

The Priorities of People with Mesothelioma: A Qualitative Study of Trial Participation and Treatment Decisions

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Abstract

Background

Treatment options for mesothelioma are increasing, as are the number of clinical trials available to patients. However, little is known about patients' and relatives' priorities when making decisions about treatment and trial participation.

Methods

Face to face, semi-structured interviews were undertaken with mesothelioma patients who were participating in the TILT trial (a randomised trial of intra-pleural immunotherapy) and their relatives. Interviews were audio-recorded, transcribed and analysed thematically.

Results

Twelve people were interviewed, comprising five mesothelioma patients and seven relatives. Four themes were identified relating to the experience of mesothelioma: physicality, quality of life, uncertainty and risk, and anxiety and the future. A further theme related to attitudes to research participation.

Participants valued physical strength and were careful not to jeopardise this with potential side effects of medication. Quality of life was important and was often prioritised over survival. Participants found ambiguity challenging and sought certainty, potentially in response to the uncertainty surrounding their future. The desire for certainty impacted on risk perception; an important factor in decision-making. Relatives often advocated on behalf of patients and were more reluctant about research participation due to concern about potential risks.

Conclusion

The study confirmed previous qualitative findings around physicality, uncertainty and relatives as advocates, building on these themes to highlight their influence on decision-making. Important findings for practice include the challenges associated with risk communication and the differing care needs of relatives.

Background

Mesothelioma is an aggressive cancer that most commonly affects the outer lining of the lung (malignant pleural mesothelioma). It is caused by inhalation of asbestos fibres, with tumours developing between 30 to 50 years after the initial exposure.⁽¹⁾ Heavy use of asbestos in certain occupations has resulted in high incidence of mesothelioma among shipyard, construction and heavy industry workers, as well as carpenters, plumbers and brake-lining fitters.⁽¹⁾ International conventions limiting the use and disposal of asbestos were adopted in the 1980s, but because of the time between exposure tumour development, mesothelioma rates are increasing in the UK and globally.^(2, 3) Mesothelioma is currently

incurable and median life expectancy is less than a year from diagnosis.(1, 4) Palliative chemotherapy has been the mainstay of management for over a decade, with the gold standard regimen offering a survival benefit of approximately 3 months.(5) Because of this relatively limited impact on overall survival, many people with mesothelioma choose not to receive chemotherapy.(6) Over recent years, there have been several developments in the treatment landscape for mesothelioma, with randomised trials demonstrating longer survival following treatment with anti-angiogenesis agents and combination immune checkpoint inhibitors.(7, 8) To ensure maximum uptake of these new agents as they become more widely available and to ensure ongoing representative participation in research trials, we explored the decision-making processes around drug therapies and research participation in people with mesothelioma and their relatives.

Previous qualitative studies in mesothelioma have highlighted the importance placed on physical strength by people with mesothelioma who, due to the occupational nature of the disease, are predominantly men with backgrounds in industrial employment.(9) Strength and fitness had been their currency, often key to their sense of self, and the loss of this was challenging for many to accept.(9, 10) Stoicism around symptoms and reluctance to rely on other people have been reported frequently in people with mesothelioma, reflecting their preference for self-sufficiency and self-reliance.(11–13) The priority placed on physical health, and concern about potential side effects of medical intervention, has been reported as influencing some people's decision to decline chemotherapy.(6)

Developing effective management strategies for people with mesothelioma has become a research priority and, as a result, the of clinical trial numbers have increased dramatically in recent years. Although there are challenges associated with recruiting people with terminal conditions into trials, these patients are often keen to participate in research and can benefit from doing so.(14–16) A recent qualitative study embedded within a trial of thoracic surgery indicated that people with mesothelioma had many reasons for participating, including altruism, a desire to receive the trial intervention, appreciation of the enhanced support provided within the trial, and hope.(17) However, some participants experienced uncertainty due to having several different teams looking after their care, particularly when transitioning between teams. Additionally, the process of randomisation caused anxiety among some people, as they struggled with the uncertainty of not knowing which management strategy they would be allocated to receive.

This study explored people's experiences of living with mesothelioma and of participating in clinical research, with the aim of providing insight into the factors influencing decision-making about treatment and trials.

Methods

Study design, population & enrolment

We conducted a qualitative interview study with participants in a randomised feasibility trial of intra-pleural immunotherapy (the TILT trial) and their relatives (full eligibility criteria for the trial are provided in

Appendix A but, in brief, eligible participants had pleural mesothelioma, with a functioning indwelling pleural catheter in situ, a performance status of 0–3, and had not received chemotherapy in the preceding 4 weeks). Purposive sampling was designed to enable inclusion of participants who had experienced all aspects of the trial, including those who had been allocated to the control and intervention groups, as well as people who had declined to participate in the trial. Relatives were also purposively sampled, and this was complemented by snowball/chain sampling to enable invitation and inclusion of wider communities of family and friends.

Participants were provided with an information sheet about the qualitative study at their final research appointment in the TILT trial. Relatives were approached at the same time, if present, or, if not, via letter with information about the study. Once the information was received and after a further 72 hours, the study team contacted participants and provided the opportunity to discuss the study and ask questions. Following discussion, if the person verbally agreed to meet the researcher, a date and location for the interview was arranged.

Data collection

Participants chose where the interview took place. Possible locations included their own home, the home of a friend or family member, a village hall, local hospital or a non-clinical space at a local university, although ultimately all interviews took place in participants' homes or community hospitals. Most interviews involved the participant and interviewer only, however two participants (both relatives) requested to be interviewed together, for support, and in keeping with their wishes, they were interviewed together. Immediately before interview, all participants provided written informed consent, including consent to be audio-recorded and for anonymised quotes to be used in written reports of the research.

Interviews were performed by the first author (ACB) in English (the first language of all participants). All participants had previously met the interviewer during clinical care or research involvement. Interviews lasted between 24 minutes and 92 minutes and were digitally audio-recorded. A topic guide was used to ensure the main aims of the qualitative study were met (Appendix B), however there was flexibility within each interview to discuss subjects beyond the topic guide if they arose.

Data analysis

Audio-recordings of interviews were transcribed verbatim and anonymised. Pseudonyms were generated for each participant and are used throughout the manuscript. Transcripts were reviewed and checked for accuracy, then re-read and recordings listened to, to increase familiarity with the data. Transcripts were uploaded to QSR NVivo v12 qualitative analysis software. Once uploaded, we used thematic analysis, in which transcripts were coded by ACB after each interview, with the code list reviewed before each successive interview. Transcripts of four interviews were independently double-coded by RGH. Code-lists were compared and refined in discussion between RGH and ACB, followed by discussion with the whole research group, and further refinement. Once all transcripts were coded, segments were grouped into categories and themes. Themes were mapped to identify connections and a descriptive account was developed.

Results

Participants

Seven TILT participants were invited to participate, of whom five agreed. Nine relatives were approached and seven participated, two of whom were interviewed together (Ida and Janet). All participants were interviewed once, giving a total of 11 interviews with 12 people. Of the four people approached but not interviewed, one TILT participant verbally agreed to meet the interviewer and discuss participation, but died before the interview took place. Her husband (the only relative bereaved during the study) declined to participate. Another participant declined the qualitative study as he was approaching the end of his life and felt too unwell to be interviewed. His daughter-in-law was interviewed instead. One patient’s wife declined interview as she felt that her husband had spoken for both of them.

Participant characteristics are shown in Table 1 (names are pseudonyms). All trial participants interviewed were men, as the only female trial participant had died before the interview would have taken place. Two participants had received the trial intervention and two were members of the control group. One man was interviewed after withdrawing from the trial’s intervention arm, and the daughter-in-law of a man who withdrew from the control arm was also interviewed.

Themes

Analysis of interviews revealed four main themes relating to participants’ experiences of mesothelioma. These experiences informed their decision-making about treatment and trial participation. The themes were:

- i. physicality,
- ii. quality of life,
- iii. uncertainty and risk,
- iv. anxiety and the future.

A further theme related to participants’ attitudes to research and reasons for participating or not participating in the clinical trial.

The same themes were noted in interviews with trial participants and with relatives, however, the experiences within the theme often differed. Each theme is summarised below, with illustrative quotes provided in the boxes.

Table 1 - Characteristics of interview participants. All names are pseudonyms

Pseudonym	Role	Gender	Age group	Interview location
Alan	TILT participant (intervention arm)	M	70-74	Patient's home
Bob	TILT participant (control arm)	M	80-84	Patient's home
Caroline	Wife of Alan	F	70-74	Patient's home
Dave	TILT participant (intervention arm)	M	60-64	Community Hospital
Eleanor	Wife of Bob	F	80-84	Patient's home
Frank	TILT participant (control arm)	M	80-84	Patient's home
Georgina	Wife of Frank	F	75-79	Patient's home
Harry	TILT participant (withdrew from intervention arm)	M	70-74	Patient's home
Ida	Wife of Harry	F	70-74	Patient's home (interviewed with Janet)
Janet	Daughter of Harry	F	45-49	Patient's home (interviewed with Ida)
Kate	Daughter-in-law of participant (withdrew from control arm)	F	40-44	Community Hospital

Physicality

All participants commented on the physical aspects of mesothelioma. Symptoms such as breathlessness impacted on activities and elicited strong emotions, including frustration and anger (Box 1a). Despite this, men with mesothelioma tended to understate their physical problems, often emphasizing their prior fitness and strength. However, several men recognised that their physical strength was deteriorating and expressed sadness and regret at their new reality.

Relatives described the anguish of watching patients experience symptoms that they (relatives) could not alleviate. In response, some relatives assumed the role of advocate, speaking out on behalf of their husbands. However, these efforts were sometimes hindered by the patient's stoicism, causing frustration (Box 1b).

Quality of life

Quality of life was important to participants and relatives, especially in the context of limited life expectancy. Participants were able to balance the amount of time they had left to live against how they felt during that time, with an awareness that their situation was likely to change in the future. For most, living longer was not desirable unless accompanied by good quality of life. (Box 2a).

The desire to preserve quality of life (and the impact of physical health on this) influenced participants' decisions about chemotherapy. Participants were well-informed about the specific survival benefit associated with chemotherapy and of potential side effects, and many believed that the limited benefits of chemotherapy did not outweigh the risks (Box 2b).

A

"I know I've got it ... but I don't feel bad. I'm okay, I like to walk, my body still allows me to walk and I do it." Bob, 84 M, person with MPM.

"[Larry] done a lot of, 'Oh, I am fine, I am great, I am OK,'" Kate, 43 F, daughter-in-law of person with MPM.

"[Doctor] said, 'Would you like to come up to my office by lift?' and I said I would walk up, so I walked up five flights of stairs." Frank, 81 M, person with MPM.

"I can remember on the Wednesday a friend came round wanting the concrete mixer, and I was humping and carrying, and I felt absolutely wonderful, I felt fine." Alan, 71 M, person with MPM.

"I've only got to walk up the garden and I can feel it, I'm struggling to breathe." Harry, 74 M, person with MPM.

"If he did anything physical, he'd spend three or four days recovering from [it], and for [Alan] he just hated it, every second of it." Caroline, 71 F, wife of person with MPM.

"It has been a shock for me to realise that I'm going to have to give up my golf and table tennis." Frank, 81 M, person with MPM

B

"It's pitiful to see him absolutely gasping for breath... [and] you can't fix it, you can't make it easier, you just have to watch." Ida, 72 F, wife of person with MPM.

"I felt so helpless, [Alan] thought he was going to die and to be honest I think the ambulance people did too... it wasn't a good experience, and, yes, it was me that took up the cudgels, but [Alan] was too poorly to do anything about it." Caroline, 71 F, wife of person with MPM.

"I was told you can't have a nurse specialist because [Larry]'s gone, 'Oh, I am fine, I am fine,' and I go, 'You actually have to tell her you are breathless! You need this, I am not doing it all'." Kate, 43 F, daughter-in-law of person with MPM.

Box 1 Quotes demonstrating the theme of physicality.

A: Participants often displayed stoicism and emphasized prior physical strength. For others, the severity of their symptoms limited their activities, causing sadness and frustration.

B: Relatives described a sense of powerlessness in the face of physical symptoms, often assuming the role of advocate, speaking up on their relative's behalf.

A

For us at the moment, quality of life is the first priority. For the years that we have got left, and hopefully there will be quite a few, we [want to] appreciate the quality of life." Eleanor, 81 F, wife of person with MPM.

"Long may the situation reign that I've got, but I can't bank on it, can I?" Bob, 84 M, person with MPM.

"Yeah, I'm happy to carry on like this, if I could stay like it." Harry, 74 M, person with MPM.

"If I got some extra time that's brilliant, but I couldn't face it like this." Frank, 81 M, person with MPM.

B

"He said, 'If it was only going to give me two months extra, I wouldn't have treatment, because the impact of having the treatment would affect the quality of life I was having, potentially.'" Kate, 43 F, daughter-in-law of person with MPM.

"We'd seen the results of chemo and it didn't work, it was absolutely hell to go through, so there didn't seem any point; if you're not going to get more than a couple of months out of it, what is the point? That was the decision that was reached." Caroline, 71 F, wife of person with MPM.

"We had this long discussion about should he have the chemo or not, and we were both of the opinion that he shouldn't have it... He looked at it from a much more practical side, went into all the statistics and found out how short a time it would prolong his life and thought, 'Well, on balance it's not worth it.'" Georgina, 79 F, wife of person with MPM.

"[Doctor] sent me a recent paper, which he was very positive about. But when I looked at it, it talked about dramatic improvements, doubling of life expectancy from six months to twelve months type of thing, so I thought, mmm, and with some really serious side effects, and so I decided that wasn't for me because quality of life is important." Frank, 81 M, person with MPM.

"That first [trial], what I, what I backed out of... I thought, well, with all my ailments another one ain't gonna be very nice, so that's the reason why." Harry, 74 M, person with MPM

Box 2 Quotes demonstrating quality of life theme

A: Participants prioritised quality of life, while recognising that their circumstances may change in the future.

B: The wish to preserve quality of life and avoid further physical symptoms influenced participants' decisions around chemotherapy and trial participation.

A similar pattern emerged in participants' descriptions of the decision to participate in clinical trials. People with mesothelioma sought out information and were able to evaluate the potential benefits of receiving a trial medication against the possible impact of side effects on their quality of life. One participant who withdrew from the trial explained it was due to concern about adverse effects of the trial medication impacting negatively on his quality of life.

Uncertainty

People with mesothelioma were knowledgeable, actively seeking information from multiple sources to assist their decision-making. They showed a preference for factual, numerical data, often wanting information to be presented as unequivocal or absolute (Box 3a). Participants disliked uncertainty and expressed frustration if they felt the information they were given was ambiguous or not specific to them.

The desire for certainty had implications on participants' understanding of equipoise and perception of the risks involved in the trial. Several people expressed a belief that clinicians had existing knowledge about the efficacy of the trial drug, and some thought that doctors could predict their individual response to it (Box 3b). This impacted on two participants who experienced adverse reactions. Despite receiving written and verbal descriptions of all possible adverse effects and their severity, both participants felt underprepared for the reactions they experienced. They described wanting specific descriptions of the severity and duration of the symptoms they experienced, seemingly not realising that this was impossible to predict.

A

"I mean reading various leaflets and [wife] going on the internet and kids doing various stuff, [son] particularly, they're quite convinced that I've only got two and a half years to live." Alan, 71 M, person with MPM.

"A statistic I used to have at the back of my head for meso is that – I'll just get this right – five per cent of people live for five years, and that's the sort of figure, that's the statistic I want." Frank, 81 M, person with MPM.

"You know, one person says, 'It is not going to really do you a lot of good'. Another person says, 'Well, we don't know, it might do'. So, what do I do? I would rather somebody say, 'It is of no use to you whatsoever and don't bother' or, 'Go for it'. But don't wishy-washy in between either a yes or a no." Dave, 61 M, person with MPM.

B

"I felt at that time you wouldn't have offered him something that would have fundamentally made him a lot worse." Caroline, 71 F, wife of person with MPM.

"Yes, the leaflet said, you know, 'You may feel terrible' and then went on [with the] various other things you can get, but... err, had anyone told me I could feel so rough?" Alan, 71 M, person with MPM.

"Yeah. I didn't realise at the time, after you gave me the drug, how bad I was going to feel." Dave, 61 M, person with MPM.

"I accept you don't know how I am going to react to something [but] It would also be nice to say, 'OK, you'll probably take 3-6 months to get over this.'" Alan, 71 M, person with MPM.

"If you ever said, 'Well this is going to put you in bed for a couple of days or it possibly could put you in bed for a couple of days' ...then I would have gone, 'Yeah, okay I can live with that.'" Dave, 61 M, person with MPM.

Box 3 Quotes demonstrating the desire for certainty

A: Participants sought out factual and numerical information and disliked ambiguity or uncertainty.

B: The desire for certainty impacted on participants' and relatives' appreciation of equipoise and perception of risks involved in trial participation.

A

"Sometimes I sit there and dwell and think, I wonder what the actual end is going to be like. You know, am I going to be in pain, am I going to be this, am I going to be that?" Dave, 61 M, person with MPM.

"I've heard a lot, a few people, gone [died] working with asbestos and I thought, well, I'm next." Harry, 74 M, person with MPM.

One of the reasons I'm interested in knowing how much time I've got is how do I prepare? I mean, if it's 18 months away I'm not going to start thinking about funerals et cetera." Frank, 81 M, person with MPM.

"I think [wife] is struggling a little bit... But as I don't talk about it then I don't really know how she feels." Dave, 61 M, person with MPM.

"Yeah, it has been a big shock for [wife] because I did all the, um, I did a lot of work in the house and with the shock of me having this relapse... I've been trying to work hard to get her to do a lot of things I used to do. For example, how do you check the pressure on the tyres? How do you order oil for the central heating? I've been trying to work through it all." Frank, 81 M, person with MPM

B

"I can't just sit and think about it day in day out. Otherwise, I don't know what I would do. Go nuts, I think. I am not saying I put on a brave face, but it is no good dwelling on it... Rather than sit and wait and think, is it coming? I just put it to the back of my mind and don't even give it another thought." Dave, 61 M, person with MPM.

"I think he's lucky, to be honest, there's a lot of people worse than him, so he's lucky." Ida, 72 F, wife of person with MPM.

"The [patient-reported outcome measures] were asking me to comment on situations where I wasn't feeling particularly bad. Most of the answers to the questions were either high or in the affirmative and I tended to get the feeling that I was, perhaps, a very fortunate man. I think I am." Bob, 84 M, person with MPM.

Box 4 Quotes illustrating the theme of anxiety and the future

A: Men with MPM were aware of their limited life expectancy but while this caused anxiety in some, most participants were stoical and focussed on practical issues.

B: Participants and relatives tried not to dwell on future uncertainties, preferring to maintain a positive outlook where possible.

Anxiety and the future

Participants may have sought certainty as a coping strategy to manage the uncertainty affecting their future. People with mesothelioma were aware that they were likely to die as a result of their illness, but the unpredictable nature of the disease generated anxiety (Box 4a). As with physical symptoms, however,

most men with mesothelioma were stoical about death and preferred to focus on the practical issues facing them, rather than the emotional. Several participants and relatives maintained remarkably positive outlooks, despite the limited prognosis.

Attitudes to research

Participants were generally positive about research, recognising that clinical trials were crucial to develop knowledge about mesothelioma and generate new treatment options (Box 5a). Most people participated in research for altruistic reasons in the hope of helping other people in future. Some people were aware that trial participation could potentially benefit them, although this was rarely a primary motivational factor. Other participants expressed a desire to repay the care they had received from clinicians. In keeping with prior themes, people with mesothelioma were well-informed about the science underpinning the research and, in several cases, this motivated them to participate.

Relatives were generally supportive of their family member's decision to participate in research (Box 5b). However, they expressed a greater recognition of potential downsides, and some were reluctant for their family members to participate in the trial. The wife of one man who withdrew from the trial after being randomised to receive the trial drug described her relief, as she had been concerned about the risk of side effects.

A

"There's got to be trials because otherwise you're never going to find anything that's going to help this dreadful disease." Caroline, 71 F, wife of person with MPM.

"If it's not right for me, hopefully it'll be right for someone else" Alan, 71 M, person with MPM.

"Of course, once you've decided you're going to do it, you're this focus of all this attention and all these extra things are being done to look at what's wrong with you, and that can't be bad." Bob, 84 M, person with MPM.

"I was keen to show that I appreciate what your team had been doing for me." Harry, 74 M, person with MPM.

"I'm always interested in the most recent scientific data and if I think there's potential there, I would get involved." Frank, 81 M, person with MPM

B

"He's very up for going for things, and he wanted to help, and I supported him in that, as did our family." Eleanor 81 F, wife of person with MPM.

"Obviously, I'd support whatever decision he made, but seeing him, well, I was worried that if he got [side effects], yeah, it's flu and whatever, but also, I had to think about my mum, 'cause she's the one looking after him and it's taken its toll on her as well." Janet 48 F, daughter of person with MPM.

"I wasn't keen for [husband] to be involved, to be honest... If he'd wanted, I would have gone along with it and supported him... but I would rather he hadn't done it because I know he doesn't like being ill." Georgina, 79 F, wife of person with MPM.

"I think the desire to be part of research and perhaps doing some good was stronger than his fear of having side effects at that stage. I'm more reticent because I'm aware of what comes afterwards in so many of the options we've had." Caroline, 71 F, wife of person with MPM.

"I knew that [husband] would say he would help in any way, but when you mentioned this [trial], and he'll be feeling like he's got the flu for a while, I thought, 'Oh, I don't know, he don't need any of that'. That did play on my mind. But he said he's not gonna, he wouldn't do that... I was, yeah, I was relieved." Ida, 72 F, wife of person with MPM.

Box 5 Quotes illustrating attitudes to research and reasons for research participation.

A: People with MPM were motivated by altruism, awareness of potential personal gain, gratitude and scientific interest.

B: Relatives, whilst supportive of their family members' decisions, were more aware of the potential downsides of research participation and generally more reluctant for them to take part.

Discussion

This study provides insight into the experiences and priorities of people living with mesothelioma and their relatives, and the role these experiences and priorities play in influencing decisions about treatment and research participation. As more effective therapies are approved for use in mesothelioma and clinical trial portfolios expand, it has become increasingly important to understand people's motivations for accepting or declining treatment and trial participation. Without an appreciation of the factors influencing these decisions, low uptake could undermine the clinical effectiveness of novel treatments and the external validity of clinical trials could be affected by selection bias.

Our study highlighted several key points, including the importance of physical strength for people with mesothelioma and its role in overall quality of life. Similar themes have been reported previously and the current study furthered this, revealing how patients balance the potential negative impact of side effects on their physical health against the survival benefits of treatment.(12, 18, 19) Our study also reinforced previous findings about the impact of uncertainty on people with mesothelioma, again broadening our understanding to show how this translated into a desire for certainty and preference for absolutes. By developing the themes of physicality, quality of life and uncertainty, specifically in relation to treatment and trial decision-making, our study augments the existing literature and furthers our understanding of the experience of people with mesothelioma.

The desire for certainty had important consequences for participants' perceptions of risk and acceptance of equipoise in trial settings. It raised important questions about how to effectively communicate equivocal or unpredictable outcomes to this population. Patient surveys have shown that people with mesothelioma were highly activated and engaged when it came to seeking out information about their disease and about clinical trials. (17, 20–23) Based on this and on our findings, it could be thought that more information is better for people with mesothelioma. However, not everyone is eager to know everything. Previous qualitative work described the varying amounts of information that different people with mesothelioma desired and were able to process.(23–25) Some people found it upsetting to be reminded of the short life-expectancy and limited treatment options associated with the condition.(23, 24) There is a balance required, therefore, between provision of the desired level of information (which may vary between patients) whilst maintaining optimism and preserving hope.

This tension is not unique to mesothelioma, as a questionnaire study of 56 patients receiving palliative care for various terminal diseases revealed.(26) Patients wished their doctors to be honest with them, but the majority (91%) also wanted them to be optimistic. The key to achieving this balance appears to lie in the manner in which information is imparted.(27) The RADIO-meso study confirmed that the 'shock' and 'devastation' of receiving a diagnosis of mesothelioma was lessened if communicated in a sensitive and caring fashion.(25) Respondents to the Mesothelioma UK patient survey described similar experiences, whereby the warmth of the staff helped relieve some of the trauma of receiving the diagnosis.(20) Other key communication elements included keeping the patient at the centre of discussions, being led by their information requirements and ensuring information was provided carefully and sensitively.(25)

Optimism and hope were important motivators to research participation, something that was also noted in qualitative interviews with participants in the mesothelioma surgical trial MARS2. Similar to TILT, MARS2 participants were motivated by altruism and the hope of receiving a treatment not available in routine care.(28) Recognition of the enhanced care received during trial follow up was also acknowledged by MARS2 and TILT participants alike. In contrast, the finding that some people with mesothelioma were motivated to participate in the trial because of scientific interest and understanding is novel, although unlikely to be unique to TILT participants. Future work could explore this in more detail.

Another novel finding from this study was that relatives were less enthusiastic about research. Their reluctance may reflect the higher levels of anxiety experienced by carers of people with mesothelioma or may be an example of relatives advocating on behalf of stoical patients.(9, 12, 29) Either way, it emphasizes the different experiences and concerns of relatives compared with patients; something that should not be overlooked in clinical practice. Several studies have described the heavy emotional burden experienced by carers of mesothelioma patients, with challenges including the change in role from partner to care-giver, awareness of future bereavement, and the demands of legal processes and post-mortem requirements.(9, 10, 12, 30–32) As a result of these pressures, relatives have described tiredness, sleep disturbance, feelings of helplessness and neglect of their own health.(10, 12, 29–31) These factors deserve recognition and require dedicated support. Mesothelioma specialist nurses play a crucial role in supporting relatives as well as patients, providing personalised care alongside an understanding of many of the nuances and complexities specific to mesothelioma.(20, 24, 25)

This study has strengths and weaknesses. Purposive sampling ensured that people with different experiences of research participation were interviewed, including people who received a trial intervention, control participants and two people who had declined to participate in the trial. Our findings resonate with and extend previous qualitative research in mesothelioma, suggesting the results have high credibility. A thematic approach to analysis enabled us to develop themes inductively from the data and our approach to coding and double coding enhanced rigour in the process and our confidence in the results. The sample size of twelve provided sufficient information power,(33, 34) and previous studies indicate that 12–14 interviews is sufficient to achieve theme saturation (i.e. the point at which no new themes relating to the research question are identified).(35, 36) In our study, theme development after each interview suggested that saturation had been achieved after the ninth interview, and additional interviews with three more participants confirmed this.

Reflexivity is important in qualitative work, and it is important to acknowledge that the interviewer was known to all participants in either a clinical or research context prior to the interviews. This could have influenced the interviews in one of several ways. From a positive perspective, the interviewers familiarity with mesothelioma facilitated discussions, and participants did not need to explain medical processes or terminology. Additionally, some interviews were enhanced by the presence of an existing relationship with mutual trust and respect already established. Contrastingly, it has been suggested that patients interviewed by healthcare providers may try to please them by saying what they think the clinician wants to hear, and this was a consideration in our study.(37) However, the openness with which several

interviewees discussed their concerns about treatments and trials, and their willingness to express reluctance about aspects of their care was reassuring. It suggested that interviewees felt free to present their genuine feelings and experiences and were not trying to gratify the interviewer.

Not everyone who was invited to participate in the qualitative study agreed to do so. Two TILT trial participants were not interviewed, in both cases because they were nearing the end of their life. Consequently, we acknowledge that our findings may not reflect the experiences of people in the final stages of mesothelioma; a time at which time peoples' perspectives may alter. The experiences and perspectives of people at the end of life are worthy of future investigation.

The study sample only comprised White British participants in late middle age or older, and all participants with mesothelioma were male. Although not representative of the general population, this is an accurate reflection of the UK mesothelioma population and the findings are likely to be transferable. (38) However, the experience of mesothelioma differs across gender and is likely to so do across ethnic groups, as will attitudes to research participation.(39) To fully understand the lived experience of mesothelioma, voices from all patient groups should be heard.

As well as exploring the experience of minority groups with mesothelioma, our study generated several areas worthy of future research. To identify effective ways to convey equipoise or ambiguity without compromising coping strategies there is an urgent need to conduct research into information requirements and preferences in relation to risk communication. Such work could include qualitative work to refine communication methods, and co-design research to develop information resources.

Declarations

Funding

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Conflicts of interest

The authors have no conflicts of interest to declare relating to this work.

Availability of data and material

Source data, which comprises audio-recordings of interviews, contain potentially identifiable information and are therefore not available. Anonymised transcripts of interviews are available on request from the corresponding author, and all participants provided written informed consent for sharing of their data in this way.

Code availability

Not applicable.

Authors' contributions

ACB, NAM and RGH conceived the study and designed it. ACB, AJM, RGH and EK recruited participants and collected and analysed data. RGH and NAM reviewed and refined the analysis. The first draft of the manuscript was written by ACB and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Ethics approval

The qualitative study was approved by NHS Research Ethics Committees (ref 17/SW/0080) and the HRA (IRAS ID 215394) as part of the protocol for the TILT trial.

Consent to participate

All participants provided written informed consent to participate in the qualitative study.

Consent for publication

All participants provided written informed consent to for publication of data arising from this study, including use of verbatim quotes.

Clinical Trial registration

The TILT trial, including the qualitative element reported here, was registered prospectively on the European Clinical Trials Registry (EudraCT number 2016-004727-23) and the ISRCTN Register (10432197) on 04/12/2017.

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