Study Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
• Qualitative studies investigating decisions/experiences of enrolment in a clinical trial reporting qualitative data • Studies reporting any aspect of participant enrolment in a trial of active cancer treatment. • Peer-reviewed studies in English • Adult human patients only • Dissertations and theses	• Nested studies reporting quantitative data only • Nested studies of cancer-related studies without anti-cancer treatment • Grey literature (eg, government or professional organisation documents)

and duplicate records removed. Titles and abstracts were then screened by two independent reviewers (BV, NR) for assessment against the inclusion criteria. These two reviewers independently screened 100% each of the articles. A list of potential studies for inclusion was circulated between BV and NR. Disagreements on study eligibility were resolved through discussion.

The full text of selected studies was retrieved following the initial screening and assessed in detail. Authors were contacted in cases of incomplete data or irretrievable articles. If the article was irretrievable (ie, not accessible from any source or from the authors), the study was excluded. The full text of each selected article was screened by the two independent authors (NR [100%], BV [100%]) to determine eligibility against the inclusion and exclusion criteria.

To ensure that all relevant studies were included, a manual search of citations and references of eligible studies was also conducted. Resulting references were exported separately and provided to the two reviewers (BV, NR) for independent review. Where necessary, study authors were contacted for missing information. To ensure impartiality the inclusion and exclusion criteria was constantly referred to (see Table 2). The results of the search are reported according to the PRISMA guidelines

for systematic reviews, detailing the number of papers identified by the search strategy and the number of papers that were included and excluded are stated. Any disagreements that arose between the reviewers were resolved through discussion. A PRISMA flow diagram of the study selection is outlined in Figure 1.[17]

Data Analysis and Synthesis

Data were extracted by two independent authors (BV, NR) for a random 10% (selected by simple random sampling) of the included studies. For the remaining studies, one author (BV) extracted the data and checked by a second author (NR). Any disagreements were resolved through discussion. The PDF files (or equivalent) of manuscripts were download and imported into NVivo and data extracted.

Data were synthesised by utilising a thematic analysis approach, which enables extraction of concepts and hypotheses from multiple qualitative studies.[18] Data were coded using NVivo and identified themes were categorised and presented as a narrative. All aspects of the thematic analysis were reviewed against the data. This involved several readings of each paper. The analysis and its explanations were repeatedly discussed among the researchers until consensus was reached.[19] The findings from the systematic review are described using meta-synthesis. Qualitative meta-synthesis aims to synthesise qualitative data to further develop identified themes and provide a more extensive interpretation of the findings.[20] In this qualitative review, quotations were included (see Table 3) to allow readers to assess the validity of the domains.

Patient and Public Involvement

No patients from the included studies were involved in this review.

Quality Assessment

Two independent reviewers (BV, NR) performed quality assessment. Each included study was critically appraised using a quality assessment tool drawn from the Standard

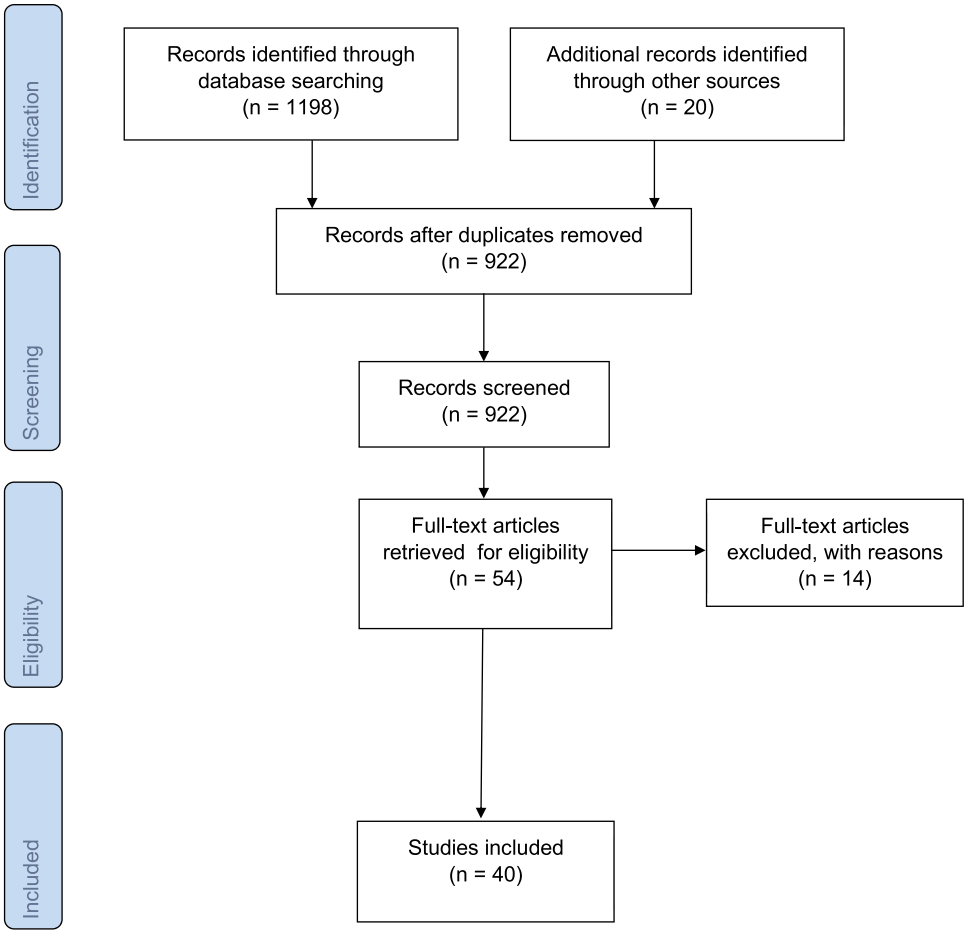

Figure 1 PRISMA flow diagram.
Notes: Moher D, Liberati A, Tetzlaff J, et al.Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. BMJ. 2009;339(jul21 1):b2535. doi:10.1136/bmj.b2535[17]

Table 3 Themes and Quotations

Themes	Sub-Themes	Quotes
Need for Trial Information	Reactions to a worsening cancer situation	"You know I just couldn't believe you know, just the shock. The shock".[12] "My family and I were so scared when the doctor said 'cancer'; I don't think I heard anything else that was said. I really couldn't think about a trial at that time. I had to digest how scared I was to know I had cancer."[41] "I heard the words lung cancer and I felt I was kicked in the gut …. I was terrified".[40] "[I would] have to control my emotions first, before I could make a decision".[31] " … He said 'cancer' straight away, well, it terrifies you".[29] "And that was the first time he ever mentioned that word (cancer) to me. So that was kind of a shock and I was by myself".[34] "I just can't throw my hands up and say, 'I give up', I mean, 'cause you got, you know, you got kids".[28] "It was panic city. I have never been more afraid of anything in my life".[45]
	Need for Health Professional Support	"My mind was like on overload. I felt like I went to nursing school in a real short amount of time".[24] "I thought well (the doctor) was pushing me (to consent) when he/she shouldn't have been … and that really annoyed me …… he/she is quite abrupt … I felt isolated".[38] "I think you are so stunned really you don't always ask questions that you probably should have done. I still think sometimes I just try and shut it away. I don't know whether this is normal".[27] "Sometimes is seems like they [the doctors] are dealing with us, I don't know, like animals".[31] "Being pressured put me off – obviously they need to get started, I understand that, but you need time to think about the diagnosis let alone to think about whether to take part in a trial".[46]
	Need for Tailored Information	"As I said it doesn't give you any information as to whether what they feel would be adequate for you, if it was on a banding system … ".[24] "It did not tell you anything because it was all in medical words and that it was purely a means of the doctors covering themselves".[27] "[Patients] … need to get somebody that can talk to them in terms that, you know, fit their mental capacity".[28] "I really believe information reduces uncertainty and gives you power".[31]
Trepidation towards Participation	Fear	"It brings up fear, it is frightening—animal testing and the unknown and pain".[41] "It was absolutely overwhelming for me. I was scared. I'd wake up in the morning with fear".[40] "There is uncertainty with new drugs; there is no guarantee".[36] "It's like walking on a plank and you don't know where the end is – you know whether you are going to drop off nor not"[26] "I was afraid to take a chance. If I only have a limited time left I don't want to waste my time with research where the outcome is unknown".[41] "Testing, it's scary. It is like you are a guinea pig and have no control over what will happen".[41] "It's like walking on a plank and you don't know where the end is – you know whether you are going to drop off or not".[26] "The biggest barrier to me, the one and only really, is fear, because cancer is fear itself and it compounds it. You don't want to put yourself at risk in any way whatsoever. And its absolute terror you see".[46]
	Leaving Treatment to Chance	"I want to decide for myself and not let luck or others decide for me".[36] "You're gonna put my name in a hat and draw us out and see which one I'm gonna get?"[58] "The only thing I don't understand is when you are pulled out of the computer … that's when the problem started (I withdrew) 'you will be picked out at random' was what they said … and I had no more control … I got out".[38] "It's like putting them in a hat and rolling them around and pulling one out and saying, "go for the operation"".[63] "To me it's your life, to let a machine decide, oh no, that didn't appeal".[63]

(*Continued*)

Table 3 (Continued).

Themes	Sub-Themes	Quotes
	Sensing No Other Alternative	"Listen love … when you get to my age and you have a choice of living or dying, you pick to live. Believe me or not!".[24] "What I wanted most was to have as much removed as possible to avoid death at an early age"[12] "If I am stage four, I do not mind trying".[54] "If it was gonna help me get through it, you know, even the slim chance of it making it better … Yeah, anything I could do to not have to burn or not go through anything, I was willing to try".[39] "I thought that clinical trials were only for a last resort when you have nothing to lose".[42] "I can lay down and die, or I can make myself available to the therapies that are available to me".[56] "I feel I have no choice. I do want to get well, if that's possible, and then you have to catch at all the straws you can find".[53] "[The] alternative was death and [I] didn't want to die".[64] "[It's] the best option, I had to do something".[64] "I can lay down and die, or I can make myself available to the therapies that are available to me".[56] "Not everyone gets the change to take part in something like this".[26]
Justifying the Decision	Need for Social Validation	"So it (support groups) wasn't nearly as easy as I had imagined … they weren't there when I need them. They really weren't".[12] "I was informed by Dr. X and then I talked to my husband. I looked at my husband and said "We have to join this"—and so we did".[54] "Family experience definitely affected how I chose treatments since I had a sister die of breast cancer and had two cousins die of it in their 30's".[12] [My] youngest [daughter] got her mind set on this one particular … thing. She found that particular one [clinical trial] and she is just determined that that's going to be the cure".[28]
	Need for Health Professional Rapport and Validation	"I came here for only the best … If he came to me, my doctor, and said let's do a clinical trial, I would do it. I trust him".[51] "I would [participate in a clinical trial] if my doctor recommended and I trust him, I would participate because I trust his medical advice".[33] "To be honest and truthful I am going to tell you I was asked and said yes and that was it. I don't think I thought anymore".[27] "I felt they knew what they were doing, and I trusted them completely. And I certainly haven't gone back on that. I felt that I'm in the best hands I could be in".[28] "Participating in a clinical trial is very much about trusting, that these people will not put me at unnecessary or irresponsibly risk … They will take care of me … if the confidence is broken it will be very dangerous to participate in trials …."[37] "I would choose whatever had been recommended to me by the doctor or doctors …. I think that applies to pretty well everything … ".[61] "You trust an authority, don't you? And I kind of believe that the doctors here, who are like specialised in this sphere of diseases, of course you trust them. Who else would you trust?."[53] "I would choose whatever had been recommended to me by the doctor or doctors … I think that applies to pretty well everything … ".[61]

Quality Assessment Criteria for Evaluating Primary Research Papers from a Variety of Fields[21] with the additional of: a statement of human research ethics committee approval. To assess the reliability and validity of included studies, studies had to meet the criteria provided in Table 4.[21] Studies were independently screened and scored (0–22) by two reviewers (BV, NR). The two reviewers also referred to the Consolidated Criteria for Reporting Quality Research (COREQ)[22] guidelines to discuss study quality and appraise the standard of evidence. Each paper could achieve a maximum score of 22. On each criterion two points were awarded for yes, one for partial and zero for no. All studies were judged to be either of high quality (scores of 17–20 points), adequate (scores of 11–16 points) or weak (scores of 0–10 points). High-quality studies were subsequently included in the final analysis (Table 5).

Table 4 Standard Quality Assessment Criteria for Evaluating Primary Research Papers from a Variety of Fields[22]

	Criteria	Abhyankar et al[24]	Asiedu et al[57]	Brown et al[51]	Brown et al[49]	Burke[25]	Catt et al[62]	Cox[26]	Cox[52]	Cox[27]	Coyne et al[28]	Davis[29]	Dellson et al[53]	Dimond nd Holifield[30]	Ebbert[48]	Ellington et al[31]	Godskesen et al[54]	Gordon and Daugherty[64]	Harrop et al[32]	Haynes-Maslow et al[33]	Hercinger et al[34]
1	Question/objective sufficiently described?	+	+	+	+	+	+	+	+	+		+	+		+	+		+	+	+	+
2	Study design evident and appropriate?	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
3	Context for the study clear?	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
4	Connection to a theoretical framework/wider body of knowledge?	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+	+
5	Sampling strategy described, relevant and justified?	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
6	Data collection methods clearly described and systematic?	+	+	+	+		+	+	+	+	+	+	+		+	+	+	+	+	+	+
7	Data analysis clearly described and systematic?	+	+	+	+			+	+	+	+	+	+	+	+	+	+	+	+	+	+
8	Use of verification procedure(s) to establish credibility?	+	-	+	-	-	-	-	-	-	-	+	+	+	+	+	+	+	-	-	+
9	Conclusions supported by the results?	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
10	Reflexivity of the account?				+	-	-	-		-				+							+
Additional	Statement of Human Research Ethics Committee Approval	+	+	-	-	-	+	+	-	-	+	+	+	+	+	+	-	+	+	-	+
Overall Score (/22)		21	19	19	18	17	17	18	17	16	18	21	21	20	22	20	21	19	21	17	22
Yes	+																				
Partial																					
No	-																				

	Criteria	Hopper[35]	Huizinga et al[47]	Krieger et al[58]	Lee et al[36]	Madsen and Holm[37]	Madsen & Holm[55]	Mills et al.[63]	Moynihan et al.[38]	Palmer-Wackerly et al.[39]	Quinn et al[40]	Quinn et al[41]	Ramers-Verhoeven et al[42]	Ridgeway et al[43]	Sanders[44]	Schutta and Burnett[56]	Shah et al[14]	Skousen[45]	Spittler[12]	Stevens et al[46]	Townsley et al[61]
1	Question/objective sufficiently described?	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
2	Study design evident and appropriate?	+	+	+	+	+	+	+		+	+	+	+	+	+	+	+	+	+	+	+

(Continued)

Table 4 (Continued).

Criteria			Abhyankar et al[24]	Asiedu et al[57]	Brown et al[51]	Brown et al[49]	Burke[25]	Catt et al[62]	Cox[26]	Cox[52]	Cox[27]	Coyne et al[28]	Davis[29]	Dellson et al[53]	Diamond nd Holifield[30]	Ebbert[48]	Ellingtton et al[31]	Godskesen et al[54]	Gordon and Daugherty[64]	Harrop et al[32]	Haynes-Maslow et al[33]	Hercinger et al[34]
	3	Context for the study clear?	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
	4	Connection to a theoretical framework/wider body of knowledge?	+		+	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
	5	Sampling strategy described, relevant and justified?	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
	6	Data collection methods clearly described and systematic?	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
	7	Data analysis clearly described and systematic?	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
	8	Use of verification procedure(s) to establish credibility?	+	–	+	–		–	+		+	+	+	–	–	+	–	–	+	+	+	+
	9	Conclusions supported by the results?	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
	10	Reflexivity of the account?		–		+	+	+		+						+	–		+	+	–	+
	Additional	Statement of Human Research Ethics Committee Approval	+	+	–	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+
Overall Score (/22)			21	16	19	20	20	20	19	20	21	21	21	17	19	22	18	19	18	22	20	20
Yes												**+**										
Partial																						
No												**–**										

Discrepant scores were resolved through discussion and consensus. The main methodological issues included inadequate explanation of the researcher-participant relationship, how this may have influenced conclusions and inadequate explanation of analytical rigour.

Results

Of the 40 studies reviewed, 11 were of local and 3 of advanced cancers; 19 included mixed cancer types and 7 did not specify. The phase of the trial was reported inconsistently throughout studies with 4 Phase I and 6 Phase III; 11 studies reported patients across a number of trials at different phases and 19 were not specified. All studies were conducted in countries with highly developed health-care systems such as USA (21), UK (10), Sweden (2), Netherlands (2), Denmark (2), England (1), Canada (1) and Singapore (1). Following meta-synthesis, three themes were identified representing the overarching domains of experience in deciding to participate in a cancer trial: (1) need for trial information; (2) trepidation towards participation; and (3) justifying the decision. Selected quotations reported in primary studies are included in Table 3 to demonstrate the correlation between the identified themes and patients' perspectives on treatment decision making. A summary of the included studies is provided in Table 5.

Need for Trial Information

Consideration of trial participation was reported in most studies (25/40) to stem from "reactions to a worsening cancer situation".[12,23–46] This situation could be described as a rapid change in health status or prognosis. Throughout the context of distress, confusion, uncertainty and illness, patients desperately attempt to identify and understand all of the appropriate treatment options available to them.[41]

Reactions to a Worsening Cancer Situation

Once cancer patients were informed their cancer was worsening, they experienced feelings of shock, fear and disbelief.[27,28,33,44,45] "You know I just couldn't believe it you know, just the shock. The shock"[12] (see Table 3). As patients tried to comprehend this change in health status, treatment options were introduced, including the invitation to take part in a clinical trial.[12,47] Due to the overwhelming emotions at this stage of their cancer trajectory, patients expressed a desire for their physician to consider their emotional concerns and offer support before providing them with trial information.[30] The patients' distressed state affected the amount of information they absorbed and impeded their ability to make health-related decisions.[23,40,45,48] Making the decision to enrol in a clinical trial of an active anti-cancer treatment is complex and personal for all cancer patients. Being confronted with trial information and not receiving enough emotional support during this time, led to decisional conflict.[49]

Need for Health Professional Support

The interaction and information exchange between physician and patient was reported as a significant issue in most of the included studies (31/40).[12,23–28,30–37,39–46,48,50–55] Patients experienced one-sided, dismissed or rushed conversations with physicians, resulting in feelings of alienation, pressure, coercion and an absence in autonomy.[37,41,45]

> (…) I thought well (the doctor) was pushing me (to consent) when he/she shouldn't have been … and that really annoyed me … … he/she is quite abrupt … () I felt isolated[37]

This hindered most patients' desire and ability to make treatment-related decisions (see Table 3).[37] In some cases, patient autonomy and ethical practice were not upheld, often due to a perceived lack of time to consider information about the trial.[37,56] Patients clearly stated that if physicians acknowledged their concerns, offered reassurance and took the time to listen, they felt they could then trust that the physicians recommendation on clinical trial participation.[30] Patients also reinforced the importance of having enough time to comprehend a cancer prognosis and filter through treatment information before making decisions.[12,45,47]

> Being pressured put me off – obviously they need to get started, I understand that, but you need time to think about the diagnosis let alone to think about whether to take part in a trial.[45]

Need for Tailored Information

The treatment information patients received was mostly described as confusing (25/40).[23,24,26–34,36,37,41–48,52,53,57,58] Written information was reported as lacking in detail[23] and difficult to read in terms of sentence length and word complexity.[26,43] "It did not tell you anything because it was all in medical words and that it was purely a means of the doctors covering themselves"[26] (see Table 3). Most participants used internet-based sources to better understand the material they received or to obtain information described in more layman's terms.[30,31,33,44,56] Even with this initiative,

Table 5 Characteristics of the Included Studies

Study	Country	Aims	Data Collection	Data Analysis	Study Population	Cancer Type	Findings
Abhyankar et al (2016)[24]	UK	To investigate the efficacy of consent information in supporting women in clinical trial decision-making.	Survey; Face-to-Face Semi-Structured Interviews	Thematic Analysis	21 participants	Breast, Ovarian & Endometrial Cancers	Patients evaluated all treatment options with reference to abating cancer and the desired to live longer. The perception of 'no choice'/only option available prevailed. Patients were overcome with the amount and content of information.
Asiedu et al (2018)[57]	USA	To understand how relationships with family members and care providers influence clinical trial decision-making for patients with ovarian cancer.	In-depth Interviews	Thematic Analysis	72 participants (33 patients; 39 family members)	Ovarian Cancer	Patients experiences, social status, doctor's recommendation to enrol, the involvement of family members and autonomy affected decision making.
Brown et al (2011)[51]	USA	To identify decision-making processes and explore patients views on clinical trial information.	Focus Groups	Thematic Analysis	26 participants (20 patients; 6 medical oncologists)	Lung, Breast & Prostate Cancer	Patients assessed the risks alongside the benefits of the clinical trial. Trust in doctor's recommendation and severity of patients disease influenced decision making.
Brown et al (2013)[49]	USA	To explore the reasons why some African American cancer patients declined trial participation.	Semi-structured Interviews; Questionnaires	Thematic Analysis; Statistics	22 participants	Multiple Cancer Types	Patients described the need to share decision making and for more information. Other influencing factors include mistrust in medical providers and research, fear of adverse effects and accompanying burden. Patients misunderstood trial information, necessitating prompt lists and supportive decision aids.
Burke (2014)[25]	USA	To identify the inconsistencies in information exchanged during cancer clinical trial recruitment.	In-depth Interviews	Thematic Analysis	52 participants (37 patients; 15 providers)	Multiple Cancer Types	Patients found it difficult to keep abreast of information. Additional influences included financial difficulties, familial pressures and stress. Patients did not obtain the required knowledge for appropriate informed consent.

Catt et al (2011)[62]	UK	To examine the reasons patients enter Phase I cancer trials.	Questionnaires; Semi-structured Interviews	Statistical Analysis; Qualitative Responses provided	40 participants	Multiple Cancer Types	The main reasons for trial entry include medical benefit, hope and research benefit. Altruism was also mentioned. A clinical trial was viewed as the only/best available option. Therapeutic misconceptions and difficulty in obtaining adequate informed consent was also present.
Cox (1999)[26]	UK	To identify the primary psychosocial processes and impact of trial participation from participant's perspectives.	Longitudinal research design. Semi-structured interviews and questionnaires	Thematic Analysis (comparative method and scoring)	55 patients (22 male; 33 female)	Multiple Cancer Types	The opportunity of enrolment in a clinical trial provided patients with a sense of honour, hope and a desire to abate cancer. Patients felt feelings of altruism and perceived that their doctor would not provide the suggestion to enrol without genuine concerns. There was however a great deal of uncertainty and feelings of no choice.
Cox (2002)[27]	UK	To examine the method of recruitment in cancer clinical trials.	Longitudinal research design. In-depth interviews	Thematic Analysis	55 patients (22 male; 33 female)	Multiple Cancer Types (Lung, Breast, Gastro-intestinal)	Patients decision making was influenced by the manner in which information was presented in written form and verbally.
Cox (2002)[52]	UK	To identify the psychosocial impact of early phase clinical trial participation from participants perspectives.	Longitudinal qualitative study	Theoretical examination of key findings	55 patients (22 male; 33 female)	Multiple Cancer Types	Two major themes were identified: hope and dying. When trials were offered, patients focused on hope, recovery and a cure rather than death or dying.
Coyne et al (2004)[28]	USA	To determine the factors that influence patients decision to participate in a clinical trial.	In-depth interviews	Ethnography; Content Analysis	17 patients (2 male; 15 female)	Multiple Cancer Types	Factors the influence decision making include physician recommendation, disease status, treatment effectiveness and side effects as well as location of treatment facility.

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Table 5 (Continued).

Study	Country	Aims	Data Collection	Data Analysis	Study Population	Cancer Type	Findings
Davis (2001)[29]	England	To explore the attitudes and psychological factors that differ between clinical trial acceptors and decliners.	Questionnaires; in-depth, semi-structured interviews	Statistical Analysis; Content Analysis; Exploratory Analysis;	49 participants	Multiple Cancer Types	Identified themes include attitudes (pre-held views, impact of project, information seeking, confusion), decision-making (trial proposal, motivations, barriers, hope, nothing to lose), disease/treatment experiences (impact of disease, experience of trial treatment, the future, anger & resentment, worry, moving on).
Dellson et al (2018)[53]	Sweden	To explore the decision-making process of cancer patients in clinical trial participation.	Face-to-face interviews	Inductive Content Analysis	27 patients	Multiple Cancer Types	Decision making was influenced by an emotions, based on a trusting relationship with healthcare personnel, feeling of no choice, desire to live longer, hope, research benefit and altruism.
Dimond et al (2009)[30]	USA	To identify the factors that influence treatment decision-making among breast cancer patients.	Mixed method; Survey, Questionnaires	Content Analysis	10 patients	Breast Cancer	Factors influencing decision making include trust, physician opinion, fear of side effects, fear of recurrence, fear of subsequent surgeries, length of recovery, patients support system, information received, personal decision, faith/spirituality, previous experience/relation to someone with breast cancer, age and direction from a nurse navigator.
Ebbert (2016)[48]	USA	To identify the factors, barriers and facilitators associated with enrolment in clinical trials for patients with ovarian cancer.	Multiple-Case Study; Surveys	Qualitative comparative analysis	40 participants (20 ovarian cancer patients; 20 nurses)	Stage III & IV Ovarian Cancer	Some enrolment facilitators include being offered a trial by a physician, patient-accessible clinical trial literature, adequate discussion with the provider of care and the ability to rely on health insurance. Barriers include an absence of these factors.

Ellington et al (2006)[31]	USA	To identify the factors influencing Spanish and English-speaking cancer patients to enrol in a clinical trial.	Qualitative Focus Group Design	Thematic Analysis	55 participants (25 Spanish-speaking; 30 English-speaking)	Multiple Cancer Types	Some factors that influenced decision-making include communication and personal relationship with the provider, the involvement of others, faith, information need and the impact of discrimination.
Godskesen et al (2013)[54]	Sweden	To investigate the ethical problems associated with patient information and to identify the reasons for clinical trial participation.	Interviews	Content Analysis; Thematic Analysis	14 participants	Multiple Cancer Types	Patients expressed the feeling of renewed hope. Patients knowledge and understanding of a clinical trial was low due to a lack of information and trust in the physician.
Gordon et al (2001)[64]	USA	To identify factors affecting clinical trial decision making as well as patients perceptions of the referral process.	Semi-structured Interviews	Statistical Analysis; Descriptive/ Thematic Analysis	144 participants	Multiple Cancer Types	Factors affecting enrolment include perceiving clinical trials as a 'last resort', having no other choice and wanting to be involved in research. Trust in the physician and health system, involvement of clinical investigators and family as well as their own experiences and others (including God) provided patients with information and influenced decision making.
Harrop et al (2016)[32]	UK	To identify the factors influencing patients decision to decline clinical trial participation and the experiences of recruitment processes.	Semi-structured Interviews	Thematic Analysis	20 patients	Bladder Cancer	Reasons for declining participation include preferences for a particular treatment arm. Patients were influenced by their own internet research, discussions with previous patients, friends and family, clinical encounters, personal history and lifestyle factors.

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Table 5 (Continued).

Study	Country	Aims	Data Collection	Data Analysis	Study Population	Cancer Type	Findings
Haynes-Maslow et al (2014)[33]	USA	To determine the factors that influence African American women's willingness to participate in clinical trials.	Focus groups	Thematic Analysis	82 participants in 8 focus groups	Multiple Cancer Types	Patients lacked clear knowledge of clinical trials and identified trust in the physician and health system to be an important factor in their willingness to participate in a trial. Patients desired the involvement of community members with a previous cancer diagnosis and clinical trial experience as well as physicians who were trustworthy, compassionate, engaged and provided adequate education.
Hercinger (2007)[34]	USA	To understand the experience of treatment decision making in older patients with cancer.	In-depth Interviews	Phenomenological Analysis	13 participants (4 Male; 9 Female)	Multiple Cancer Types	Main findings include the importance of relationships with others, spirituality, therapeutic communication, positive coping methods and feelings of powerlessness.
Hopper (2007)[35]	USA	To determine the willingness and opinions of African American cancer patients in clinical trial participation.	In-depth Interviews	Grounded Theory	10 participants	Multiple Cancer Types	Factors influencing patients willingness to participate include fear, concerns about becoming a 'guinea-pig', hope, trust in research and providers and the way information is provided to them. There was an evident need for more, non-misleading information, equal access for African Americans to treatment and health care and more cultural awareness.

Huizinga et al (1999)[47]	Netherlands	To better understand the decision-making process for cancer patients asked to participate in a clinical trial.	Semi-structured Interviews; Questionnaire	Descriptive Statistics; Qualitative Content Analysis	14 participants (12 women; 2 men)	Breast Cancer, Testicular Cancer & Melanoma	Patients reasons for trial enrolment include desire to improve health, hope, altruism, and distinguishing trial treatment to be superior to standard treatment. Reasons for trial refusal include concerns with randomisation, feeling like a 'guinea pig', fear of side effects, feeling overwhelmed by the amount of information and the impact the trial will have on daily life.
Krieger et al (2015)[58]	USA	To identify factors that may prevent cancer patients ability to provide informed consent and to examine their understanding of the randomisation process.	Semi-structured Interviews; Self-Administered Survey	Coding; Descriptive Analysis	49 patients	Multiple Cancer Types	Patients at all levels of understanding experienced uncertainty about randomisation. Patients associated clinical trials with 'trial and error' and were concerned about becoming a 'guinea-pig'.
Lee et al (2016)[36]	Singapore	To investigate the barriers and facilitators for clinical trial participation among multi-ethnic Asian breast cancer patients.	Focus Groups	Thematic Analysis	16 female participants	Breast Cancer	Factors influencing patients willingness to enrol in a trial include hope, trust in physician and health system, opinion of family members and friends, perceiving the trial as a 'last resort', altruism and desire to improve health. Barriers include lack of trial understanding and information, fatalism, poor experiences and fear of investigational drugs.

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Table 5 (Continued).

Study	Country	Aims	Data Collection	Data Analysis	Study Population	Cancer Type	Findings
Madsen et al (2007)[37]	Denmark	To explore patients strategies experiences of decision making.	Questionnaire; In-depth Interviews	Grounded Theory	29 participants	Breast & Ovarian Cancer	Patients developed a significant treatment preference which affected decision making. Patients felt their freedom to choose was restricted by randomisation, focusing on adverse effects and requiring more trust in their physician. All patients expressed a feeling of loneliness and lack of autonomy. Some patients lacked sufficient knowledge and sources to render an educated decision.
Madsen et al (2007)[55]	Denmark	To explore the attitudes of women with cancer invited to participate in one of three randomised trials.	Interviews	Constant Comparative Method	29 female participants	Breast & Ovarian Cancer	Patients expressed positive attitudes toward clinical trials and perceived a moral obligation to participate in order to improve research. Reasons for declining to enrol include a change in focus, concerns with randomisation, no experience of equipoise and a lack of trust in physicians.
Mills et al (2003)[63]	UK	To explore patients opinions of trial randomisation and their reasons for accepting or declining participation in the ProtecT study.	In-depth Interviews	Constant Comparison	21 male participants	Prostate Cancer	Patients view and belief in clinical equipoise was essential to randomisation consent and trial participation. Most of the patients who understood and accepted clinical equipoise consented to randomisation. Patients who were unaccepting were more inclined to refuse participation.

Moynihan et al (2012)[38]	UK	To determine patients' perceptions of clinical trial participation in a comparing selective bladder preservation against surgery in muscle invasive bladder cancer.	Semi-Structured Interviews	Constant Comparison	24 patients (10 decliners and 14 accepters)	Bladder Cancer	The majority of patients felt confusion and ambiguity caused by inadequate communication. This impacted ethical concerns enveloping informed consent and caused a sense of hostility between health care personnel and patients.
Palmer-Wackerly et al (2018)[39]	USA	To determine how and why patient illness identity relates to cancer treatment decision-making.	Interviews	Thematic Analysis	46 participants	Multiple Cancer Types (Breast, Multiple Myeloma & Prostate)	Patients decision making was influenced by illness identity perceptions, goals and conflicts in reference to themselves, close relationships and others.
Quinn et al (2011)[40]	USA	To utilise the planned behaviour framework to better understand the process of clinical trial decision making.	Open-ended, Semi-structured Interviews	Content Analysis	12 participants	Lung Cancer	Patients declined participation due to issues with transportation, treatment preference, lack of family, previous family history of cancer, trust in physician, control, reaction to diagnosis and their attitudes at the time impacted the decision-making process.
Quinn et al (2012)[41]	USA	To determine patients knowledge and attitudes towards clinical trial participation.	In-depth Interviews	Content Analysis	48 patients	Lung, Breast, Genitourinary, Head & Neck Cancer	Majority of patients discussed fear surrounding the trial, their cancer diagnosis, participation and of the unknown. Participants accepted physician's recommendations to enrol if they had a trusting relationship.
Ramers-Verhoeven et al (2014)[42]	Netherlands	To identify cancer patients attitudes towards clinical trial participation.	Interviews	Content Analysis	120 participants (48 cancer patients; 72 caregivers)	Multiple Cancer Types	Patients expressed trial misunderstandings and described feeling that conversations with physicians about clinical trials were one-sided, dismissed or rushed. Other decision-making factors included hope, concerns about being a 'guinea-pig' and apprehensions of the 'unknown'.

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Table 5 (Continued).

Study	Country	Aims	Data Collection	Data Analysis	Study Population	Cancer Type	Findings
Ridgeway et al (2017)[43]	USA	To examine the experiences of patients with ovarian cancer and their families in considering clinical trials.	Interviews	Thematic Analysis	72 participants (33 patients; 39 nominated family members)	Ovarian Cancer	Patients stated that conversations with providers about clinical trials was rare. Patients worried that they might miss opportunities as they found trials difficult to ascertain. If clinical trials were discussed with the provider, it was overpowering and patients viewed trials as the 'last resort'. There was a need for trust in providers and some family support.
Sanders. (2000)[44]	UK	To investigate patients treatment decision-making process.	Observations; In-depth Interviews	Thematic Analysis	Observations of 87 oncologists and patients interactions. 37 patients initially interviewed; 28 interviewed later; a further 11 interviews carried out with oncologists & nursing staff	Colorectal Cancer	Most patients required discussions with their physician and relied on their opinion and recommendations. Patients expressed feelings of 'no choice', found it difficult to understand information, felt uncertain about their disease and it subsequent treatment and required time to adequately decide.
Schutta et al (2000)[56]	USA	To investigate the factors that affect patients decision to participate in a phase I clinical trial.	Focus Groups	Thematic Analysis	22 patients with cancer	Multiple Cancer Types	Patients expressed trust in physician's recommendations and hope were primary influences in decision-making. The majority of participants believed that no one would participate in a trial solely due to altruism.
Shah et al (2012)[14]	USA	To investigate patients willingness to participate in a clinical trial.	Semi-structured Interviews	Thematic Analysis; Constant Comparison	46 participants	Prostate Cancer	Factors affecting patients willingness to participate include altruism/need to compare treatments, concerns with randomisation, physician opinion, financial enticements and time demands/scheduling.

Skousen (2006)[45]	USA	To describe the treatment decision making of men under the age of 60 years diagnosed with prostate cancer.	Interviews	Grounded Theory	28 participants (18 men; 10 significant others)	Prostate Cancer	Factors influencing decision making include physician communication, beliefs, personality traits and support systems. Patients engaged in processes of expectation (health care orientation, crisis of diagnosis, investigating prospects, determining choice and reflections).
Spittler (2011)[12]	USA	To explore the factors affecting decision-making and processes of women with breast cancer.	Mixed-Methods; Surveys; Questionnaires	Frequencies & Multiple Regression; Qualitative Content Analysis	102 participants	Breast Cancer	Factors include hope, need for more information, emotions at diagnosis, delivery of treatment options, threat of dying, fear of the unknown and reoccurrence, decision aids, treatment team strengths and deterrents.
Stevens et al (2004)[46]	UK	To identify the motives for declining clinical trial participation in breast cancer patients.	Qualitative, Longitudinal Design, Interviews	Thematic Analysis	22 patients	Breast Cancer	The reasons patients declined participation include fear of their illness and treatment, having a limited understanding of medical research due to poor presentation and unsupportive discussions with medical personnel. Patients who declined participation experienced guilt, uncertainty and wanted to review their decision.
Townsley et al (2006)[61]	Canada	To establish the attitudes elderly patients have towards clinical trial participation.	Questionnaire; Semi-structured Interviews	Statistics; Grounded Theory	94 patients (17 interviewees)	Multiple Cancer Types	Factors that influenced patients willingness to participate include physician recommendation to enrol, the desire to improve their health and help others. Reasons for declining enrolment include physician recommendation against enrolment and concerns with trial effectiveness.

confusion was still evident and the level of knowledge about trial basics was considerably low amongst most cancer patients.[26,27,37,53,59,60] "[Patients] … need to get somebody that can talk to them in terms that, you know, fit their mental capacity".[27] This lack of trial understanding demonstrated a clear disconnect between trialists and their patients, to the extent that not all patients understood their position in the consent process. Some even believed that withdrawal from a trial was impossible, affecting treatment decision-making.[37]

> (Once randomised) you couldn't volunteer for the other (treatment) because you only got that if you went into the trial and got away with it through randomisation.[37]

Trepidation Towards Participation

A substantial finding across reported studies (29/40) was patients experience of trepidation, most commonly expressed as "fear".[12,14,25,27–29,31–33, 35–46,48,50,51,54,57,60–62] This was frequently associated with cancer diagnosis, prognosis and treatment options.[29,40] Trepidation towards participation was associated with fear of cancer diagnosis, prognosis and treatment options.[29,40] Common reasons for trepidation included cancer fatalism,[35] the lack of time to decide on treatment,[40] concern about the "unknown"[47] and the possibility of a negative response to the trial.[47] Patients with a history of cancer, not only expressed uncertainty but the fear of cancer reoccurrence as well.[12,27,40] These factors formed a mental barrier and delayed the decision to enrol in a clinical trial.[12,27,35,47]

Participants described not wanting to lose control, feel isolated, alienated or powerless during decision-making.[33,37] Common statements associated with the idea of participating in a clinical trial included "I am scared",[29] "I am nervous" about joining a trial,[47] concerns about feeling like a "guinea pig", or an "experiment", "trial and error",[32] "feeling alone" and "having no say"[34,37,45,46,48,57,61] (see Table 3). Another primary influence in considering treatment options was patients' fear of potential adverse side effects associated with clinical trial participation[27,29,33,43,44,46]. This included both the known and unknown risks intrinsic in clinical trial medicines.[27,35] There was a clear need for patients to consider the potential side effects and its impact on future quality of life (QOL) against the therapeutic advantages of the trial.[48] Patients desired and suggested that their health-care providers offer detailed discussions and deliver general and specific information about clinical trials in order to improve their understanding of the risk-to-benefit ratio in clinical trial enrolment.[35,40,54]

Leaving Treatment to Chance

Before enrolling in a clinical trial, most participants expressed concerns about the process of randomisation and wanted to know the treatment group in which they would be placed.[14,48,54,62] As depicted in Table 3, the idea of randomisation made most patients feel uncomfortable or stressed[46] and made some unwilling to join a clinical trial.[35] Patients wanted to make an informed choice and felt "unpleasant" leaving treatment decisions to chance.[31,35] There was a general lack of knowledge about the concept of random assignment and the need for comparing two different treatments.[32,46,57] Patients struggled to make sense of their involvement in the trial process while questioning scientific principles.[37]

Sensing No Other Alternative

Evident in 30 out of the 40 included studies, was patients tendency to simplify their treatment options by evaluating them in terms of life versus death, regardless of fear or randomisation.[12,23,25,27–30,32–36,38–44,46,48,50–54,60,61,63]

There was a predisposition to perceive the active pursuit of treatment as the only option available and there was "no real choice" to make.[23,25,28,30,43,52,63] The use of the term "last resort" was used by many patients offered Phase III clinical trials.[32,35,42,50,63] As validated in Table 3, the majority of participants suggested that treatment options presented were considered with reference to the goal of living longer and hopefully abating cancer.[43,44,46,60] This goal seemed to influence the way in which the options were comprehended, evaluated and experienced within decision making.[12] For most, the offer to participate in a clinical trial provided some form of hope.[25,26,28,33,43,46,51–53,61] Hope was viewed as complex, affected by spirituality and faith, interpersonal relationships, trust, positivity and vital to the coping process.[29,48,51,53] When patients sensed they had no other alternative they tended to make the treatment decision quickly. Patients frequently described, "having already made their mind up", "seeing trial as just a natural thing to do", "going with their gut feelings" and even suggesting "it never entered my mind to say no".[23,25,28,47,52,53]

Justifying the Decision

Patient decision-making processes are influenced by the knowledge and support received from their family, friends and physician. This is viewed as important in order to justify their decision about clinical trial participation.[56] Many participants further expressed a moral obligation to participate in a clinical trial for altruistic purposes[14,23,25,28,30,35,46,52,55,61]

and the desire to assist in furthering clinical research.[23,52,54,63,64]

Need for Social Validation

Twenty-nine out of the forty studies suggest that patients' approach to decision making is influenced by their sociodemographic, social and cultural backgrounds, their experiences with health-care services and their relationships with their health-care providers.[14,23,25–29,31,33,34,36–44,48,51–56,60,61,63] The opinion and knowledge of patients' physician, family and friends were predominantly noted as important in decision-making and facilitators for clinical trial enrolment.[35] Brown (2013) states that patients actively want to share decisions.[48] The support of family, peers and health professionals was fundamental in being able to comprehend their diagnosis, treatment options and treatment experience.[12]

With the established difficulty in decision-making and processing treatment information, many patients wished to seek the opinion of others and/or hear from previous trial participants' experiences of clinical trial treatment.[23,27] Patients stated they would try and contact previous clinical trial participants to enquire about "what they tried and what they used"[56] to assist them in understanding the actuality of trial participation and inform decision-making.[27,31,42,56] Patients also wanted to be aware of support groups before enrolment.[12] Participants who heard about successful trials emphasised that hearing stories allowed them to feel more enthusiastic about the research, some even went online and/or approached clinical providers about trials[42] as indicated in Table 3. Speaking with previous survivors was verbalised as decision aids, helping participants know they were not alone, providing an additional viewpoint and gave them a sense of feeling valued.[12,23]

Participants sought some form of family involvement in the clinical trial decision-making process. This was identified as a significant finding across the included studies (23/40).[26–31,33–36,38–40,42–44,46,48,52,53,56,61,63] The involvement of family was either to assist patients in their search for more information about the trial, help them stay informed about the clinical trial process and/or support their final decision about treatment. The opinions of friends and family was viewed as an important facilitator if the opinions were positive and seen as a barrier if the opinions were negative.[35] To manage this, patients selectively involved family members in their decision making, engaging with those they shared a strong and close relationship or when they had scientific or medical training.[47,56] Patients also determined when and how to share particular types of information. Some reasons for excluding family members from discussions about trial participation included a desire to avoid creating perceived emotional and psychological burdens for family members.[56]

Patients who witnessed friends or family members who had experienced cancer, positive and negative results with treatment and any long-term outcomes impacted their treatment considerations and decision-making.[12,29,44] As demonstrated in Table 3, some patients stressed the importance of making decisions in partnership with family members, as portrayed in the use of plural pronouns such as "we" and "our" in talking about the final decision.[56] These relationships were essential; family members attended appointments, participated in discussions around clinical trial enrolment, showed concern, provided physical and emotional support, shared expert knowledge and therefore influenced the treatment decisions that were made.[56]

Need for Health Professional Rapport and Validation

Trust in a physician's recommendation or opinion concerning enrolment in a clinical trial was reported as vital in majority of included studies (31/40).[14,25–37,39–44,47,50,52–56,60,61,63,65] A commonly-held belief in one study was that the doctor would not offer trial participation if it was not in the patients' best interest.[26] Patients indicated that, if they held a long-standing relationship and developed trust in their doctors' medical judgment, they would most likely adhere to their doctors' guidance.[30,39,50] Being content with decision-making appeared to be influenced by the trust, respect and relationships patients had with health-care providers and health-care personnel[26,28,31,33,36,37,40,42,43,52,55,63] (see Table 3). Enabling trust and building rapport over time were identified as an important basis to facilitate good communication, willingness to participate in a trial and ultimately affected decision-making.[14,25,43,55] Participants wanted their physician to be honest with them, providing reassurance and clarity through quality consultations and discussions.[24,37,41,43,50] Trust in the doctor, specialists and medical team were crucial in considering the available treatment options.[14,27] This trust, as well as trust in local governance, drug development processes and government legislation were all viewed as facilitators to clinical trial enrolment.[35] Patients yearn for the knowledge that clinical trials are conducted in an ethical manner and cited confidence that adequate care is given during trial procedure as facilitators for clinical trial enrolment.[35]

Discussion

To our knowledge, this is the only review that comprehensively synthesises evidence from qualitative studies reporting the experience of patients deciding whether to enrol in a clinical trial. Our findings show that after a cancer diagnosis and being invited to enrol in a clinical trial, deciding to enrol revolves around the "need for trial information"; "trepidation towards participation"; and "justifying the decision". Our data highlights several points among which is an overarching need to better address informational and decision-support needs in individuals deciding to enrol in a cancer trial.

Firstly, there is a need to improve the way patients are informed about clinical trials and supported to make a decision that is right for them. Moreover, given the broad array of needs voiced by patients across most included studies as well as the role of health professionals in meeting them, finding effective decision-support interventions should be a priority for health systems and clinical trialists everywhere.

Secondly, understanding decision-making in the context of a clinical trial and individuals' associated needs for decision-support should be prioritised. Our findings bear similarity to the domains of Charles' Shared Decision-Making Framework[66] in which patients make decisions in the context of (1) "information exchange"; after (2) "deliberation" happens; and towards (3) "deciding on treatment to implement". Given the broad applicability of Charles' framework[66] to health contexts, our thematically similar results suggest the decision process of enrolling in a clinical trial may not be dissimilar to other health-related decisions experienced by cancer patients. Instead, where the decision-process may differ is context; clinical trials present as uncertain and unfamiliar to many participants and health professionals lack the interventions that comprehensively address informational, psychological and decision support needs. For instance, a Cochrane review reported inconclusive results on whether individuals who were provided with a decision aid experienced changes in comprehension and/or uncertainty during decision making.[10] Recently, decision aids adaptable to the clinical trial context have become available via the International Patient Decision Aids Standards (IPDAS) Collaboration however their effectiveness in the trial context remains unknown thus far.[67–69]

Thirdly, across every theme, participants reported a desire for personalised support from the clinician inviting them to participate in a trial. The communication style of the clinician plays an important role in patients understanding of information and willingness to join a trial.[70] Poor communication techniques used by a physician can lead to insufficient patient understanding.[71] Information provision should therefore be tailored to address patients' needs, questions and concerns.[70] For trialists and patients, addressing prospective participants' emotional needs, actively listening and promoting opportunities to converse with, inform, question and interact with each other may provide the best mechanism for addressing negative aspects of the decision-making experience. It is important for clinicians to implement a variety of communication strategies to enhance participants understanding of clinical trial information.[71] Efficacious communication ensures participants receive relevant information customised to their individual learning requirements and encourages informed decision-making.[72]

A focus for decision support may therefore be on improving communication skills using a shared decision-making framework to structure any proposed intervention. According to the IPDAS Collaboration how information is presented can have a significant impact on the knowledge patients acquire, by affecting patient ability to understand and integrate the information.[68] These points are supported by Nishimura's 2013 review of interventions for improving informed consent in trials insofar as conversational opportunities may lead to enhanced understanding of the study among participants, a greater sense of partnering in the research process, and heightened rapport between trialists and participants.[73] The evaluation criteria for assessing the quality of patient decision aids as part of the IPDAS Collaboration, identified coaching/guidance in deliberation and communication as one of twelve broad dimensions in the field of patient design and development.[74] Patients and physicians may therefore profit from receiving coaching and guidance in order to cultivate high-quality and productive two-way communication.[74]

Fourth, we would argue that the experiences synthesised from the data of 40 included studies show a need for interventions that address all facets of the decision-making process described herein. Supporting people to learn about trials in their preferred way and in view of their own circumstances is crucial for any decision support intervention. Participants should also be given the opportunity to express their emotions and be provided with the space to deliberate about the best course to take for their circumstances. Two-way communication that is accompanied by

a strong-patient provider relationships, that recognises individual preferences and values and incorporates and evaluates the use of effective evidence-based information, leads to greater treatment satisfaction and positive health outcomes.[74] Interventions therefore should be multimodal to reflect diverse learning styles in the broader community while space to make a decision should be better incorporated into the informed consent process.[75] Nevertheless, with many failed interventions for supporting the decision to enrol in a clinical trial,[10] more work is needed to build on the process identified in our review and identify ways to measure outcomes of decision support and design effective interventions for cancer survivors deciding whether to enrol in a clinical trial.

Strengths and Limitations

We used a carefully designed and systematic search strategy, rigorous inclusion criteria, and a validated quality assessment process to determine the merits of our review findings. Moreover, several experienced researchers reviewed the protocol and were involved in the key phases of the review. Additionally, we used a popular and robust approach to synthesising qualitative data for systematic reviews.[18] Our review was limited by being unable to access raw qualitative transcripts from any authors identified for inclusion in the study due to either a lack of ethical approval, failure to reply or unavailability of transcripts mostly due to the elapsed time of some studies. All of the studies were conducted in the health systems of highly developed economies. Therefore, there is a limitation that these results may not apply to low-and-middle-income counties. Additionally, we have included studies that have focused on the experiences of patients involved in enrolling in a clinical trial however, of note is that six of these studies also included interviews of patients who subsequently declined clinical trial participation. While it was not possible to identify those who declined within the data from included studies, we believe the experiences of individuals declining to participate in a clinical trial is a gap in the literature and should be a topic for further research.

Conclusion

Our review findings indicate that the decision to participate in a clinical trial is an experience marked by complex informational, emotional and psychological needs. With a lack of evidence on effective interventions, further work is needed to design strategies for individuals considering whether to enrol in a trial which pair quality decision support with effective psychosocial and supportive care.

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