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The Mesothelioma and Radical Surgery Trial 2 (MARS 2): Qualitative Assessment Study

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Project Summary

The Mesothelioma and Radical Surgery Trial 2 (MARS 2): Qualitative Assessment Study

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This Qualitative Assessment Study (QAS) explored the patient experience of participation in a UK based clinical trial - the Mesothelioma and Radical Surgery Trial 2 (MARS 2). The MARS2 trial assessed the role of lung sparing surgery and chemotherapy compared to chemotherapy alone for the treatment of Malignant Pleural Mesothelioma. The purpose of the QAS was to generate insights into the patient experience of recruitment, consent and randomisation to the trial as well as the experience of the MARS2 interventions. It also aimed to identify recommendations for the presentation of trial information and the support required by patients.

Methods

The study used longitudinal semi-structured patient interviews scheduled at specified points within the trial and treatment plan. 15 participants took part in the study, and a total of 41 interviews were carried out over the telephone by two researchers between August 2015 and March 2017. Interviews ranged in duration from 8 to 45 minutes and were digitally recorded and transcribed verbatim. Analysis of the data was carried out using framework analysis (Ritchie & Lewis, 2013). The interviews explored experiences and views on recruitment and randomisation along with influences on decisions to participate in the trial. Patients were also asked about their expectations and experiences of the treatments received and associated care and support needs.

Findings

The findings in relation to the key project themes were as follows:

The context of trial information

Participants were given trial information and made decisions about participation at a time when they had recently encountered a diverse range of new and concerning experiences. These included worrying symptoms, hospital visits, investigations and procedures, along with being given life-changing information about diagnosis and prognosis. These factors shaped the context in which they were then given information about the MARS 2 trial.

Learning about the trial

All of the participants reported being given information and opportunities to discuss both treatment options. The depth and quality of information about treatment and the trial provided verbally by the staff was praised. However, some found the language and detail provided in the written information confusing. There was evidence that some participants had inferred from their consultation that surgery might be the preferred or more effective treatment option. This may have been influenced by the way in which information about the aim and intention of surgery was presented.

Deciding to join the MARS 2 trial

Reasons given by participants for participation in the MARS 2 trial included: altruism, gaining access to surgery, a positive self-assessment of their ability to cope physically with treatment and a belief that enhanced support might be available to trial patients.

Understanding randomisation

Variation in understanding regarding randomisation procedures were revealed. Misunderstandings included perceptions that treatment decisions were made by the doctor or a computer based on an assessment of their particular health characteristics.

Treatment preference

Eleven participants stated a preference for a specific arm of the trial prior to randomisation and waiting for the outcome was a time of anxiety. Five participants did not get their preferred treatment choice. Those who did not get surgery described feeling disappointed and contrasted this to their earlier optimism on being eligible for randomisation. For some this was influenced by a perception that chemotherapy might not be as effective as surgery.

Experience of chemotherapy

Negative experiences of chemotherapy included fatigue, nausea, reduced appetite, taste changes, constipation, infections, excessive tears, sore eyes and skin reactions. Admission to hospital to manage serious side effects such as neutropenic sepsis and dehydration occurred for three participants. The negative impact of nausea, anorexia, taste changes, fatigue and feeling generally unwell on eating and drinking was a significant concern for those who experienced this.

Experience of surgery

Post-operative complications were reported by some which had resulted in extended hospital stays. Reasons included a chest infection, post-operative bleeding, surgical emphysema and complications with the chest drain. Difficult journeys home on being discharged from hospital were recounted suggesting inadequate anticipatory pain management.

Post-operative problems in the weeks and months after surgery included pain, breathlessness, tiredness, feeling weak, numbness at the operation site, constipation and reduced appetite. Being discharged home with a post-operative chest drain was associated with pain and difficulty sleeping. Some felt unprepared for having a chest drain at home.

Sources of support

Family members played a vital role in providing practical and emotional support during trial and treatment procedures and recovery. The most frequently mentioned sources of professional support post treatment were district nurses and General Practitioners. People did have contact numbers for the treatment centres which were used during chemotherapy but less often post-surgery. Transitions between treatments and moving 'off trial' were difficult, partly due to losing contact with staff they had built a relationship with. In some cases this appeared to be exacerbated by the absence a clear plan for on-going care and support.

Conclusions

The longitudinal approach used in this study identified changing priorities and care needs of patients across the trial and post treatment. There were many examples of positive experiences particularly relating to the information and care provided pre, during and immediately post treatment.

Recommendations

- Consideration needs to be given to the presentation of trial information and the development of formats that can be tailored to individual needs and preferred ways of learning.
- All staff involved in recruitment, information and support regarding clinical trials need to be aware how easily their words can be misinterpreted by patients. Developing information that communicates the trial procedures that reduces the potential for misunderstanding should be a priority
- Pro-active symptom management and enhanced communication between treatment and service providers should be seen as part of the treatment plan. New roles such as care navigators or nurse-led services should be considered to support transitions in the treatment pathway.
- The development of exit consultations and the implementation of elements of the Macmillan recovery package could help to manage patient expectations and bridge gaps between primary and secondary care.

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1. Background

Malignant pleural mesothelioma (MPM) is an aggressive cancer of the lining of the chest wall and lung, its aetiology lies in asbestos exposure. With over 2,500 people diagnosed each year, the UK has the highest incidence of mesothelioma in the world. Chemotherapy is an established treatment for MPM but response rates are variable, evidence is lacking in new drug therapies and mortality remains high (in the UK half of patients die within 8.5 months of diagnosis). Surgery is therefore an important option.

Very little robust, randomised controlled trial evidence (RCT) exists regarding surgical interventions for mesothelioma and many studies are observational (Cao et al 2014). There are also challenges in conducting clinical research in surgical treatments. Influencing factors include reluctance to accept randomisation, restrictive trial regulation and difficulties in presenting trial arm options neutrally (Treasure and Morton 2012, Horton, 1996). There is a lack of qualitative research into the patient experience of randomised clinical trials involving surgical interventions. There is also an absence of research to understand mesothelioma patient's motivations to participate in trials of surgical treatments. A recent survey has indicated that barriers exist to participation in mesothelioma clinical trials (British Lung Foundation, Unpublished). This study did not focus on surgical trials, but did point to fear of being allocated to the placebo arm, and a lack of information and support about available trials as barriers to participation.

The Mesothelioma and Radical Surgery Trial 2 (MARS 2) examines the role of radical surgery in the treatment of pleural mesothelioma. This trial has provided a unique opportunity to conduct an embedded qualitative evaluation to generate insights into the patient experience of recruitment, consent and randomisation as well as the experience of the MARS 2 interventions.

The aims of study were to:

1. Provide understanding of the patient experience of:
 - trial treatments (radical surgery and chemotherapy)
 - recruitment procedures (informed consent, factors influencing decisions to participate and understanding of randomisation)
 - care and support received prior to, during and after treatment
2. Identify recommendations for the conduct of future trials, including the presentation of trial information alongside the information and support needs of patients before and up to 12 months after treatment

Research questions

1. What is the patient experience of the MARS 2 study interventions?
 - What are the support and information needs of people receiving the interventions (surgery and no surgery)?
 - What is the impact of the interventions on their quality of life?
2. What is the patient experience of the MARS 2 recruitment process?
3. What factors influence patient decisions regarding MARS 2 including participation and randomisation?

2. Methods

The MARS2 QAS is a longitudinal qualitative exploration of patient experiences of recruitment and treatment interventions within MARS2. Semi-structured patient interviews were scheduled at 3 or 4 points within the trial and treatment plan dependent on treatment arm (see figure one). Interviews were carried out over the telephone by two researchers, CW and KL, between August 2015 and March 2017. Interviews ranged in duration from 8 to 45 minutes and were digitally recorded and transcribed verbatim. Analysis of the data was carried out using framework analysis (Ritchie & Lewis, 2013).

Interviews were conducted using a topic guide developed in collaboration with relevant members of the trial management group, lay consultation and with reference to the relevant literature. Patient interviews explored experiences and views on recruitment and randomisation, as well as influences and motivations underlying decisions. Reasons for consenting to participate in the trial were elicited. Patients were also asked about their expectations and experiences of the treatments received and associated care and support needs.

Sample

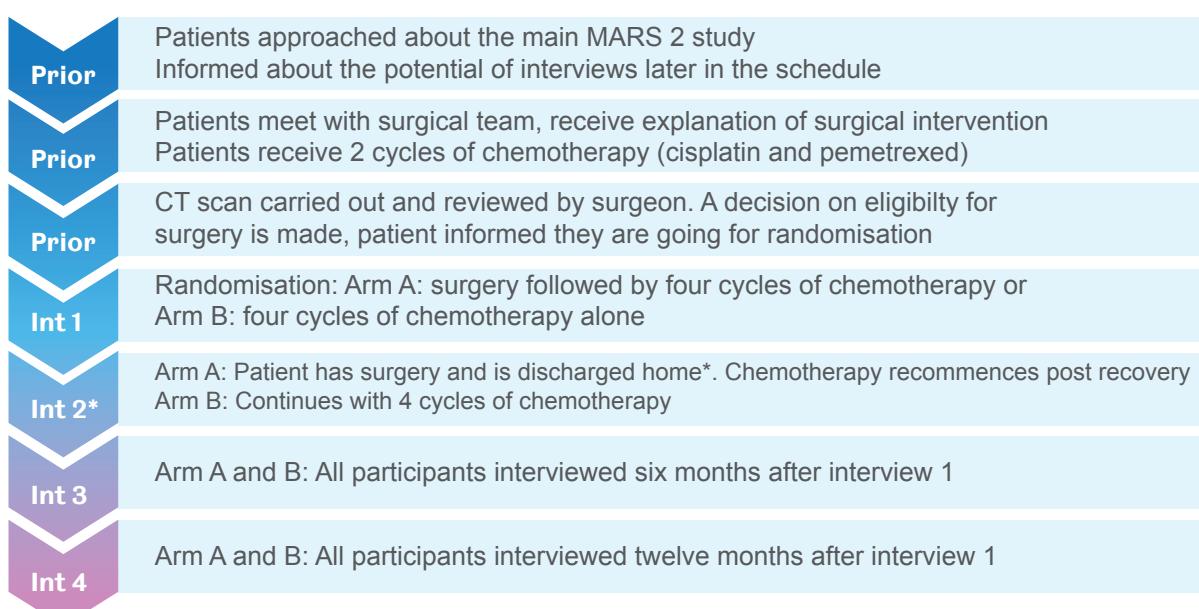
The process of recruitment and randomisation is detailed in Figure 1. Following randomisation patients were approached regarding the interview study. 15 people were recruited, with 9 participants receiving chemotherapy and surgery and 6 receiving chemotherapy alone (arm A and B). Interview schedules were as follows (also see figure 1):

Arm A: 4 interviews: post randomisation but prior to surgery, within 4 weeks after surgery and at 6 and 12 months after the initial interview.

Arm B: 3 interviews: post randomisation and at 6 and 12 months following the first interview.

Demographics and number of interviews conducted for each participant is detailed in table 1.

Figure one: Qualitative study interviews and trial interventions



*Interview 2 carried out with participants who received surgery only

Table one: Demographics and treatments summary

Study number	Study arm	Gender	Age	Marital status	Interview 1	Interview 2	Interview 3	Interview 4
1	Surgery	Male	74	Married	Yes	Yes	No (died)	NA
2	Surgery	Male	66	Married	Yes	Yes	Yes	No (no reply to contacts)
3	Surgery	Male	59	Married	Yes	Yes	Yes	No (died)
4	Surgery	Male	63	Married	Yes	Yes	Yes	Yes
5	Chemotherapy	Male	69	Married	Yes	NA	Yes	Yes
6	Surgery	Male	82	Not known	Yes	No (died)	NA	NA
7	Surgery	Male	73	Married	Yes	Yes	No (no reply to contacts)	No (died)
8	Surgery	Male	78	Widower	Yes	Yes	No (withdrew)	No (died)
9	Chemotherapy	Male	65	Married	Yes	NA	Yes	Yes
10	Chemotherapy	Male	69	Married	Yes	NA	Yes	No (died)
11	Surgery	Female	63	Married	Yes	Yes	Yes	Yes
12	Chemotherapy	Male	77	Married	Yes	NA	Yes	Yes
13	Chemotherapy	Male	68	Married	Yes	NA	Yes	Yes
14	Surgery	Male	78	Widower	Yes	Yes	Yes	No (withdrew)
15	Chemotherapy	Male	68	Married	Yes	NA	Yes	Yes

3. Findings

Experiences prior to the trial

Participant's accounts of their experiences leading up to trial participation revealed a series of worrying events, most of which were new experiences. These were accompanied by multiple episodes of information provision on unfamiliar and troubling subjects. All of this had occurred within a relatively short period of time. A summary is presented in Figure one (p 15).

Getting a diagnosis

Participants described their own pathways to diagnosis. There were shared elements but also a significant amount of variation. Breathlessness, pain and/or cough were the most frequently mentioned presenting symptoms but the speed of onset, and the time it took to seek medical advice, differed. Some people had delayed seeking advice hoping symptoms would improve. Other participants had waited until symptoms were having a significant impact on daily living, while others "mentioned it" opportunistically, when they were seeing the General Practitioner (GP) for another reason. Two participants presented at A&E due to the severity of their symptoms, all others were first seen by their GP.

The speed of referral to the hospital for investigations again varied. Some were treated initially with antibiotics and were then referred as their symptoms did not change or deteriorated. Others recounted that their GP referred them immediately, in some cases this was attributed to perceived occupational risk factors.



"Because I had worked on the railways she recommended that I had an X-ray". (Participant 10)



"GP said it was probably mesothelioma because of where I live, because quite a few people round here, it's a big asbestos factory, or it was, where I worked". (Participant 4)

During symptom investigations, many were found to have a pleural effusion, which was followed by drainage and biopsy procedures. Participants often described the volume of fluid drained - this ranged between 1 ½ to 4 ½ litres. Having fluid on the lung was described by some as a sign to them that something was seriously wrong.



"Because I had spent over a day in hospital having the drain done and looking at what was coming out of my chest, I sort of realised then that they weren't going to say, you've got a little bit of infection, there's some antibiotics, do you know what I mean"? (Participant 1)

Many contrasted their new situation to how they had felt prior to their symptoms and diagnosis. They described how fit and active they had been up to the time of their symptom onset, for example, going to the gym or playing golf. For most participants, this was the first time they had attended hospital for investigations and procedures or been unwell apart from accident related injuries; for them, this was a new and unexpected experience.

"Before that I was in the gym every other day....for my age I thought I was quite fit and I didn't expect, I just thought I had a chest infection which people get now and again". (Participant 5)

Being told the diagnosis

Prior to their consultation with the doctor who gave their diagnosis, many participants described how they had suspected they would be hearing significant or worrying news. A small number had been forewarned by their GP but others had suspected it from their symptoms or clues they picked up from others during the process of investigations.



"I was talking to the woman who took it (the x-ray). She said, when do you go back to your doctor? I said, oh, next Thursday. She said, I think you'd better go sooner than later. That was the first time I heard, like, you know. And then I told my wife and she went grey". (Participant 2)

All participants recalled the words mesothelioma and cancer being used at the time they were given their diagnosis. Not everyone talked about the moment they received their diagnosis but those who did described different reactions including anger and shock. The variation is illustrated in the following examples of phrases used.

- *"Not very pleased, but it didn't shock me".*
- *"Disappointed but not surprised".*
- *"Can I swear? I was really pissed off".*
- *"Unexpected shock".*
- *"It knocked me sideways".*

When participants were given their diagnosis this often included a discussion of prognosis and outcomes. There was good evidence in all the interviews that participants were aware that their cancer could not be cured and had a potentially poor prognosis. However, some had been given a particularly negative picture at the point of diagnosis.



"Because of what the doctor had said to me I just presumed that it was it, there was nothing he could do. I didn't know there was anything they could do". (Participant 4)

For these patients, being told there was a trial they might be eligible for contrasted with their initial negative understanding of their treatment options and outcomes.



"She came back up to me with the results and that and told me I'd got this mesothelioma and she told me it was terminal and it is inoperable... She said it had spread to my chest wall or something and it's on your lung and she said it's inoperable and there was nothing as sure as that, because we were amazed when eventually we came out of hospital and made another appointment to see [doctor] back at our own local hospital... and it was him who suggested the MARS2 trial". (Participant 9)

Understanding of mesothelioma

Although asbestos was a familiar word to all, prior knowledge of mesothelioma ranged from never having heard the term before to personal experience of the disease.



"I'd never heard the word in my life – and then they clarified it by saying asbestos- related lung cancer and then I woke up to that effect". (Participant 14)



"It is (new information) I mean I've heard about asbestos and stuff like that, but it doesn't really sink in until somebody that's close that's got it. I don't know anybody really close that's got mesothelioma". (Participant 3)

In contrast, a few participants lived and worked in areas with a high incidence of mesothelioma and were very familiar with it.



"I worked in the factory, but also there's tips of it everywhere round where I live..... loads of lads at work had died and even a neighbour two doors up, and she had never worked there..... because of things how it is over there I did expect something, sometime maybe".(Participant 4)



"The consultants and myself.....we had an inclination that the reason might be mesothelioma. That was reinforced by my own work history going back to my teens where I was significantly exposed to asbestos". (Participant 13)

At the time of their diagnostic consultation, all participants described how they had been asked about exposure to asbestos. Some could recall this immediately while others had to think back over the course of their employment to pinpoint a potential time when this might have occurred. Occupations identified were skilled manual, technical and engineering and included working in the navy, railways, shipyards, factory work and building trades. All described how they had been given information at or since their diagnosis about the legal aspects of mesothelioma, compensation and claiming benefits. Again, for the majority this was new information and a new set of experiences and challenges.



"I've never claimed in my life for anything...He (support group member) came round and he went, right what do you claim for? I went, well, I'm lucky I've never claimed and he went right, we'll get this and get that. So they've been really good". (Participant 3)

For some, mesothelioma was perceived as being different from lung cancer as mesothelioma was caused by asbestos rather than tobacco smoking, as illustrated here:



"I used to smoke and lung cancer would be self-inflicted because I smoked. But this illness is not, is it?" (Participant 10)

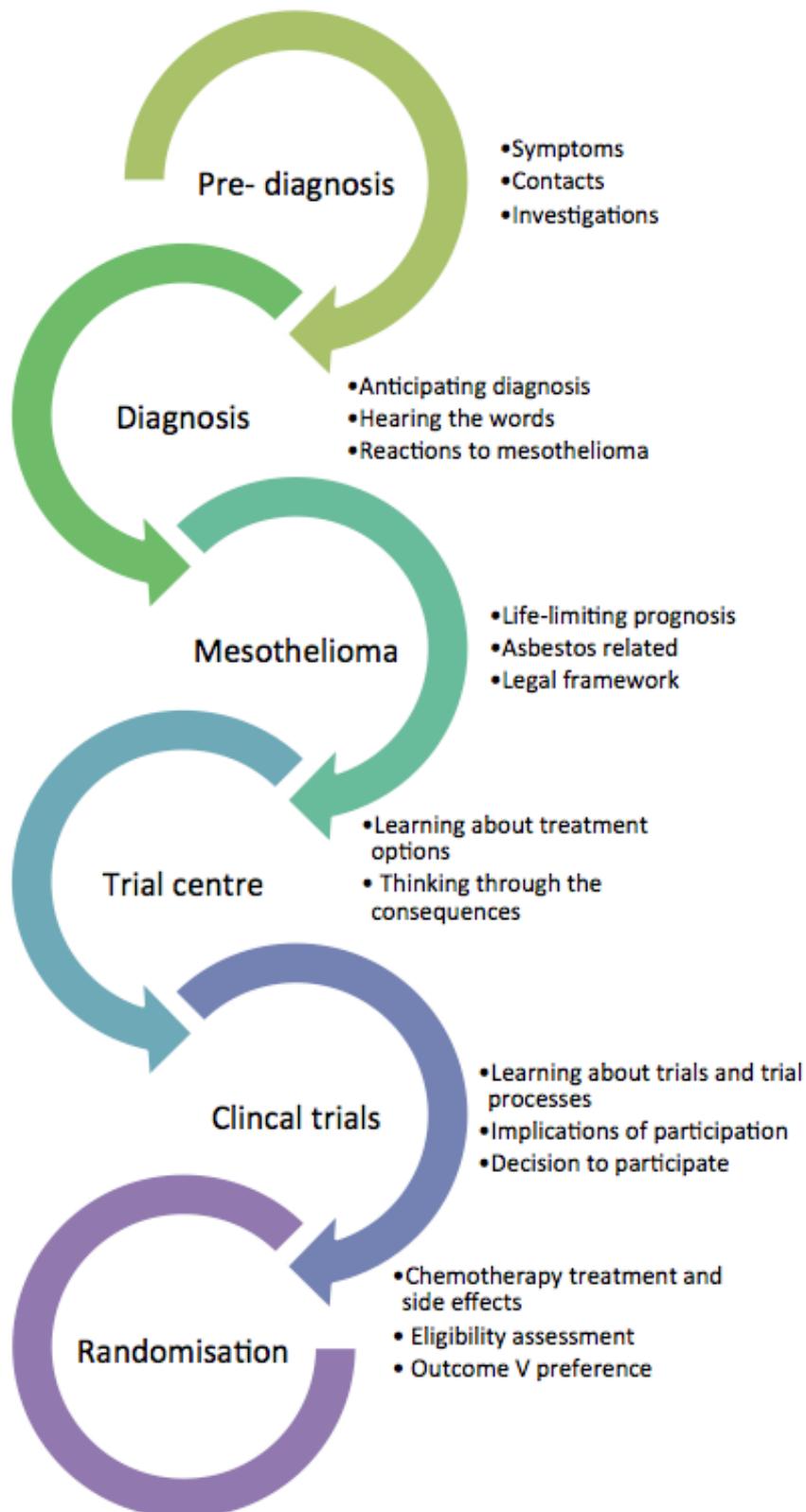
In summary, up to the point of their consultation about the MARS 2 trial participants had encountered a diverse range of new and concerning experiences. These included worrying symptoms that were significant enough for them to seek help, GP and hospital visits, scans and investigations and the drainage of litres of fluid from the lung. They had also been provided with an array of life-changing facts including being informed that they had a rare incurable cancer associated with a poor prognosis. At this point they were also informed that their illness was an occupational disease caused by exposure to a substance that they may have worked with many years previously that had legal and financial ramifications. There were variations in the pathways each participant had experienced prior to their trial consultation but they shared most of the elements summarised here. Many of these had taken place within a relatively short period of time. These factors shaped the context in which they were then given information about the MARS 2 trial.



I: "Has it been easy to understand what people have been telling you"?

R: "Yes, well, you know, it's in a different field that you've not been experienced in before, and for somebody to turn around and say that you've got this condition and your time is limited it is very daunting". (Participant 6)

Figure one: Context of trial participation: information pathway leading to randomisation



Learning about the trial

Participants attended their trial consultation soon after they had been given their diagnosis of mesothelioma. Their descriptions of the explanation and decision-making process revealed variation in understanding the trial procedures, specifically decision-making regarding treatments and the process of randomisation.

Understanding the treatment options

All the participants understood that the treatment included chemotherapy and/or surgery. Most knew they would receive two cycles of chemotherapy before a decision about the next stage of treatment was made. However, one person described being surprised to find this out.



"It was after the first bout of chemo I think. I went to see (Dr) and he said, right we'll give you one more and then you'll be randomised for the operation. And I went, oh right, do you not have all the chemo and then have the operation? And he went, no, we can't do that". (Participant 3)

All reported being given information about both treatment options and having opportunities to discuss them with the doctor and specialist nurses at the hospital. No one reported feeling as if they had felt any pressure to participate in the trial and some felt that the opposite was the case.



*I: "Did you feel under any pressure to say, yes"?
R: "No, I don't think I did at all. I think it was more the other way really if they talked about things". (Participant 4)*

Many praised the depth and quality of verbal information that they had received about the trial. Being shown scans and computer images were described as particularly helpful in supporting understanding of their diagnosis and the surgical procedures. However, some found the language and detail provided in the written information confusing and felt it did not meet their needs.



"I mean, we tend to get bombarded with paperwork and booklets, and I've tried to read them all and some of it makes sense and some of its way over my head... sometimes understanding the expressions that they use and the descriptions of various things... sometimes it does seem an awful lot of stuff to take in...not all of it will apply to all people. I mean, some bits, I know, don't apply to me but other bits. It's sometimes a bit confusing sorting out the exact very important bits, but it is all there, I feel". (Participant 4)

Achieving equipoise

While all participants recalled being informed about both treatments, there was evidence in a small number of interviews that they felt it had been inferred that surgery might be the preferred treatment option from the perspective of the medical staff.



"He explained to me that... given the current state of medical knowledge and techniques available... if it was him personally that had mesothelioma, if surgery was available as well as chemotherapy he would probably go down that, if he had the ability to affect the outcome he would hope for it and probably would want it and equally if it was his family". (Participant 13)



"Well, I think he said the surgery's proven to be a bit more... you know, whatever the symptoms are, a bit more controllable or something". (Participant 2)

However, many understood that the trial was being carried out because the optimal treatment pathway was not known. This included some who had reported that the doctor had inferred a preference.



"It has been explained to me in words of one syllable – in a very compassionate way I might add...that there is no evidence that adding radical surgery will make a massive difference.....To be fair to them they said we just do not know and that is the reason why we are conducting the trial". (Participant 13)

In some cases, this positive slant regarding surgery could have simply reflected the surgeon's description of the intention of surgery. The participant may have then interpreted this as an endorsement or an expression of a preference



"He said, well, if you had the surgery he said two things, he said it will extend your life and make it easier. So if you can get that, that's fine". (Participant 1)



"He said at the moment, he said looking at your screen, he said you are right on the borderline for me to do this procedure of stripping all around your lung. He said, I wouldn't be doing this operation if I didn't think it was going to give you a better time of life - he didn't say what length of life, he said better time of life". (Participant 6)

Deciding to join the MARS 2 trial

Many factors were cited as influencing the decision to join the MARS 2 trial. These included:

- To get surgery (if this was their preferred treatment option).
- A positive self-assessment of their ability to cope physically with treatment, particularly surgery.
- To support a "positive" approach to coping with diagnosis and treatment (for example, I want take the latest treatment on offer, I am not giving up and I want treatment).
- Altruism through supporting research.
- Being able to overcome perceived barriers to participation, such as the logistics of travelling to a distant treatment centre.
- To get enhanced support and care that might be available to trial patients.

Many of these elements were inter-connected and occurred within and across the participant's accounts. This is demonstrated in the following extracts from one participant's interview:



"My thinking was, well, if you've got something bad and they can cut it out, then it's obviously got to be a favoured route. And then I thought, well, if I don't bother to do anything about this.....I'm just giving my life up too easily. So I came to the conclusion that yes I would participate in the trial and wherever I was directed from that then that would be okay.....I thought it would suit me best to participate and then maybe give me a better chance. And I was keen to participate from a point of view of maybe people in the future.....I thought it was a worthwhile project. I think it's important that these things are put into place. I also think it's important that people take part as well if they can". (Participant 1)

All had joined the trial because they felt it offered a potential advantage to them, but this was frequently twinned with the hope that it could have potential future benefits for others.



"What I wanted from MARS was that...it has given me some hope, because in the beginning they were.. a little bit, oh you've only got so long and all the rest of it, you know what I mean? And I was thinking, oh...bugger this for a game of soldiers! That...apart from giving other people a chance, that it would also give me a chance, if you understand". (Participant 10)

Examples of altruism featured in nearly all the interviews suggesting this was an important factor in supporting trial participation. Some additional examples are provided below:



"Well, as (surgeon) explained, no one knows really if there's a cure and if I can help in some small way to find a cure, you know, it won't have been in vain, if you see what I mean". (Participant 5)



"I just thought, I'll do that, you know. If it doesn't work for me, you're like a guinea pig really aren't you, it will work for somebody else, won't it. Experimenting with things isn't it, so that's the way I look at it". (Participant 2)



"The way I kind of look on this kind of study, I'm 77 years old and if it does good then it's okay. I mean, let's face it, I know I'm towards the end of my life and I just hope it does some good. It sounds very...you know what I mean. It sounds very much over the top on my part but that's the way I kind of feel". (Participant 8)



"I am a philosophical chap and I always think if it doesn't help me, it will help somebody else further on down the line, you know". (Participant 9)

While the participants had all decided to participate in the trial some had initially been put off the idea by the logistics associated with receiving treatment some distance from home. This was both for surgery and chemotherapy as some had to pass local chemotherapy providers to reach the participating treatment centre. Organising travel and hotel accommodation were challenges for some and information regarding this was not always readily available.

These logistical issues continued to be a source of concern for some participants throughout the trial treatments. Having these recognised and acted on by the healthcare team, was viewed positively where it had been experienced. An example was scheduling appointments to co-ordinate with train times when there was a long distance to travel.

Treatment decisions

Understanding randomisation

One of the aims of the study was to explore participants understanding of randomisation. The findings showed a variation in levels and accuracy of understanding. (See Table two for a summary). Many participants did understand randomisation. This was implied by the use of certain phrases, for example, statements such as “a 50:50 chance” or “could go either way” indicated they were aware that they could get either treatment at the randomisation point.



“They explained it well. There would be 50 people on the trial, 25 would go one way and 25 would go the other way and it would be entirely randomised”. (Participant 10)

However, six participants did not fully understand randomisation and the way in which decisions about the treatment they would be receiving were made. Three thought the doctor made the decision based on what was best for the patient. Two thought the computer was given information that helped to select the most appropriate treatment.



“I said to the doctor, if you want to operate I am not frightened of surgery. If you want to do chemotherapy, go down that way. Use your judgment, do what’s best in my case”. (Participant 8)



“They put all the results of the two, what happens on the chemotherapy side of it...and put it into a computer and then the computer spits out a name.....I don’t want her, I don’t want her, yes we’ll have him....presumably there’s a criteria that it has to meet and obviously, because I had responded to the treatment and that’s why I got picked for the surgery”. (Participant 11).

Treatment preferences and randomisation

Participants were asked if they held a treatment preference prior to randomisation. Three had no preference and wanted to let the doctors or “fate” decide. Seven stated they preferred surgery, giving two reasons for this. The first was a belief that surgery was inherently a more effective treatment and the second was a desire to receive all of the treatment that was available.



“As a lay person, I felt that if I can use this term the full loaf if you like, the whole loaf was really, really a process of receiving both aspects chemotherapy and the radical surgery”. (Participant 13)



"For me, personally, I would have loved to have had the operation, but that was because I thought the operation would be a quick fix".
(Participant 10)



"Because I'm a mechanic, maintenance, I see it as a hands-on thing so I was going for the surgery. That's what I would've gone for because I can see it plain in my mind; they cut it out, get rid of it". (Participant 4)

Four declared a preference for chemotherapy, based on their evaluation of the potential challenges associated with surgery and their concerns about taking this on.



"I still consider myself quite fit and I thought to myself maybe if I had that op it could flatten me like and put me out for months and months. So, I wasn't too upset, put it that way... If it had been offered to me I would have taken it but secretly I was glad that it wasn't". (Participant 5)

Table two: Understanding of randomisation along with treatment preferences and outcomes

Participant number	Treatment preference	Randomisation outcome	Understanding of randomisation
1	Surgery	Surgery	Good
2	Surgery	Surgery	Good
3	Surgery	Surgery	Not clear, initially explains he could get either treatment but later states he got surgery as chemo wasn't working
4	Surgery	Surgery	Good
5	Chemotherapy	Chemotherapy	Good
6	No preference	Surgery	Poor - doctors makes the decision; the trial is comparing types of surgery
7	No preference	Surgery	Not clear from discussion
8	No preference	Surgery	Poor – doctor makes the decision
9	Surgery	Chemotherapy	Good
10	Surgery	Chemotherapy	Good
11	Chemotherapy	Surgery	Poor – computer makes decisions by assessing their individual situation from information provided
12	Chemotherapy	Chemotherapy	Poor – computer makes decisions by assessing their individual situation from information provided
13	Surgery	Chemotherapy	Good
14	Chemotherapy	Surgery	Poor – doctors makes the decision; the trial is comparing types of surgery
15	No preference	Chemotherapy	Good

Table two: Understanding of randomisation along with treatment preferences and outcomes

For some who had a strong preference the waiting period from consenting to the trial and the decision to proceed to randomisation was a time of anxiety.



I: "Were you aware that you might not have got into that treatment arm?"

R: "Oh, yes, of course I was, all the time until the other day. I was wanting the operation from the beginning and I knew that it was random on a computer and that's what panicked me... don't know whether chemotherapy works or the other type works but what I'm saying is I knew my best way would be an operation... I was worried I might not get the randomisation and get the operation".

(Participant 4)

Treatment preferences and randomisation outcomes

Five participants did not get their preferred treatment choice. Those who did not get surgery described feeling disappointed and deflated. This was contrasted to their earlier optimism on getting through to the point of randomisation.



"I sort of got my hopes built up, you know. I had a scan.....blood tests and then the breathing tests and everything and the surgeon.....said that I would be an ideal candidate for it. So, I was sort upbeat for that, if you understand what I mean..... and then it came up with the chemo.....then, to be perfectly honest with you, I was a little bit, oh. You know what I mean? It was like someone putting a pin in a balloon. Not with it going bang, but deflated". (Participant 10)

The implication in these interviews was that participants thought that chemotherapy might not be as effective as surgery. One of the ways in which they managed this disappointment was to remember the overall purpose of the trial.



"I was a bit disappointed that I hadn't been picked obviously for the operation because I thought (pause) Well that's being a bit selfish sort of thing, you know. That was the whole idea of the trial. Some going down one path and some going down the other". (Participant 9)

One participant who had wanted chemotherapy but had been randomised to surgery was stoical and became resigned to the treatment allocation. The other had managed to reframe surgery and its consequences in a more positive light than he had originally.



"[I] sort of wished I hadn't got to go through it but you take what is given and offered". (Participant 11)



"Very hesitant. I was still very dubious... But I think it's the best way for me to go actually..... got my head round it and with (wife) being registered disabled I look after her as well and I think it'll gee me on to get things done and sorted so I can carry on looking after her". (Participant 14)

Experience of trial treatments

Chemotherapy

By the time of the first interview most participants had already received at least two cycles of chemotherapy. Some recalled feeling anxious beforehand due to their pre-existing beliefs



"The horror stories that I've heard about chemotherapy in the past". (Participant 8)



"You don't know what to expect, especially with the chemo because I've heard horror stories". (Participant 5)

The experience of receiving chemotherapy varied widely between participants. One person was surprised and self-conscious that he experienced few side effects.



"I've had no problems at all. I'm still looking for the side effects... I feel a bit of a fraud at times because I don't feel ill in myself". (Participant 12)

However, the majority described some negative experiences with a smaller number having a particularly troubled time, as is seen in the following descriptions.



"Well, the side effects were quite horrendous". (Participant 3)



"It does knock you backwards". (Participant 9)



"Chemo was really bad, it knocks you out...I thought, oh, it's just a nightmare". (Participant 2)

Participants described a cyclical pattern of treatment and side effects, which some had not expected. While the repetition of treatment cycles was challenging it did afford some the opportunity to anticipate problems and learn how to manage them.



"It was always the same... I seem to go downhill for about seven to 10 days but then pick up and get back and you just feel as though you got back to where you started when it was time for another dose of chemotherapy, unfortunately... I can feel myself getting better and better and when I feel at my peak, come back we'll give you some more of this poison!" (Participant 9).



"But the second time you know a little bit of what to expect so you're able to sort of combat it". (Participant 13)

Experience of chemotherapy side-effects

The most frequently recalled side-effects of chemotherapy included fatigue, nausea, reduced appetite, taste changes, constipation, infections, excessive tears, sore eyes and skin reactions. Admission to hospital to manage serious side-effects such as neutropenic sepsis and dehydration occurred for three participants, one of whom had two admissions, the second for a blood transfusion.

Nausea was largely pro-actively managed and controlled. However, steroids used for anti-emetic purposes could also cause side effects, such as nausea, anorexia, taste changes, fatigue and feeling generally unwell had a negative impact on the ability to eat and drink. This was a significant concern for those who experienced it. There was a sense of fear when eating was difficult, as it was regarded as an indicator of wellbeing. For some this led to disagreement and conflict between participants and their partners.



“Being sick, not being able to eat... You’ve got to eat because otherwise you get knackered don’t you, so you’ve got to eat. But eating’s terrible. I used to get porridge every morning, I couldn’t face it.... It was terrible... my wife keeps feeding you, she wants to feed you up and you don’t want to eat and it causes conflict”.

(Participant 2)



“In the last two or three days, I’m improving every day massively because my chemo’ has worn off now, my second lot, and I’m sort of getting better. I mean food has been shocking because nothing tastes how it should be, and I’ve left a lot of food and then had other stuff instead, and it does cause a bit of aggravation”.

(Participant 12)

Tiredness and fatigue could have a major impact on daily living and how participants felt in general.



“The first day after the chemo I just went to bed all day. Just felt absolutely knackered... like the next day I felt really, really crap and then for about a week it sort of went down... the chemo was terrible for me”. (Participant 10)

A range of strategies for coping with chemotherapy were described. These included following the advice of the healthcare team (such as temperature monitoring) and finding ways to manage side effects. Some were able to develop self-management strategies that were seen as a way to maintain a sense of resourcefulness and maintain their usual approach to life (and health).



“On the first lot I had mouth ulcers... I’ve got a two year old grandson and he’s got Bonjela so I could use his like. So, you know, I’m one of them guys who fixes himself”. (Participant 5)

Managing to carry on with some normal activities was an important measure of coping. These activities included taking regular exercise, such as walking, creative activities, and maintaining hobbies. These also were seen to help maintain a positive approach.



“At the moment I’m painting and I get out and walk every day – I try and walk every day, you know; only for an hour maybe but enough, ...I’m not saying I’m superman or nothing like, but I feel that you could do more for yourself if you have the positive mental attitude”. (Participant 5)

Experience of surgery

All participants having surgery recalled being warned at their pre-operative consultations that they were having major surgery that would be painful and that recovery would take a few months. Immediate post-operative symptoms and experiences varied, but many were surprised that they had less pain while in hospital than they had anticipated. Post-operative complications occurred for some which led to extended hospital stays of between two to seven days longer than the 14 days they had expected. Reasons for the delayed discharge included a chest infection, post-op bleeding, surgical emphysema and complications with the chest drain. Some participants also described difficult journeys home on being discharged from hospital following surgery, suggesting inadequate anticipatory pain management

 *"When I got in the car to come home... it was like I was in a cardboard box and somebody had actually kicked the box all the way home". (Participant 14)*

Post-operative problems in the weeks and months after surgery included pain, breathlessness, tiredness, feeling weak, numbness at the operation site, constipation and reduced appetite. Some had fewer problems than anticipated or felt any difficulties or problems were manageable

 *"I felt better than I expected to. I wasn't on any painkiller... I had discomfort because of the drain I think... the problems that I had were normal things, constipation, tiredness, a lack of appetite, all the things that you generally find if you're poorly". (Participant 1)*

Others struggled more with their symptoms at times, particularly those who had pain and breathlessness.

 *"I mean I'm not like a hard bloke or anything, I mean I've been in pain, I've cried over it and stuff like that but at the end of the day it's just a bit of pain... I'm not sort of a miserable person, but you do think, oh, God what am I doing with this". (Participant 3)*

In the weeks and months after surgery, pain was a problem for many participants but the experience of pain control was variable. Those who reported good pain control were those who had a level of pain that was controllable with simple analgesia, such as regular paracetamol and those who followed the advice of the healthcare team in taking opioid analgesia.

 *"I did try coming off the morphine the other week... and it wasn't really a good idea... Well the doctors and the nurses have said you should not be in pain and that's why we have given you the medication and stuff... I've gone back. I mean I'm not taking as much as I was in hospital, but I am a couple of times a day". (Participant 3)*

There were participants who did not have adequate pain relief. Two different reasons were identified to explain this. Some had not been given analgesia that was effective for them and they had not contacted anyone for advice about pain management. Others did not take the medication provided due to fear of constipation (a side effect of opioid analgesia). Prophylactic laxatives had not been prescribed alongside opioid analgesia in many cases.

Increased pain and difficulty sleeping was a particular problem among those who were discharged home with a post-operative chest drain in place.



"That's a killer, the drain in the side...It's just like every time you move, you get a pain. You get pain in your side. You can't sleep at night because of the pain". (Participant 2)



"... one of them sticking out all the while, you've got to be careful you don't...knock it. When you go to bed you've got to lay in a certain position, so you can't move because if you turn over it all comes out because you know, it's got a vent. It was a disciplined sleep as you might say, you could only lay in one position".

(Participant 7)

Some who had a chest drain at home reported not being informed that this could happen in advance and so felt completely unprepared. There was also uncertainty expressed about the plans for removal adding to concerns about its presence.

Breathlessness was experienced to varying degrees by all participants. For most it affected activities of living, particularly walking longer distances, upstairs and uphill. Breathlessness was an enduring symptom for many that persisted for months following surgery.



"If I forget to take my time going up the stairs, I get out of breath. If I remember, I take it nice and easy, it's not a problem. I can walk around all day on a flat surface but it's just when you come to the stairs". (Participant 2)

The physical changes due to surgery could also impact on function, such as lifting light weights in shops or at home. This endured for months after treatment as is seen in this six month post-op interview:



"You feel silly because you can't even pick anything up in a shop.....you're stood at the counter, at the till, and my missus had to carry my bags out for me, anything like that, it was difficult to carry....It's, like, as though you've taken your muscles away from the front and....you can feel it when you pick something up".

(Participant 4)

Evaluation of care and support received

The most frequently mentioned sources of support from healthcare staff were district nurses and General Practitioners (GP). There were descriptions of GP interventions to try and control symptoms, such as cough and pain, but little evidence of specialist input such as oncology or palliative care services. People did have contact numbers for the chemotherapy treatment centre and the specialist nurses which were used while treatment was underway. However, they were rarely used outside of this time.

Family members played a vital role in providing practical and emotional support during trial and treatment procedures and recovery. Many participants described concerns about the impact of their illness and treatment on their family and the additional demands it placed on them.



“Because it doesn’t make any odds to me because I’m in hospital but there’s people who have got to come and see you, that’s the trouble. I’m worried about my wife more than anything”.

(Participant 2)



“My sons and my two excellent daughters-in-law are rallying round her, you know what I mean like; absolutely brilliant. And she (wife) is...not taking it bad but not taking it as good as me, you know”.

(Participant 5)

Overall the care received by the centres involved in trial recruitment, chemotherapy and surgical treatment delivery were described in a positive light. This was particularly true in the initial interviews that occurred before, during and immediately post treatment. This positive perspective was underpinned by an appreciation that treatments were available for their mesothelioma. It was further reinforced by positive feelings towards the NHS in general. Other factors relating to care were also praised, such as the behaviours and attitudes of staff towards them as individuals.



“They’re all there together, even down to the cleaner. I tell you, it’s absolutely inspirational... when they’re doing something now, whether it’s a cook or a nurse, surgeon, everybody seems to care about you personally... Oh, I think they’re marvellous. They work like a jigsaw and everybody fits together and they’re all on the same button, all going for the same thing, you know, to get you better”. (Participant 4)



“Everyone seems to be helping me all the way sort of thing; it’s quite heart-lifting”. (Participant 5)

Participants recalled positively the amount of time that staff had taken to give them information and explanations. They particularly valued the ways in which information had been tailored to their own situation or needs.



“I was lucky because I went first to see [surgeon] and there were a nurse there. She (nurse) gave me more literature, but she told me in our term of speaking exactly what it was. So it were down to her... who broke it into my language for me, to understand fully what was going on”. (Participant 14)



"I did really have a lot of trust in both...(oncologist and surgeon). They explained everything, any questions I had they would answer me and... if I had forgotten to ask something, I would write it down and go back next time and ask them. So, I was really pleased about that. It's not like it used to be where...they stand around your bed, talk about you and never speak to you, you know; now they actually communicate with you and I am really pleased about that". (Participant 4)



I: "Did you think you could ask questions"?

R: "You could definitely do that. He was dead keen to find out what my thinking was". (Participant 1)

Participants indicated that information regarding the trial, chemotherapy and surgical treatments and their immediate impact was in plentiful supply in a range of formats to meet individual needs. However, some gaps in the information and support were described in the interviews. These included:

- Practical and financial support with logistical issues such as travel and accommodation.
- Clear plans regarding the scheduling of surgery post randomisation: some had a period of time when they did not know what the plans were, others recalled being given very little notice such as being informed of the date a few days before admission.
- Expectations of recovery post-treatment, including what was normal and what they could or should not do to improve their recovery.
- Pro-active management of side effects, particularly tiredness, pain, anorexia and constipation.
- Ongoing treatment plans, specifically, communication between the surgical and oncology centres regarding the resumption of chemotherapy post-surgery.
- Post-trial plans including what will happen after the trial, who will be responsible for their on-going treatment, who they can contact for advice, future treatments that might be needed or available.

There was evidence of fragmented care between the different treatment and service providers, for example the chemotherapy centre not being aware of the potential date for resumption of treatment post-operatively. This created a sense of uncertainty and added to participant's anxiety. The end of treatment and the trial were also points that triggered uncertainty among participants. Some found these transitions difficult because they were losing contact with healthcare staff they had built a relationship with. This appeared to be exacerbated by the absence a clear plan for on-going care and support during the post-treatment recovery phase as well as on-going disease surveillance as they continued to live with mesothelioma.



"I'm not saying that they're not bothered about you.. it just seems they pass you on from one to another and you don't get the same like personal attention sort of thing. It's not as though they're doing anything personal but you don't get the same feedback, the information, they seem to know more about you if you're seeing somebody all the time". (Participant 9)



R: "There were times when there was a long gap with apparently nothing happening... it was a long time with no clinics... nothing happening at all. It seemed a long time in fact".

I: "Would you have preferred someone to have contacted you"?

R: "Oh that may well have eased things knowing that you were not forgotten". (Participant 12)

4. Discussion

The Mars 2 Qualitative Assessment Study is the first longitudinal in-depth exploration of the impact and influences on participants of a randomised controlled trial for mesothelioma surgery. The study has generated a unique insight into the motivations of participants to enter the trial, and their experiences of participation

This is a qualitative study and so caution is needed regarding any claims of generalisability of the findings. However, the results do raise some useful questions on how to support and care for people having chemotherapy and surgery for mesothelioma. The study also gives some indication of how to support people on complex mesothelioma trials.

Key findings from the study are summarised below and implications for future care and trials are highlighted.

Volume and complexity of trial information

Information regarding the trial was provided verbally and in writing. Positive feedback was given about the time staff provided for explanation and efforts to tailor this to individual needs. Examples included follow-up discussions to clarify understanding and answer questions, employing “lay” language that was non-technical and using pictures and scan images to aid understanding. Alongside these positive elements a challenge was also identified relating to the volume and complexity of the information which some found difficult to understand or identify the content that was relevant to their situation.

Implications

Consideration needs to be given to the presentation of trial information and the development of formats that can be tailored to individual needs and preferred ways of learning. Some participants had used on-line sources of information as a supplement and electronic approaches to structuring information could be helpful. This is an area for further exploration. Involving patients in the development and review of trial materials could help to ensure this is achieved.

Achieving equipoise, providing neutral information on treatment options

Some participants felt that surgery would result in better outcomes than chemotherapy. In some cases, this arose from individual beliefs around cancer surgery (for example, removing the cancer must be the better option). However, some also felt the doctors had expressed a view that surgery was the optimum treatment. It is not possible to know if this was actually the case or was a misunderstanding from the patient’s perspective. It is also possible that the description of the rationale for surgery, for example, improved length or quality of life, was interpreted as an endorsement. Either way, this finding highlights an area for improvements in information provision. This is particularly important as some participants were subsequently randomised to receiving the treatment they felt was perceived to be less effective by healthcare staff involved in trial procedures.

Implications

All staff involved in recruitment, information provision and patient support regarding clinical trials need to be aware how easily their words can be misinterpreted by patients. Ways to communicate the intention and purpose of

a trial needs to be carefully thought through to ensure patients do not feel they are receiving a lesser treatment by being selected to a particular treatment arm. Consultations where patients are given information about randomisation outcomes should be seen as a moment when significant information is given. When this information differs from the patient's preferred outcome it should be seen as "breaking bad news" with attention being given to providing pro-active support and follow up to help manage patient's concerns.

Understanding randomisation

Understanding of randomisation was found to be variable. It is possible that the trial procedures may have contributed to this. The surgeon had to review a scan prior to randomisation to determine whether the patient was eligible for surgery and this could have been misinterpreted by them making a decision on surgery as a treatment option. However, this again highlights a gap in the information provided.

Implications

Some participants had a good understanding of the process of randomisation and used phrases such as "toss of the coin" and "50/50" to describe it. Working with patients to co-produce information that communicates this effectively, may be a useful approach to meeting this challenge. This could help to identify language and phrases that have less scope for misunderstandings.

Consequences of trial participation: uncertainty and logistics

Agreement to enter the trial created additional concerns and challenges for the study participants. These included:

- Uncertainty associated with trial procedures for example, waiting for confirmation of eligibility for randomisation followed by decision regarding treatment arms
- Short notice scheduling of dates for surgery
- Practicalities of organising travel and accommodation in an unfamiliar city
- Care fragmentation due to distance from the treatment centre and/or multiple care providers. This was exacerbated when there was poor co-ordination or communication between surgical and chemotherapy centres and/or between cancer treatment centres and community services.

Implications

While the factors identified are part and parcel of trial participation, interventions can be put in place to mitigate and manage their impact. These issues were a concern to participants and acknowledging the logistical implications of participating in the trial in initial discussions, such as providing written information about travel, parking, accommodation and reimbursement of costs, may ease concerns. One other approach that could be of benefit is the development of a care coordinator or navigator role that provides up to date information about practical issues and also tracks the patient's progress along the treatment pathway facilitating communication between service providers.

Experience of side-effects

Participants described a series of well-documented side effects. There were gaps identified in the information and support provided for managing commonly occurring side effects of treatment, some of which could have been avoided

or reduced with pro-active interventions. Areas for care improvements were identified.

- 1) Post-operative pain management, on the journey home from hospital and in the months during recovery
- 2) Education and interventions to prevent and manage constipation (post-operative, chemotherapy related and induced by opioid analgesia)
- 3) Symptom management and care plans for post-operative chest drains in the community. In particular identifying who is responsible for on-going care, contacts for advice on pain and symptom management and an anticipated duration and removal plan

Implications

Symptom management outside of the hospital should be seen as part of the treatment plan and include clear lines of communication for the patient and community services with the treatment centre. The findings suggest the positive potential for developing a nurse-led service to support patients following discharge and during recovery. Participants found it helpful when they were forewarned about potential problems beforehand and given a time estimate for duration and improvements. Having achievable goals was a frequently used coping strategy in the treatment phase and providing patients with information to help manage expectations and set appropriate goals could help to achieve this. In addition, family carers were found to have a vital role in supporting participants and should be included when discussing symptom management and recovery during and post treatment.

Post-trial care – transitioning off the trial

The period of transition at the end of the trial was challenging for participants. Moving to post-treatment recovery and surveillance was characterised by uncertainty. Participants were unclear who to contact for information and support and were uncertain about possible future treatment options and the possible course of their disease. Some accounts provided stark comparison between the intensity of support at recruitment and during treatment compared to when they are exiting the trial with some feeling abandoned.

Implications

The study identified the need to manage patient's expectations by identifying a transition point at which they leave the trial accompanied by a clear plan for their future care. One way to achieve this could be the introduction of an exit consultation where patients are thanked for their participation and are given an opportunity to provide feedback on their experiences. This consultation can also be used to outline the future treatment and surveillance plans including identifying who responsible for their care from this point forwards. Implementing elements of the Macmillan Cancer Support Recovery Package such as treatment summaries, cancer care review, holistic care assessment and access to education and care events may also ease such uncertainty post clinical trial and help to bridge gaps between secondary and primary care.

5. Conclusion

The longitudinal approach used in this study identified the changing priorities and care needs of patients across the phases of the trial and onwards to the post treatment and recovery period. There were many examples of positive experiences recalled by participants, particularly relating to information and care received regarding chemotherapy and surgical treatment. However, there were also missed opportunities where pro-active interventions could have significantly improved the patient experience in identifiable ways such as reducing uncertainty, preventing unnecessary symptom distress and aiding understanding. The findings suggest there is a requirement to reflect on what patient's want and need, at different points during and post-trial participation, in order to develop interventions to pro-actively assess, manage and meet their expectations and needs.

The study also highlighted the challenges patients have in absorbing and understanding the volume of complex information associated with trial participation. Developing and embedding interventions to support care navigation, with clear lines of responsibility for communicating with patients and between trial and treatment centres, may have the potential to improve patient experiences of trial participation.

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