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Report of a patient/public involvement group.**

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# What do families want to improve in the management of paediatric febrile neutropenia during anti-cancer treatment? Report of a patient/public involvement group.

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## Abstract

### Background

This study reports how parents and young people who had experience of febrile neutropenia improved the design of a trial to inform the management of this condition. Five parents, a young person who had completed treatment, and three clinician-researchers contributed.

### Methods

The group formed after an invitation via social media and met via video conference. Many participants were from an existing childhood cancer parent-involvement group. The initial questions for the discussion asked about the importance of the topic, the views of the need for a trial, which important outcomes should be measured, and practical aspects which would make it easier or more difficult for people to take part in it. The conversation occurred across an entire afternoon, was audio and video recorded, transcribed, analysed, and checked by those involved. A fifth parent added to this via email.

### Results

The group altered the trial structure, proposing to randomise each child to one of the two management methods through the whole of their anti-cancer treatment, rather than randomising the study sites or the child at each visit. They felt even if people declined taking part in the study in the first weeks of diagnosis, their views may change and they should be allowed to consent later. They also proposed methods of collecting patient and family important data, enriching the medical information gained in the study. Active follow-up, negotiated for each individual family, was also suggested.

### Conclusion

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3 Trials improving the management of febrile neutropenia for children and young people who are  
4 undergoing anti-cancer treatments should consider individual-patient randomisation, collection of  
5 'quality of life' and 'experience of care' aspects using digital and paper methods, engage families in  
6 shared decision making around management choices and ensure adequate supportive information is  
7 available and accessible to all patients, regardless of background, geographical location, or age.  
8  
9

## 10 11 12 13 **Key Messages**

### 14 15 **What is known**

- 16 • Febrile neutropenia is a common complication of childhood cancer therapy which is disruptive  
17 and resource intensive
- 18 • Trials of reduction in intensity of treatment for febrile neutropenia has previously been  
19 challenging to accept for parents
- 20 • Parent/patient and public involvement in trials has modified designs and information leaflets  
21  
22

### 23 24 **What this study adds**

- 25 • Parent/patient and public involvement in a proposed trial of reducing antibiotic treatment for  
26 febrile neutropenia led to changes in fundamental aspects of trial design
- 27 • Proposed outcome assessments were enhanced by experts by experience describing the burden  
28 of the treatment for febrile neutropenia and trial procedures
- 29 • Video conferencing was effective despite the participants not already being well known to each  
30 other  
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## 36 37 **Introduction**

38 The treatment of malignancies in childhood is associated, in high-income countries, with five-year  
39 survival rates in excess of 80%<sup>1</sup>. This is possible through the use of intensive, toxicity inducing,  
40 regimens, where one-third of deaths in this group are the result of complications of therapy rather than  
41 directly due to the disease<sup>2,3</sup>. The cancer treatment often produces acute complications requiring  
42 unplanned hospitalisation, disruption, distress and strain upon the young person and their family<sup>4</sup>. One  
43 such complication is the co-occurrence of fever in the presence of neutropenia; this combination heralds  
44 a possible overwhelming infection and is considered a medical emergency<sup>5</sup>. The absolute risk of death  
45 or requirement for intensive care in such episodes is low; approximately 3%<sup>6</sup>. The challenge for families  
46 and health care professionals is to effectively treat each episode, with minimum exposure to antibiotics  
47 and disruption of family life.  
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50  
51 Research into episodes of febrile neutropenia, and subsequent clinical practice guidelines have  
52 emphasised the need to treat promptly, assess the risk of each episode, and treat with antibiotics  
53 chosen to address individual and local resistance patterns<sup>5</sup>. The methods of risk assessment and  
54 discontinuing antibiotic therapy are, however, precautionary and conservative, treating two thirds of  
55 patients with broad spectrum antibiotics unnecessarily<sup>7</sup>. Studies have shown that biomarkers of  
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3 infection/inflammation seem to predict the risk of serious infection and its resolution, but have not been  
4 used to guide management <sup>8</sup>. Further refinement of the approach to febrile neutropenia has been  
5 identified as a research priority <sup>5</sup>.  
6  
7

8 In analogous situations with critically ill or immunocompromised hosts, such as adult or neonatal  
9 intensive care units, the traditional management is similar to febrile neutropenia, with the prompt use  
10 of antibiotics and discontinuing when infection has been excluded. Procalcitonin-led guidelines have  
11 been shown to reduce exposure to antibiotics and potentially improve mortality rates <sup>9 10</sup>.  
12  
13

14 The need to improve the management of febrile neutropenia led to the development of a research  
15 proposal to use procalcitonin, which is tested on a blood sample, to assist antibiotic decision making  
16 episodes of febrile neutropenia. Deciding how to conduct such a study, which outcomes were important  
17 to measure, how to measure them, and possible barriers and solutions to a trial, was felt to be best  
18 undertaken with the engagement of clinicians, academics, and parents and young people who had direct  
19 experience of anti-cancer treatment in childhood.  
20  
21

22 This paper reports the findings of a patient/public involvement (PPI) group of clinical academics, parents  
23 and young people convened to design a study to investigate procalcitonin-assisted decision-making in  
24 the management of febrile neutropenia in children undergoing anti-cancer therapy.  
25  
26

## 27 **Method**

28 A request was made on social media for parents and young people who had experience of childhood  
29 cancer therapy to consider taking part in a group to discuss the proposed trial. Volunteers were  
30 gathered, and after initially attempting a face to face meeting, a video conference platform (Zoom) was  
31 used to overcome geographical barriers. The clinical academics all met in one location; the service users  
32 took part from their own homes. One participant could not get integrated audio working, so joined the  
33 conversation via telephone and mute video. The discussion lasted 2h 15 minutes.  
34  
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36

37 The session was video and audio recorded. The entire meeting was transcribed, after audio immersion,  
38 and the content thematically studied. Elements of the conversation related specifically to the design and  
39 conduct of a study were developed into themes and sub-themes. Elements related to the management  
40 of febrile neutropenia were examined in a framework derived from the themes developed in a relevant  
41 PhD <sup>11</sup>.  
42  
43

44 The costs of the group were small; transport costs and light refreshments only for the researchers, and a  
45 small fee for the video conferencing platform. The platform and the technologies were already owned  
46 by the participants. The participants volunteered their time and did not receive payment.  
47  
48

49 As this was a patient/public engagement group of experts through experiences in the development of a  
50 study, consistent with the INVOLVE definition of public involvement in research as “research being  
51 carried out ‘with’ or ‘by’ members of the public rather than ‘to’, ‘about’ or ‘for’ them” <sup>12</sup> no ethical  
52 review or confirmation was required.  
53  
54

## 55 **Results**

### ***Participants***

Four volunteer parents were part of the UK-based PORT (Paediatric Oncology Reference Team) organisation, which consists of parents of children and young people who had experience of childhood cancer. Each was the mother of a child who had undergone cancer treatment; two with leukaemia, two with neuroblastoma. Three of these four parent's children had died of their disease. A patient who had leukaemia when a teenager also took part in the group. Of the three clinical academics, two were higher specialist trainees in paediatric oncology, and one a Consultant, who was the only male in this group. Each member of the group had prior experience with research in children's cancer beyond participation. The discussions involved descriptions of past experiences of admissions with fever and neutropenia. The experiences were from around 2006-2017. During that time period, there has been a move to some reduction in length-of-stay and marginally more consistency between centres in the UK<sup>13</sup>. Additional comments were added by a fifth PORT parent via email following the video conference.

### ***Study-specific themes***

Information regarding the undertaking and conduct of the study was described under three major themes; 'importance', 'how PPI changes trialists' views' and 'practical and ethical'. The theme of 'importance' was formed by concepts of 'medical consequence', 'psychological consequence', 'impact', 'unpredictability' and 'frequency of FN'. (See Figure)

*Importance:* The volunteers unanimously agreed that the management of episodes of febrile neutropenia was important because of its unpredictability, frequency, and medical, psychological and social ('impact') consequences. They described particularly how variation in care across different hospitals was a source of concern to them and consistency would be a positive by-product of undertaking a trial:

*"we've got the 20-odd centres and pretty much everybody follows the same protocols [for anti-cancer treatment]... and I think it would be really reassuring for families if the POSCUs [Paediatric Oncology Shared Care Units] you know if we knew that everybody was doing the same thing" [P1]*

*'How PPI changes trialists' views'* describes how PPI is important in modifying the initial, genuinely held presumptions and beliefs about the best ways to conduct such a trial for families and CYP. These beliefs were drawn from the trial development group, the group of clinicians and researchers involved in designing the trial, which has over a century of experience working in children's cancer in a variety of units and countries and specific expertise in studying supportive care in this group of patients. The PPI group altered the initial trial suggestion in the following aspects:

*Allocation.* The initial suggestion was for group randomisation, assigned arms to by clinical unit, rather than individual patients. However, the PPI input strongly steered towards individual randomisation, but with each individual receiving the same arm of management throughout the whole trial:

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2  
3 *with paediatric oncology unlike many other things... everybody is on a trial... everybody... I*  
4 *mean... <snip>... I think everyone just expects that their treatment may be a bit different than*  
5 *everyone else's... [P2]*  
6  
7

8  
9 *once you're randomised rather than each time coming in and by randomised each time, you're*  
10 *better off having "this family is procalcitonin, this family is not" [P1]*  
11  
12

13  
14 Outcome assessment. The trial group felt direct measures of patient experience would be important,  
15 more than 'quality of life' checklists. They suggested offering a daily experience journal of some form  
16 (paper, or 'app' based electronic), and believed this would supplement and enrich the medical data  
17 collected, such as admission duration, antibiotic duration, and infective organisms.  
18

19  
20 *capturing that idea of burden beyond the hospital based stuff and things that matter to the*  
21 *family, [P3]*  
22  
23

24 They described how it would be important to measure the extra resources required because of FN  
25 admissions. The word 'impact' was felt to capture this rather than 'costs'.  
26

27  
28 *impact, because it's not just about extra costs, I mean if you're having to call in grandparents*  
29 *and you're having to call in favours left right and centre, <snip> I mean how many times can you*  
30 *ask the next door neighbours to collect your kids from school [P1]*  
31  
32  
33

34 Active safety netting. The trialists initially felt the standard approach after discharge of responsibilities  
35 passed to the family to 'return if unwell' would be safe and acceptable, but the PPI group thought an  
36 active approach to safety-netting was necessary, but should be individually negotiated:  
37

38  
39 *I think it needs to be more than just you phone up the hospital if you have any concerns, it should*  
40 *be either somebody coming around or phoning you and saying "Do you have any concerns, do*  
41 *you have any concerns at all" and actually if you say yes ..... giving you the option of coming*  
42 *back or having somebody over [P4]*  
43  
44  
45

46 Gaining consent. The trialists proposed, as with usual practice, the study would be offered once to  
47 families when the clinician believed it appropriate. The PPI group, with their experience of studies and  
48 information being exchanged, thought it would be fair to allow people to decline early on, but have the  
49 opportunity to join the study if they changed their mind as their treatment journey progressed. They  
50 also floated the idea of families approaching clinicians to join, rather than being invited.  
51

52  
53 *I don't think I even knew what febrile neutropenia was though, at the time when we were first*  
54 *giving our consent to all the other things? I think that's something that possibly comes with...*  
55 *further on... down the line... even a week or two weeks after you've given all those other*  
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3 *consents. Because actually, the other consents are almost live-saving things... whereas this is a*  
4 *real choice... and I think that batching it in with those initial forms of consents is almost taking*  
5 *away your flexibility of trying to consider it whether you want to do it or not [P4]*  
6  
7  
8  
9

10 *You might also get people saying 'No' right at the beginning, if it's something they don't have to*  
11 *agree with, and then subsequently further on during their treatment when they can really see*  
12 *the how much of a headache that this can be... [giggles]*  
13

14  
15 - *Do you think it's OK then to offer it twice? If somebody says no the first time? [R1]*  
16

17 *Yes – I think I do [P4]*  
18  
19  
20

21 *Because it's not like chemo A vs chemo B, it's not ... it's not crucial like... you can opt in whenever*  
22 *you want [P2]*  
23  
24  
25

26 The theme of 'practical and ethical considerations' included the ethical aspects of; consent,  
27 randomisation, delays introduced by undergoing the trial, equity and equality, and the sharing of trial  
28 data. The practical aspects described outcome collection, safety netting, and ensuring the veracity of  
29 information collected in the trial.  
30

31 Randomisation was considered a fair and ethical approach when in clinical equipoise. Along with this, a  
32 later discovery one arm proving better than the other was not considered unethical; however if being on  
33 the study disadvantaged everyone (for example, by meaning treatment would be delayed while forms  
34 were completed) then it would not have been supported. A design which was accessible for the diversity  
35 of social, cultural and economic backgrounds of potential participants was essential. Confirmation of the  
36 scientific validity of the proposal and clinical equipoise was important to the PPI team. Prior systematic  
37 reviews with meta-analysis were felt to be a very comprehensive answer to this question.  
38  
39  
40

41 Two of the three clinical academics have a strong interest in individual participant data meta-analysis. A  
42 question was asked about data sharing in this context, and the PPI were very enthusiastic in being  
43 involved.  
44  
45

46 *Definitely share. I think the thing with paediatric oncology is that we do so many international*  
47 *trials together, because thankfully it is rare, but ultimately I think that... [snip] we're here*  
48 *ultimately to try to make things better for kids of the future and if that's part of it, and it is with*  
49 *these meta-analysis, then definitely. [P1]*  
50  
51  
52

53 The PPI group were concerned with ensuring the veracity of information collected during the study.  
54

55 *"are they [study groups] actually going to tell you the truth?" [P2]*  
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5 The PPI group were keen to know there would be some ways of determining if the data collected were  
6 truthful and accurate: this seems to speak of a greater public awareness being required of the nature of  
7 health research governance within the country generally.  
8  
9

### 10 ***Febrile neutropenia themes***

11 Conversations in these discussions mapped onto the framework proposed by Morgan, developed to  
12 understand the decision-making processes involved in managing episodes of febrile neutropenia<sup>11</sup>. The  
13 overarching concepts she described were of the quest for certainty, attaining mutual trust, and the  
14 potential for realised discretion. These were all strongly endorsed in analysis of the group discussion.  
15  
16

17 The quest for certainty involves balancing the uncertainty of outcome of each episode of febrile  
18 neutropenia, including an appreciation of probability, the use of protocols and guidelines to manage the  
19 risk, and acknowledging the adverse elements of hospitalisation. The use of protective isolation, where  
20 the child and family are kept in a single room to avoid infections being caught from other hospitalised  
21 children, or source isolation, where the child is kept in a single room to avoid an infection they have  
22 spreading onwards to others, were viewed particularly negatively.  
23  
24

25  
26 *It was his cupboard – [child] called it his cupboard [P3]*  
27  
28

29 Mutual trust had been a challenge, with the group describing individual health care practitioners in  
30 whom they did not place trust, and the reciprocal of this, along with the negating of parental concerns;  
31

32  
33 *the first time that I thought it was that they were taking too much precaution and I would have*  
34 *much preferred him to be at home taking tablets and things... monitored every so often..*  
35 *whereas the second time I think he needed more than what he was getting... and I think we were*  
36 *right both times actually [P4]*  
37  
38

39  
40 The ideal management of an episode of febrile neutropenia was one where safety was assured,  
41 hospitalisation was minimised, decisions discussed with families, and support provided at home provided  
42 as desired by the family: the potential for realised discretion. The group readily acknowledged the  
43 decisions would need to be based on a range of factors, including home-to-hospital distance and the  
44 variability between parents and families in self-expressed confidence:  
45  
46

47  
48 *my sort of worry is that... the responsibility is even more on the parent as well. .on top of like*  
49 *running the house... and its that sense of responsibility as well... like they're monitoring their*  
50 *child and being responsible for it... and like if something did happen would they feel guilty about*  
51 *it or not? [P5]*  
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3 Exploring how the professionals were thinking about the episode, in terms of the likelihood of adverse  
4 outcomes and their considerations, was a strength in a shared decision making approach which had  
5 been absent in many prior experiences:  
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7  
8 *I think it would be really helpful, [imitates Dr speaking] ... we think its' like this [left] or we think*  
9 *it's like this [right]... and then chatting... and ..... You know where you are coming from and*  
10 *where there is a difference and you know talking about ... [P2]*  
11

12  
13 *seem to recall being in negotiations... situations where... ringing [PTC] consultants saying "This is*  
14 *our situation .... can you speak to them and and so on..." [P4]*  
15

### 16 17 18 **Reflections of clinical academics**

19 The group discussions encouraged the three clinical trialists to reflect on their previous approaches to  
20 febrile neutropenia and PPI involvement in other studies. The more experienced clinical academics had  
21 undertaken PPI before, but always on a face-to-face basis. The video conferencing allowed for a more  
22 diverse group of individuals to undertake the work, with the clinicians in the same room on one screen  
23 facilitating. The makeshift re-positioning of audio for one participant through the phone served to  
24 reduce hierarchies, with collaborative suggestions and problem solving forming an early 'win' for the  
25 group. The protocol changes suggested by the group had been unexpected, as was the emphasis on the  
26 emotional burden of physical isolation. The researchers all took away from this experience the value of  
27 listening to expert parents and young people, and considering video or telephone conferencing to allow  
28 a greater number and range of people to take part in PPI events.  
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### 35 **Discussion**

36 The engagement of a group of parents and an ex-patient who had experience of CYP cancer with  
37 clinician-trialists developing a study to improve the management of febrile neutropenia led to changes  
38 in the proposed design of the trial, and brought out a deeper understanding of the potential concerns of  
39 participants in such a study. The wider discussions about the nature of the experience of an episode of  
40 febrile neutropenia were congruent with prior work in the field<sup>11</sup>. pointing particularly to actively  
41 involve parents and young people in sharing decisions about care.  
42  
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45 The PPI involvement altered how the trial would be structured, randomisation of each child to one of  
46 the two management methods through the whole of their anti-cancer treatment, rather than  
47 randomising the study sites or the child at each visit. The suggestion of multiple opportunities to be  
48 involved in the study was welcome, and congruent with the description of an emerging expertise and  
49 empowerment in people through the childhood cancer journey<sup>14</sup>. They discussed practical methods of  
50 collecting data which went beyond simple admission statistics and questionnaires, to enrich the  
51 information gained in the study. Active follow-up, with healthcare initiated contact with the family, but  
52 negotiated in light of their individual family, had not been originally considered by the trialists. The  
53 discussion also shed light on the experiences of people in being involved in treatments of episodes of  
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3 febrile neutropenia, with the ideal being an individualised, negotiated approach within clear, safe,  
4 guidance, consistently used across all centres.  
5

6  
7 The expertise and prior relationships in the group members of similar situations may have enhanced the  
8 easy flow of ideas and conversations in this event. All members knew at least one other participant  
9 through in-person interactions, in similar group settings or clinical interactions. Ice-breaking activities  
10 were extremely brief, as there was little ice to be broken. Future PPI work with similar groups of people  
11 would benefit from considering holding the group conversations via a video conferencing platform. The  
12 ready availability of web-cams and front-facing cameras on phones, tablet and laptop computers, and  
13 the common use of video conversations in work and home life mean these are acceptable methods to  
14 have discussions. It may be beneficial to have a 'test run' period prior to the meeting to allow any  
15 technical challenges to be met; we would suggest a period of time when 'drop in' connections to  
16 confirm all is working well would be a sensible way forwards. A backup approach, as simple as a  
17 telephone line, is also very helpful.  
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21 The findings of this study have immediately influenced an application for a feasibility study of  
22 procalcitonin guided management of febrile neutropenia. They will also influence the ongoing  
23 development of clinical practice through dissemination through the children's and young people's  
24 professional network groups. Finally, the participants in this group have expressed a wish to be part of  
25 the steering committee of a trial addressing this issue, and one has joined the study as a co-applicant,  
26 enhancing further the study design.  
27  
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### 31 32 **Figure legend**

33 Interaction of themes and sub-themes  
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40 profit sectors. BP was supported by an NIHR Post-doctoral fellowship: grant number PDF2014-10872.  
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42  
43  
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### 45 **Competing Interests**

46 There are no competing interests to declare.  
47  
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### 51 **Contributorship**

52 This study was conceived by BP and SD, and developed with the assistance of JM. The audio was  
53 transcribed and analysed by BP initially with input from JM and SD. BP drafted the paper, and was  
54 critically revised and developed by JM and SD. The PPI group read and agreed with the content of the  
55 paper. The authors very gratefully acknowledge their input into this specific work.  
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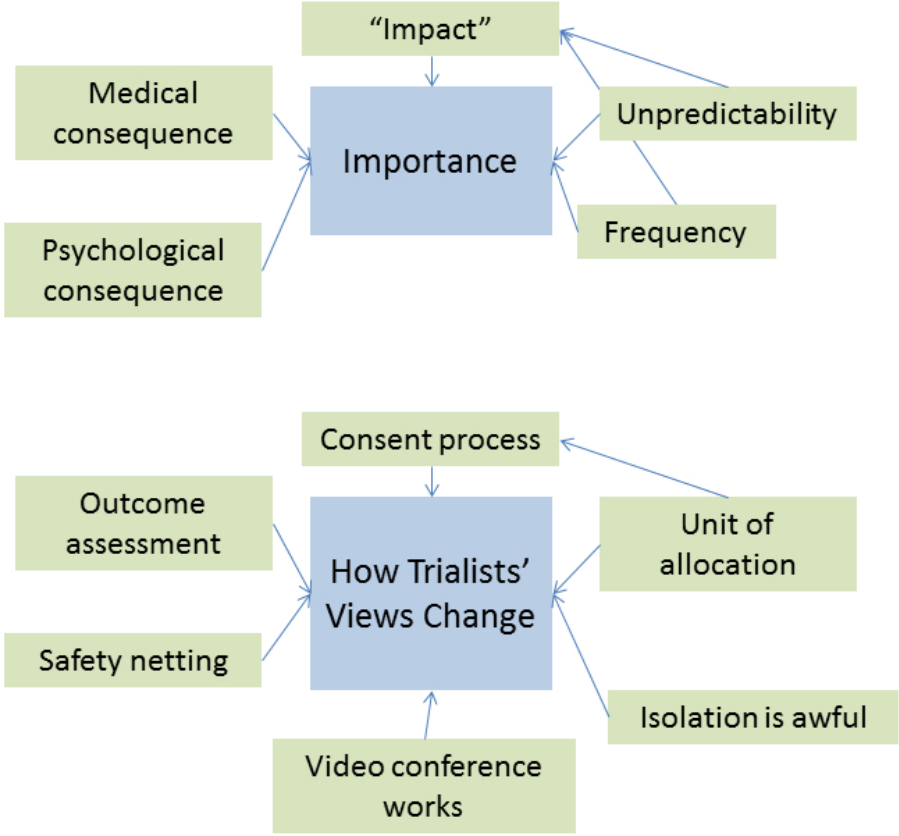
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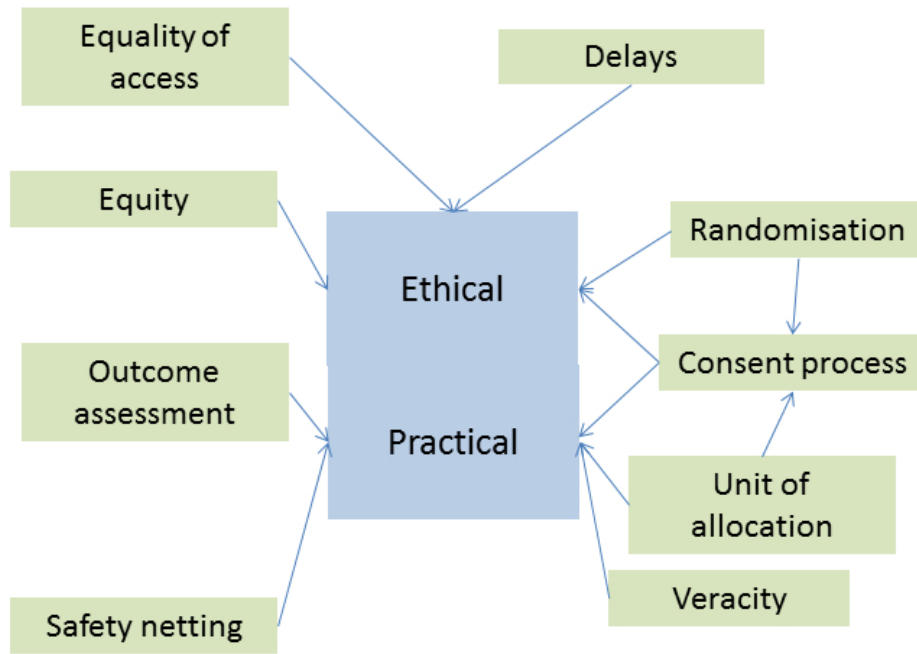
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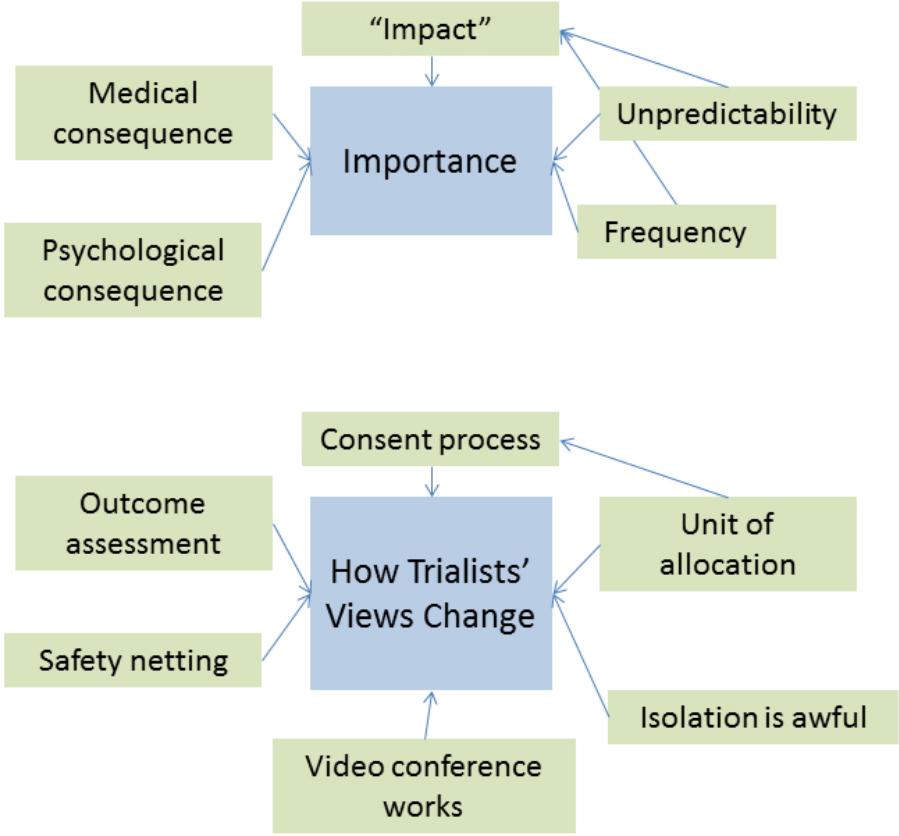
# BMJ Paediatrics Open

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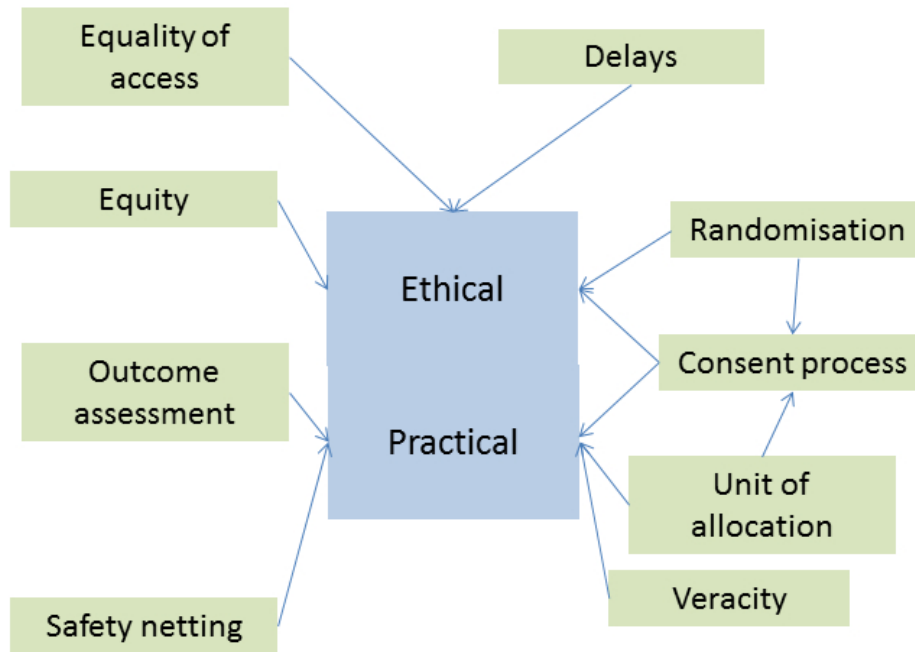
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# What do families want to improve in the management of paediatric febrile neutropenia during anti-cancer treatment? Report of a patient/public involvement group.

## Authors

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## Abstract

### Background

This study reports how parents and young people who had experience of febrile neutropenia improved the design of a trial to inform the management of this condition. Five parents, a young person who had completed treatment, and three clinician-researchers contributed.

### Methods

The group formed after an invitation via social media and met via video conference. Many participants were from an existing childhood cancer parent-involvement group. The initial questions for the discussion asked about the importance of the topic, the views of the need for a trial, which important outcomes should be measured, and practical aspects which would make it easier or more difficult for people to take part in it. The conversation occurred across an entire afternoon, was audio and video recorded, transcribed, analysed, and checked by those involved. The fifth parent added to this via email.

### Results

The group altered the trial structure, proposing to randomise each child to one of the two management methods through the whole of their anti-cancer treatment, rather than randomising the study sites or the child at each visit. They felt even if people declined taking part in the study in the first weeks of diagnosis, their views may change and they should be allowed to consent later. They also proposed methods of collecting patient and family important data, enriching the medical information gained in the study. Active follow-up, negotiated for each individual family, was also suggested.

### Conclusion

Trials improving the management of febrile neutropenia for children and young people who are undergoing anti-cancer treatments should consider individual-patient randomisation, collection of

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2  
3 'quality of life' and 'experience of care' aspects using digital and paper methods, engage families in  
4 shared decision making around management choices and ensure adequate supportive information is  
5 available and accessible to all patients, regardless of background, geographical location, or age.  
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## 10 **Key Messages**

### 11 **What is known**

- 12 • Febrile neutropenia is a common complication of childhood cancer therapy which is  
13 disruptive and resource intensive
- 14 • Trials of reduction in intensity of treatment for febrile neutropenia has previously been  
15 challenging to accept for parents
- 16 • Parent/patient and public involvement in trials has improved study designs, research  
17 comprehension and engagement materials

### 18 **What this study adds**

- 19 • Parent/patient and public involvement in a proposed trial of reducing antibiotic treatment  
20 for febrile neutropenia led to changes in fundamental aspects of trial design
- 21 • Proposed outcome assessments were enhanced by experts by experience describing the  
22 burden of the treatment for febrile neutropenia and trial procedures
- 23 • Video conferencing for parent/patient and public involvement was effective despite the  
24 participants not already being well known to each other

## 25 **Introduction**

26 The treatment of malignancies in childhood is associated, in high-income countries, with five-year  
27 survival rates in excess of 80%<sup>1</sup>. This is possible through the use of intensive, toxicity inducing,  
28 regimens, where one-third of deaths in this group are the result of complications of therapy rather  
29 than directly due to the disease<sup>2,3</sup>. The cancer treatment often produces acute complications  
30 requiring unplanned hospitalisation, disruption, distress and strain upon the young person and their  
31 family<sup>4</sup>. One such complication is the co-occurrence of fever in the presence of neutropenia; this  
32 combination heralds a possible overwhelming infection and is considered a medical emergency<sup>5</sup>.  
33 The absolute risk of death or requirement for intensive care in such episodes is low; approximately  
34 3%<sup>6</sup>. The challenge for families and health care professionals is to effectively treat each episode,  
35 with minimum exposure to antibiotics and disruption of family life.

36 Research into episodes of febrile neutropenia, and subsequent clinical practice guidelines have  
37 emphasised the need to treat promptly, assess the risk of each episode, and treat with antibiotics  
38 chosen to address individual and local resistance patterns<sup>5</sup>. The methods of risk assessment and  
39 discontinuing antibiotic therapy are, however, precautionary and conservative, treating two thirds of  
40 patients with broad spectrum antibiotics unnecessarily<sup>7</sup>. Studies have shown that biomarkers of  
41 infection/inflammation seem to predict the risk of serious infection and its resolution, but have not  
42 been used to guide management<sup>8</sup>. Further refinement of the approach to febrile neutropenia has  
43 been identified as a research priority<sup>5</sup>.

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2  
3 In analogous situations with critically ill or immunocompromised hosts, such as adult or neonatal  
4 intensive care units, the traditional management is similar to febrile neutropenia, with the prompt  
5 use of antibiotics and discontinuing when infection has been excluded. Procalcitonin-led guidelines  
6 have been shown to reduce exposure to antibiotics and potentially improve mortality rates<sup>9 10</sup>.  
7  
8

9 The need to improve the management of febrile neutropenia led to the development of a research  
10 proposal to use procalcitonin, which is tested on a blood sample, to assist antibiotic decision making  
11 episodes of febrile neutropenia. Deciding how to conduct such a study, which outcomes were  
12 important to measure, how to measure them, and possible barriers and solutions to a trial, was felt  
13 to be best undertaken with the engagement of clinicians, academics, and parents and young people  
14 who had direct experience of anti-cancer treatment in childhood. Previous work had shown how  
15 such involvement led to improved research focus, better interview questions, and enhanced the  
16 skills of children and young people undertaking such work<sup>11</sup>.  
17  
18  
19

20 This paper reports the findings of a patient/public involvement (PPI) group, where researchers,  
21 parents and young people convened to design a study to investigate procalcitonin-assisted decision-  
22 making in the management of febrile neutropenia in children undergoing anti-cancer therapy.  
23  
24

## 25 **Method**

26 A request was made on social media for parents and young people who had experience of childhood  
27 cancer therapy to consider taking part in a group to discuss the proposed trial. Volunteers were  
28 gathered, and after initially attempting a face to face meeting, a video conference platform (Zoom)  
29 was used to overcome geographical barriers to promote inclusiveness and working together. The  
30 researchers, all clinical doctors with additional academic roles, all met in one location; the public  
31 contributors took part from their own homes. One participant could not get integrated audio  
32 working, so joined the conversation via telephone and mute video. The discussion lasted 2h 15  
33 minutes.  
34  
35  
36

37 The session was structured to introduce febrile neutropenia, the existing evidence for the proposed  
38 intervention, and the rationale for a randomised feasibility study (see Box 1 for the initial plan). The  
39 PPI group all had knowledge of clinical studies, including trials, in children and young people with  
40 cancer. The discussion followed a series of questions about the experience of febrile neutropenia,  
41 it's management, the perceived challenges with current approaches and how the study would be  
42 best organised to meet these.  
43  
44  
45

46 The session was video and audio recorded. The entire meeting was transcribed, after audio  
47 immersion, and the content thematically studied. Elements of the conversation related specifically  
48 to the design and conduct of a study were developed into themes and sub-themes. Elements related  
49 to the management of febrile neutropenia were examined in a framework derived from the themes  
50 developed in a relevant PhD<sup>12</sup>. Following the meeting, a summary was shared and agreed, and the  
51 full report from which this paper is derived was reviewed by the PPI group.  
52  
53  
54

55 The costs of the group were small; transport costs and light refreshments only for the researchers,  
56 and a small fee for the video conferencing platform. The platform and the technologies were already  
57 owned by the participants. The participants volunteered their time, in line with their voluntary  
58 involvement with similar charitable activities, and did not receive payment.  
59  
60

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3 As this was a patient/public engagement group no ethical review was required. This is consistent  
4 with the INVOLVE definition of public involvement in research as “research being carried out ‘with’  
5 or ‘by’ members of the public rather than ‘to’, ‘about’ or ‘for’ them”<sup>13</sup>, Despite the lack of a formal  
6 requirement for research ethics committee oversight, and ethical approach to such work is  
7 necessary. Such an approach has been described<sup>14</sup>, and the key elements of a fair choice to partake  
8 in the work, appropriate training and support to understand the questions asked, making sure access  
9 was as equitable as possible and providing recognition for the work were all considered in this  
10 project.  
11  
12

## 13 14 **Results**

### 15 16 ***Participants***

17 Four volunteer parents were part of the UK-based PORT (Paediatric Oncology Reference Team)  
18 organisation, which consists of parents of children and young people who had experience of  
19 childhood cancer. Each was the mother of a child who had undergone cancer treatment; two with  
20 leukaemia, two with neuroblastoma. Three of these four parent’s children had died of their disease.  
21 A patient who had leukaemia when a teenager also took part in the group, unrelated to the other  
22 participants. Of the three researchers, two were higher specialist trainees in paediatric oncology,  
23 and one a Consultant, who was the only male in this group. Each member of the group had prior  
24 experience with research in children’s cancer beyond participation. The discussions involved  
25 descriptions of past experiences of admissions with fever and neutropenia. The experiences were  
26 from around 2006-2017. During that time period, there has been a move to some reduction in  
27 length-of-stay and marginally more consistency between centres in the UK<sup>15</sup>. Additional comments  
28 were added by a fifth PORT parent via email following the video conference.  
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### 36 37 ***Study-specific themes***

38 Information regarding the undertaking and conduct of the study was described under three major  
39 themes; ‘importance’, ‘how PPI changes researchers’ views’ and ‘practical and ethical’. The theme of  
40 ‘importance’ was formed by concepts of ‘medical consequence’, ‘psychological consequence’,  
41 ‘impact’, ‘unpredictability’ and ‘frequency of FN’. (See Figure)  
42

43 *Importance:* The group members unanimously agreed that the management of episodes of febrile  
44 neutropenia was important because of its unpredictability, frequency, and medical, psychological  
45 and social (‘impact’) consequences. They described particularly how variation in care across different  
46 hospitals was a source of concern to them and consistency would be a positive by-product of  
47 undertaking a trial:  
48  
49

50  
51 *“we’ve got the 20-odd centres and pretty much everybody follows the same protocols [for*  
52 *anti-cancer treatment]... and I think it would be really reassuring for families if the POSCUs*  
53 *[Paediatric Oncology Shared Care Units] you know if we knew that everybody was doing the*  
54 *same thing” [P1]*  
55

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57  
58 *‘How PPI changes researchers’ views’* describes the impact of this work: of how PPI is important in  
59 modifying the initial, genuinely held presumptions and beliefs about the best ways to conduct such a  
60

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3 trial for families and CYP. These beliefs were drawn from the trial development group, the group of  
4 clinicians and researchers involved in designing the trial, which has over a century of experience  
5 working in children's cancer in a variety of units and countries and specific expertise in studying  
6 supportive care in this group of patients. The impact of the group is seen in in the following aspects:  
7  
8

9 Allocation. The initial suggestion was for group randomisation, assigned arms to by clinical unit,  
10 rather than individual patients. However, the PPI input strongly steered towards individual  
11 randomisation, but with each individual receiving the same arm of management throughout the  
12 whole trial:  
13

14  
15 *with paediatric oncology unlike many other things... everybody is on a trial... everybody... I*  
16 *mean... <snip>... I think everyone just expects that their treatment may be a bit different*  
17 *than everyone else's... [P2]*  
18

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20  
21 *once you're randomised rather than each time coming in and by randomised each time,*  
22 *you're better off having "this family is procalcitonin, this family is not" [P1]*  
23  
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25  
26 Outcome assessment. The group members felt direct measures of patient experience would be  
27 important, more than 'quality of life' checklists. They suggested offering a daily experience journal of  
28 some form (paper, or 'app' based electronic), and believed this would supplement and enrich the  
29 medical data collected, such as admission duration, antibiotic duration, and infective organisms.  
30

31  
32 *capturing that idea of burden beyond the hospital based stuff and things that matter to the*  
33 *family, [P3]*  
34  
35

36 They described how it would be important to measure the extra resources required because of FN  
37 admissions. The word 'impact' was felt to capture this rather than 'costs'.  
38

39  
40 *impact, because it's not just about extra costs, I mean if you're having to call in grandparents*  
41 *and you're having to call in favours left right and centre, <snip> I mean how many times can*  
42 *you ask the next door neighbours to collect your kids from school [P1]*  
43  
44

45  
46 Active safety netting. The researchers initially felt the standard approach after discharge of  
47 responsibilities passed to the family to 'return if unwell' would be safe and acceptable, but the PPI  
48 group thought an active approach to safety-netting was necessary, but should be individually  
49 negotiated:  
50

51  
52 *I think it needs to be more than just you phone up the hospital if you have any concerns, it*  
53 *should be either somebody coming around or phoning you and saying "Do you have any*  
54 *concerns, do you have any concerns at all" and actually if you say yes ..... giving you the*  
55 *option of coming back or having somebody over [P4]*  
56  
57

58  
59 Gaining consent. The researchers proposed, as with usual practice, the study would be offered once  
60



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3 to families when the clinician believed it appropriate. The group members, with their experience of  
4 studies and information being exchanged, thought it would be fair to allow people to decline early  
5 on, but have the opportunity to join the study if they changed their mind as their treatment journey  
6 progressed. They also floated the idea of families approaching clinicians to join, rather than being  
7 invited.  
8  
9

10 *I don't think I even knew what febrile neutropenia was though, at the time when we were*  
11 *first giving our consent to all the other things? I think that's something that possibly comes*  
12 *with... further on... down the line... even a week or two weeks after you've given all those*  
13 *other consents. Because actually, the other consents are almost live-saving things... whereas*  
14 *this is a real choice... and I think that batching it in with those initial forms of consents is*  
15 *almost taking away your flexibility of trying to consider it whether you want to do it or not*  
16  
17 [P4]  
18  
19

20  
21  
22 *You might also get people saying 'No' right at the beginning, if it's something they don't have*  
23 *to agree with, and then subsequently further on during their treatment when they can really*  
24 *see the how much of a headache that this can be... [giggles]*  
25  
26

27 - *Do you think it's OK then to offer it twice? If somebody says no the first time? [R1]*  
28

29 *Yes – I think I do [P4]*  
30  
31

32  
33 *Because it's not like chemo A vs chemo B, it's not ... it's not crucial like... you can opt in*  
34 *whenever you want [P2]*  
35  
36  
37

38 The theme of 'practical and ethical considerations' included the ethical aspects of; consent,  
39 randomisation, delays introduced by undergoing the trial, equity and equality, and the sharing of  
40 trial data. The practical aspects described outcome collection, safety netting, and ensuring the  
41 veracity of information collected in the trial.  
42  
43

44 Randomisation was considered a fair and ethical approach when in clinical equipoise. Along with  
45 this, a later discovery one arm proving better than the other was not considered unethical; however  
46 if being on the study disadvantaged everyone (for example, by meaning treatment would be delayed  
47 while forms were completed) then it would not have been supported. A design which was accessible  
48 for the diversity of social, cultural and economic backgrounds of potential participants was essential.  
49 Confirmation of the scientific validity of the proposal and clinical equipoise was important to the PPI  
50 group. Prior systematic reviews with meta-analysis were felt to be a very comprehensive answer to  
51 this question.  
52  
53

54  
55 Two of the three researchers have a strong interest in individual participant data meta-analysis. A  
56 question was asked about data sharing in this context, and the PPI were very enthusiastic in being  
57 involved.  
58  
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3 *Definitely share. I think the thing with paediatric oncology is that we do so many*  
4 *international trials together, because thankfully it is rare, but ultimately I think that... [snip]*  
5 *we're here ultimately to try to make things better for kids of the future and if that's part of it,*  
6 *and it is with these meta-analysis, then definitely. [P1]*  
7  
8  
9

10 The group members were concerned about study governance, for example ensuring the veracity of  
11 information collected during the study.  
12

13  
14 *"are they [study groups] actually going to tell you the truth?" [P2]*  
15  
16

17 The members were keen to know there would be some ways of determining if the data collected  
18 were truthful and accurate: this seems to speak of a greater public awareness being required of the  
19 nature of health research governance within the country generally.  
20

21  
22 ***An offer for expressions of interest in continuing to engage with the study governance was***  
23 ***enthusiastically met by the participants. One of the group has joined the funding***  
24 ***application as a co-applicant, and has helped develop the grant application and is planned***  
25 ***to be involved in the qualitative data collection and analysis as a co-investigator. Febrile***  
26 ***neutropenia themes***  
27

28 Conversations in these discussions mapped onto the framework proposed by Morgan, developed to  
29 understand the decision-making processes involved in managing episodes of febrile neutropenia <sup>12</sup>.  
30 The overarching concepts she described were of the quest for certainty, attaining mutual trust, and  
31 the potential for realised discretion. These were all strongly endorsed in analysis of the group  
32 discussion.  
33  
34

35 The quest for certainty involves balancing the uncertainty of outcome of each episode of febrile  
36 neutropenia, including an appreciation of probability, the use of protocols and guidelines to manage  
37 the risk, and acknowledging the adverse elements of hospitalisation. The use of protective isolation,  
38 where the child and family are kept in a single room to avoid infections being caught from other  
39 hospitalised children, or source isolation, where the child is kept in a single room to avoid an  
40 infection they have spreading onwards to others, were viewed particularly negatively.  
41  
42  
43

44 *It was his cupboard – [child] called it his cupboard [P3]*  
45  
46

47 Mutual trust had been a challenge, with the group describing individual health care practitioners in  
48 whom they did not place trust, and the reciprocal of this, along with the negating of parental  
49 concerns;  
50

51  
52 *the first time that I thought it was that they were taking too much precaution and I would*  
53 *have much preferred him to be at home taking tablets and things... monitored every so*  
54 *often.. whereas the second time I think he needed more than what he was getting... and I*  
55 *think we were right both times actually [P4]*  
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3 The ideal management of an episode of febrile neutropenia was one where safety was assured,  
4 hospitalisation was minimised, decisions discussed with families, and support provide at home  
5 provided as desired by the family: the potential for realised discretion. The group readily  
6 acknowledged the decisions would need to be based on a range of factors, including home-to-  
7 hospital distance and the variability between parents and families in self-expressed confidence:  
8  
9

10 *my sort of worry is that... the responsibility is even more on the parent as well. .on top of like*  
11 *running the house... and its that sense of responsibility as well... like they're monitoring their*  
12 *child and being responsible for it... and like if something did happen would they feel guilty*  
13 *about it or not? [P5]*  
14  
15

16  
17 Exploring how the professionals were thinking about the episode, in terms of the likelihood of  
18 adverse outcomes and their considerations, was a strength in a shared decision making approach  
19 which had been absent in many prior experiences:  
20  
21

22 *I think it would be really helpful, [imitates Dr speaking] ... we think its' like this [left] or we*  
23 *think it's like this [right]... and then chatting... and .... You know where you are coming from*  
24 *and where there is a difference and you know talking about ... [P2]*  
25  
26

27 *seem to recall being in negotiations... situations where... ringing [PTC] consultants saying*  
28 *"This is our situation .... can you speak to them and and so on..." [P4]*  
29  
30  
31

### 32 **Reflections of clinical academics**

33 The group discussions encouraged the three researchers to reflect on their previous approaches to  
34 febrile neutropenia and PPI involvement in other studies. The more experienced researchers had  
35 undertaken PPI before, but always on a face-to-face basis. The video conferencing allowed for a  
36 more diverse group of individuals to undertake the work, with the researchers in the same room on  
37 one screen facilitating. The makeshift re-positioning of audio for one participant through the phone  
38 served to reduce hierarchies, with collaborative suggestions and problem solving forming an early  
39 'win' for the group. This method worked well with the age and technological skills of this group, but  
40 may be less successful if a group with fewer technology skills or younger age were being involved.  
41 The protocol changes suggested by the group had been unexpected, as was the emphasis on the  
42 emotional burden of physical isolation. The researchers all took away from this experience the value  
43 of listening to expert parents and young adults, and considering video or telephone conferencing to  
44 allow a greater number and range of people to take part in PPI events.  
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### 52 **Discussion**

53 The engagement of a group of parents and an ex-patient who had experience of CYP cancer with  
54 researchers developing a study to improve the management of febrile neutropenia led to changes in  
55 the proposed design of the trial, and brought out a deeper understanding of the potential concerns  
56 of participants in such a study. The wider discussions about the nature of the experience of an  
57 episode of febrile neutropenia were congruent with prior work in the field<sup>12</sup> pointing particularly to  
58 actively involve parents and young people in sharing decisions about care.  
59  
60

1  
2  
3 The PPI involvement altered how the trial would be structured, randomisation of each child to one  
4 of the two management methods through the whole of their anti-cancer treatment, rather than  
5 randomising the study sites or the child at each visit (see Box 2 for specific changes). The suggestion  
6 of multiple opportunities to be involved in the study was welcome, and congruent with the  
7 description of an emerging expertise and empowerment in people through the childhood cancer  
8 journey<sup>16</sup>. They discussed practical methods of collecting data which went beyond simple admission  
9 statistics and questionnaires, to enrich the information gained in the study. Active follow-up, with  
10 healthcare initiated contact with the family, but negotiated in light of their individual family, had not  
11 been originally considered by the researchers. The discussion also shed light on the experiences of  
12 people in being involved in treatments of episodes of febrile neutropenia, with the ideal being an  
13 individualised, negotiated approach within clear, safe, guidance, consistently used across all centres.  
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18 The expertise and prior relationships in the group members of similar situations may have enhanced  
19 the easy flow of ideas and conversations in this event. All members knew at least one other  
20 participant through in-person interactions, in similar group settings or clinical interactions. Ice-  
21 breaking activities were extremely brief, as there was little ice to be broken. None of the participants  
22 were paid for their time undertaking this work. The INVOLVE guidelines suggest involvement should  
23 come with re-imburement, the group all undertook work with charities related to childhood cancer  
24 treatment, research and support and saw this as an extension of their other activities. Future PPI  
25 work with similar groups of people would benefit from considering holding the group conversations  
26 via a video conferencing platform. The ready availability of web-cams and front-facing cameras on  
27 phones, tablet and laptop computers, and the common use of video conversations in work and  
28 home life mean these were acceptable methods to have discussions with this group, though may not  
29 work with younger children or those unfamiliar with video conferencing. If the approach is used, it  
30 may be beneficial to have a 'test run' period prior to the meeting to allow any technical challenges to  
31 be met; we would suggest a period of time when 'drop in' connections to confirm all is working well  
32 would be a sensible way forwards. A backup approach, as simple as a telephone line, is also very  
33 helpful. Direct advertising of the chance to be involved in the work to young people via other groups,  
34 such as Young People's Advisory Groups hosted by organisations such as the National Cancer  
35 Research Institute or Clic-Sergant, or advertising through the Teenage Cancer Trust, may have meant  
36 more than one young person was involved.  
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43 The findings of this study have immediately influenced an application for a feasibility study of  
44 procalcitonin guided management of febrile neutropenia. They will also influence the ongoing  
45 development of clinical practice through dissemination through the children's and young people's  
46 professional network groups. The participants in this group have expressed a wish to be part of the  
47 steering committee of a trial addressing this issue, and the ongoing study development will also seek  
48 further young people to be involved, following INVOLVE guidelines<sup>17 18</sup>. One of the group members  
49 has joined the study as a co-applicant, developing the grant, and plans to be involved as a co-  
50 investigator..  
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## 57 **Figure legend**

58 Interaction of themes and sub-themes  
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## Competing Interests

There are no competing interests to declare.

## Contributorship

This study was conceived by BP and SD, and developed with the assistance of JM. The audio was transcribed and analysed by BP initially with input from JM and SD. BP drafted the paper, and was critically revised and developed by JM and SD. The PPI group read and agreed with the content of the paper. The authors very gratefully acknowledge their input into this specific work.

### Box 1

Site-randomised trial (randomising by hospital) using cluster or step-wedge approach

Sites consented

Use of single quality of life questionnaire at discharge

Patient contact for trial purposes only to occur while in-patient – not after discharge

Antibiotic decision making on procalcitonin measurements and clinical judgement without family involvement

### Box 2

Individual patient randomised trial (randomising by patient, not by episode)

Consent permissible at any point during the cancer journey while still 'at risk'

Richer patient experience measures – not just patient QoL but family experience and their costs to be captured

Active follow-up after discharge

Explicitly encouraging shared decision making and sharing of results with families to decide antibiotic use

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# BMJ Paediatrics Open

## What do families want to improve in the management of paediatric febrile neutropenia during anti-cancer treatment? Report of a patient/public involvement group.

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Keywords:	Data Collection, Infectious Diseases, Oncology, Patient perspective

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# What do families want to improve in the management of paediatric febrile neutropenia during anti-cancer treatment? Report of a patient/public involvement group.

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## Abstract

### Background

This study reports how parents and young people who had experience of febrile neutropenia improved the design of a trial to inform the management of this condition. Five parents, a young person who had completed treatment, and three clinician-researchers contributed.

### Methods

The group formed after an invitation via social media and met via video conference. Many participants were from an existing childhood cancer parent-involvement group. The initial questions for the discussion asked about the importance of the topic, the views of the need for a trial, which important outcomes should be measured, and practical aspects which would make it easier or more difficult for people to take part in it. The conversation occurred across an entire afternoon, was audio and video recorded, transcribed, analysed, and checked by those involved. The fifth parent added to this via email.

### Results

The group altered the trial structure, proposing to randomise each child to one of the two management methods through the whole of their anti-cancer treatment, rather than randomising the study sites or the child at each visit. They felt even if people declined taking part in the study in the first weeks of diagnosis, their views may change and they should be allowed to consent later. They also proposed methods of collecting patient and family important data, enriching the medical information gained in the study. Active follow-up, negotiated for each individual family, was also suggested.

### Conclusion

Trials improving the management of febrile neutropenia for children and young people who are undergoing anti-cancer treatments should consider individual-patient randomisation, collection of

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3 'quality of life' and 'experience of care' aspects using digital and paper methods, engage families in  
4 shared decision making around management choices and ensure adequate supportive information is  
5 available and accessible to all patients, regardless of background, geographical location, or age.  
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## 10 **Key Messages**

### 11 **What is known**

- 12 • Febrile neutropenia is a common complication of childhood cancer therapy which is  
13 disruptive and resource intensive
- 14 • Trials of reduction in intensity of treatment for febrile neutropenia has previously been  
15 challenging to accept for parents
- 16 • Parent/patient and public involvement in trials has improved study designs, research  
17 comprehension and engagement materials

### 18 **What this study adds**

- 19 • Parent/patient and public involvement in a proposed trial of reducing antibiotic treatment  
20 for febrile neutropenia led to changes in fundamental aspects of trial design
- 21 • Proposed outcome assessments were enhanced by experts by experience describing the  
22 burden of the treatment for febrile neutropenia and trial procedures
- 23 • Video conferencing for parent/patient and public involvement was effective despite the  
24 participants not already being well known to each other

## 25 **Introduction**

26 The treatment of malignancies in childhood is associated, in high-income countries, with five-year  
27 survival rates in excess of 80%<sup>1</sup>. This is possible through the use of intensive, toxicity inducing,  
28 regimens, where one-third of deaths in this group are the result of complications of therapy rather  
29 than directly due to the disease<sup>2,3</sup>. The cancer treatment often produces acute complications  
30 requiring unplanned hospitalisation, disruption, distress and strain upon the young person and their  
31 family<sup>4</sup>. One such complication is the co-occurrence of fever in the presence of neutropenia; this  
32 combination heralds a possible overwhelming infection and is considered a medical emergency<sup>5</sup>.  
33 The absolute risk of death or requirement for intensive care in such episodes is low; approximately  
34 3%<sup>6</sup>. The challenge for families and health care professionals is to effectively treat each episode,  
35 with minimum exposure to antibiotics and disruption of family life.

36 Research into episodes of febrile neutropenia, and subsequent clinical practice guidelines have  
37 emphasised the need to treat promptly, assess the risk of each episode, and treat with antibiotics  
38 chosen to address individual and local resistance patterns<sup>5</sup>. The methods of risk assessment and  
39 discontinuing antibiotic therapy are, however, precautionary and conservative, treating two thirds of  
40 patients with broad spectrum antibiotics unnecessarily<sup>7</sup>. Studies have shown that biomarkers of  
41 infection/inflammation seem to predict the risk of serious infection and its resolution, but have not  
42 been used to guide management<sup>8</sup>. Further refinement of the approach to febrile neutropenia has  
43 been identified as a research priority<sup>5</sup>.

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3 In analogous situations with critically ill or immunocompromised hosts, such as adult or neonatal  
4 intensive care units, the traditional management is similar to febrile neutropenia, with the prompt  
5 use of antibiotics and discontinuing when infection has been excluded. Procalcitonin-led guidelines  
6 have been shown to reduce exposure to antibiotics and potentially improve mortality rates<sup>9 10</sup>.  
7  
8

9 The need to improve the management of febrile neutropenia led to the development of a research  
10 proposal to use procalcitonin, which is tested on a blood sample, to assist antibiotic decision making  
11 episodes of febrile neutropenia. Deciding how to conduct such a study, which outcomes were  
12 important to measure, how to measure them, and possible barriers and solutions to a trial, was felt  
13 to be best undertaken with the engagement of clinicians, academics, and parents and young people  
14 who had direct experience of anti-cancer treatment in childhood. Previous work had shown how  
15 such involvement led to improved research focus, better interview questions, and enhanced the  
16 skills of children and young people undertaking such work<sup>11</sup>.  
17  
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19

20 This paper reports the findings of a patient/public involvement (PPI) group, where researchers,  
21 parents and young people convened to design a study to investigate procalcitonin-assisted decision-  
22 making in the management of febrile neutropenia in children undergoing anti-cancer therapy.  
23  
24

## 25 **Method**

26 A request was made on social media for parents and young people who had experience of childhood  
27 cancer therapy to consider taking part in a group to discuss the proposed trial. Volunteers were  
28 gathered, and after initially attempting a face to face meeting, a video conference platform (Zoom)  
29 was used to overcome geographical barriers to promote inclusiveness and working together. The  
30 researchers, all clinical doctors with additional academic roles, all met in one location; the public  
31 contributors took part from their own homes. One participant could not get integrated audio  
32 working, so joined the conversation via telephone and mute video. The discussion lasted 2h 15  
33 minutes.  
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37 The session was structured to introduce febrile neutropenia, the existing evidence for the proposed  
38 intervention, and the rationale for a randomised feasibility study (see Box 1 for the initial plan). The  
39 PPI group all had knowledge of clinical studies, including trials, in children and young people with  
40 cancer. The discussion followed a series of questions about the experience of febrile neutropenia,  
41 its management, the perceived challenges with current approaches and how the study would be  
42 best organised to meet these.  
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46 The session was video and audio recorded. The entire meeting was transcribed, after audio  
47 immersion, and the content thematically studied. Elements of the conversation related specifically  
48 to the design and conduct of a study were developed into themes and sub-themes. Elements related  
49 to the management of febrile neutropenia were examined in a framework derived from the themes  
50 developed in a relevant PhD<sup>12</sup>. Following the meeting, a summary was shared and agreed, and the  
51 full report from which this paper is derived was reviewed by the PPI group.  
52  
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55 The costs of the group were small; transport costs and light refreshments only for the researchers,  
56 and a small fee for the video conferencing platform. The platform and the technologies were already  
57 owned by the participants. The participants volunteered their time, in line with their voluntary  
58 involvement with similar charitable activities, and did not receive payment.  
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3 As this was a patient/public engagement group no ethical review was required. This is consistent  
4 with the INVOLVE definition of public involvement in research as “research being carried out ‘with’  
5 or ‘by’ members of the public rather than ‘to’, ‘about’ or ‘for’ them”<sup>13</sup>, Despite the lack of a formal  
6 requirement for research ethics committee oversight, and ethical approach to such work is  
7 necessary. Such an approach has been described<sup>14</sup>, and the key elements of a fair choice to partake  
8 in the work, appropriate training and support to understand the questions asked, making sure access  
9 was as equitable as possible and providing recognition for the work were all considered in this  
10 project.  
11  
12

## 13 14 **Results**

### 15 16 ***Participants***

17 Four volunteer parents were part of the UK-based PORT (Paediatric Oncology Reference Team)  
18 organisation, which consists of parents of children and young people who had experience of  
19 childhood cancer. Each was the mother of a child who had undergone cancer treatment; two with  
20 leukaemia, two with neuroblastoma. Three of these four parent’s children had died of their disease.  
21 A patient who had leukaemia when a teenager also took part in the group, unrelated to the other  
22 participants. Of the three researchers, two were higher specialist trainees in paediatric oncology,  
23 and one a Consultant, who was the only male in this group. Each member of the group had prior  
24 experience with research in children’s cancer beyond participation. The discussions involved  
25 descriptions of past experiences of admissions with fever and neutropenia. The experiences were  
26 from around 2006-2017. During that time period, there has been a move to some reduction in  
27 length-of-stay and marginally more consistency between centres in the UK<sup>15</sup>. Additional comments  
28 were added by a fifth PORT parent via email following the video conference.  
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### 36 37 ***Study-specific themes***

38 Information regarding the undertaking and conduct of the study was described under three major  
39 themes; ‘importance’, ‘how PPI changes researchers’ views’ and ‘practical and ethical’. The theme of  
40 ‘importance’ was formed by concepts of ‘medical consequence’, ‘psychological consequence’,  
41 ‘impact’, ‘unpredictability’ and ‘frequency of FN’. (See Figure)  
42

43 *Importance:* The group members unanimously agreed that the management of episodes of febrile  
44 neutropenia was important because of its unpredictability, frequency, and medical, psychological  
45 and social (‘impact’) consequences. They described particularly how variation in care across different  
46 hospitals was a source of concern to them and consistency would be a positive by-product of  
47 undertaking a trial:  
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49

50  
51 *“we’ve got the 20-odd centres and pretty much everybody follows the same protocols [for*  
52 *anti-cancer treatment]... and I think it would be really reassuring for families if the POSCUs*  
53 *[Paediatric Oncology Shared Care Units] you know if we knew that everybody was doing the*  
54 *same thing” [P1]*  
55

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58 *‘How PPI changes researchers’ views’* describes the impact of this work: of how PPI is important in  
59 modifying the initial, genuinely held presumptions and beliefs about the best ways to conduct such a  
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3 trial for families and CYP. These beliefs were drawn from the trial development group, the group of  
4 clinicians and researchers involved in designing the trial, which has over a century of experience  
5 working in children's cancer in a variety of units and countries and specific expertise in studying  
6 supportive care in this group of patients. The impact of the group is seen in in the following aspects:  
7  
8

9 Allocation. The initial suggestion was for group randomisation, assigned arms to by clinical unit,  
10 rather than individual patients. However, the PPI input strongly steered towards individual  
11 randomisation, but with each individual receiving the same arm of management throughout the  
12 whole trial:  
13

14  
15 *with paediatric oncology unlike many other things... everybody is on a trial... everybody... I*  
16 *mean... <snip>... I think everyone just expects that their treatment may be a bit different*  
17 *than everyone else's... [P2]*  
18

19  
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21 *once you're randomised rather than each time coming in and by randomised each time,*  
22 *you're better off having "this family is procalcitonin, this family is not" [P1]*  
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25  
26 Outcome assessment. The group members felt direct measures of patient experience would be  
27 important, more than 'quality of life' checklists. They suggested offering a daily experience journal of  
28 some form (paper, or 'app' based electronic), and believed this would supplement and enrich the  
29 medical data collected, such as admission duration, antibiotic duration, and infective organisms.  
30

31  
32 *capturing that idea of burden beyond the hospital based stuff and things that matter to the*  
33 *family, [P3]*  
34  
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36 They described how it would be important to measure the extra resources required because of FN  
37 admissions. The word 'impact' was felt to capture this rather than 'costs'.  
38

39  
40 *impact, because it's not just about extra costs, I mean if you're having to call in grandparents*  
41 *and you're having to call in favours left right and centre, <snip> I mean how many times can*  
42 *you ask the next door neighbours to collect your kids from school [P1]*  
43  
44

45  
46 Active safety netting. The researchers initially felt the standard approach after discharge of  
47 responsibilities passed to the family to 'return if unwell' would be safe and acceptable, but the PPI  
48 group thought an active approach to safety-netting was necessary, but should be individually  
49 negotiated:  
50

51  
52 *I think it needs to be more than just you phone up the hospital if you have any concerns, it*  
53 *should be either somebody coming around or phoning you and saying "Do you have any*  
54 *concerns, do you have any concerns at all" and actually if you say yes ..... giving you the*  
55 *option of coming back or having somebody over [P4]*  
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58  
59 Gaining consent. The researchers proposed, as with usual practice, the study would be offered once  
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3 to families when the clinician believed it appropriate. The group members, with their experience of  
4 studies and information being exchanged, thought it would be fair to allow people to decline early  
5 on, but have the opportunity to join the study if they changed their mind as their treatment journey  
6 progressed. They also floated the idea of families approaching clinicians to join, rather than being  
7 invited.  
8  
9

10 *I don't think I even knew what febrile neutropenia was though, at the time when we were*  
11 *first giving our consent to all the other things? I think that's something that possibly comes*  
12 *with... further on... down the line... even a week or two weeks after you've given all those*  
13 *other consents. Because actually, the other consents are almost live-saving things... whereas*  
14 *this is a real choice... and I think that batching it in with those initial forms of consents is*  
15 *almost taking away your flexibility of trying to consider it whether you want to do it or not*  
16  
17 [P4]  
18  
19

20  
21  
22 *You might also get people saying 'No' right at the beginning, if it's something they don't have*  
23 *to agree with, and then subsequently further on during their treatment when they can really*  
24 *see the how much of a headache that this can be... [giggles]*  
25  
26

27 - *Do you think it's OK then to offer it twice? If somebody says no the first time? [R1]*  
28

29 *Yes – I think I do [P4]*  
30  
31

32  
33 *Because it's not like chemo A vs chemo B, it's not ... it's not crucial like... you can opt in*  
34 *whenever you want [P2]*  
35  
36

37  
38 The theme of 'practical and ethical considerations' included the ethical aspects of; consent,  
39 randomisation, delays introduced by undergoing the trial, equity and equality, and the sharing of  
40 trial data. The practical aspects described outcome collection, safety netting, and ensuring the  
41 veracity of information collected in the trial.  
42  
43

44 Randomisation was considered a fair and ethical approach when in clinical equipoise. Along with  
45 this, a later discovery one arm proving better than the other was not considered unethical; however  
46 if being on the study disadvantaged everyone (for example, by meaning treatment would be delayed  
47 while forms were completed) then it would not have been supported. A design which was accessible  
48 for the diversity of social, cultural and economic backgrounds of potential participants was essential.  
49 Confirmation of the scientific validity of the proposal and clinical equipoise was important to the PPI  
50 group. Prior systematic reviews with meta-analysis were felt to be a very comprehensive answer to  
51 this question.  
52  
53

54  
55 Two of the three researchers have a strong interest in individual participant data meta-analysis. A  
56 question was asked about data sharing in this context, and the PPI were very enthusiastic in being  
57 involved.  
58  
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60



1  
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3 *Definitely share. I think the thing with paediatric oncology is that we do so many*  
4 *international trials together, because thankfully it is rare, but ultimately I think that... [snip]*  
5 *we're here ultimately to try to make things better for kids of the future and if that's part of it,*  
6 *and it is with these meta-analysis, then definitely. [P1]*  
7  
8  
9

10 The group members were concerned about study governance, for example ensuring the veracity of  
11 information collected during the study.  
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13  
14 *"are they [study groups] actually going to tell you the truth?" [P2]*  
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17 The members were keen to know there would be some ways of determining if the data collected  
18 were truthful and accurate: this seems to speak of a greater public awareness being required of the  
19 nature of health research governance within the country generally.  
20

21  
22 An offer for expressions of interest in continuing to engage with the study governance was  
23 enthusiastically met by the participants. One of the group has joined the funding application as a co-  
24 applicant, and has helped develop the grant application and is planned to be involved in the  
25 qualitative data collection and analysis as a co-investigator.  
26  
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### 28 ***Febrile neutropenia themes***

29 Conversations in these discussions mapped onto the framework proposed by Morgan, developed to  
30 understand the decision-making processes involved in managing episodes of febrile neutropenia<sup>12</sup>.  
31 The overarching concepts she described were of the quest for certainty, attaining mutual trust, and  
32 the potential for realised discretion. These were all strongly endorsed in analysis of the group  
33 discussion.  
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36 The quest for certainty involves balancing the uncertainty of outcome of each episode of febrile  
37 neutropenia, including an appreciation of probability, the use of protocols and guidelines to manage  
38 the risk, and acknowledging the adverse elements of hospitalisation. The use of protective isolation,  
39 where the child and family are kept in a single room to avoid infections being caught from other  
40 hospitalised children, or source isolation, where the child is kept in a single room to avoid an  
41 infection they have spreading onwards to others, were viewed particularly negatively.  
42  
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44

45 *It was his cupboard – [child] called it his cupboard [P3]*  
46  
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48 Mutual trust had been a challenge, with the group describing individual health care practitioners in  
49 whom they did not place trust, and the reciprocal of this, along with the negating of parental  
50 concerns;  
51  
52

53 *the first time that I thought it was that they were taking too much precaution and I would*  
54 *have much preferred him to be at home taking tablets and things... monitored every so*  
55 *often.. whereas the second time I think he needed more than what he was getting... and I*  
56 *think we were right both times actually [P4]*  
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3 The ideal management of an episode of febrile neutropenia was one where safety was assured,  
4 hospitalisation was minimised, decisions discussed with families, and support provide at home  
5 provided as desired by the family: the potential for realised discretion. The group readily  
6 acknowledged the decisions would need to be based on a range of factors, including home-to-  
7 hospital distance and the variability between parents and families in self-expressed confidence:  
8  
9

10 *my sort of worry is that... the responsibility is even more on the parent as well. .on top of like*  
11 *running the house... and its that sense of responsibility as well... like they're monitoring their*  
12 *child and being responsible for it... and like if something did happen would they feel guilty*  
13 *about it or not? [P5]*  
14  
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16  
17 Exploring how the professionals were thinking about the episode, in terms of the likelihood of  
18 adverse outcomes and their considerations, was a strength in a shared decision making approach  
19 which had been absent in many prior experiences:  
20  
21

22 *I think it would be really helpful, [imitates Dr speaking] ... we think its' like this [left] or we*  
23 *think it's like this [right]... and then chatting... and .... You know where you are coming from*  
24 *and where there is a difference and you know talking about ... [P2]*  
25  
26

27 *seem to recall being in negotiations... situations where... ringing [PTC] consultants saying*  
28 *"This is our situation .... can you speak to them and and so on..." [P4]*  
29  
30

### 31 32 **Reflections of clinical academics**

33 The group discussions encouraged the three researchers to reflect on their previous approaches to  
34 febrile neutropenia and PPI involvement in other studies. The more experienced researchers had  
35 undertaken PPI before, but always on a face-to-face basis. The video conferencing allowed for a  
36 more diverse group of individuals to undertake the work, with the researchers in the same room on  
37 one screen facilitating. The makeshift re-positioning of audio for one participant through the phone  
38 served to reduce hierarchies, with collaborative suggestions and problem solving forming an early  
39 'win' for the group. This method worked well with the age and technological skills of this group, but  
40 may be less successful if a group with fewer technology skills or younger age were being involved.  
41 The protocol changes suggested by the group had been unexpected, as was the emphasis on the  
42 emotional burden of physical isolation. The researchers all took away from this experience the value  
43 of listening to expert parents and young adults, and considering video or telephone conferencing to  
44 allow a greater number and range of people to take part in PPI events.  
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### 51 52 **Discussion**

53 The engagement of a group of parents and an ex-patient who had experience of CYP cancer with  
54 researchers developing a study to improve the management of febrile neutropenia led to changes in  
55 the proposed design of the trial, and brought out a deeper understanding of the potential concerns  
56 of participants in such a study. The wider discussions about the nature of the experience of an  
57 episode of febrile neutropenia were congruent with prior work in the field <sup>12</sup> pointing particularly to  
58 actively involve parents and young people in sharing decisions about care.  
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3 The PPI involvement altered how the trial would be structured, randomisation of each child to one  
4 of the two management methods through the whole of their anti-cancer treatment, rather than  
5 randomising the study sites or the child at each visit (see Box 2 for specific changes). The suggestion  
6 of multiple opportunities to be involved in the study was welcome, and congruent with the  
7 description of an emerging expertise and empowerment in people through the childhood cancer  
8 journey<sup>16</sup>. They discussed practical methods of collecting data which went beyond simple admission  
9 statistics and questionnaires, to enrich the information gained in the study. Active follow-up, with  
10 healthcare initiated contact with the family, but negotiated in light of their individual family, had not  
11 been originally considered by the researchers. The discussion also shed light on the experiences of  
12 people in being involved in treatments of episodes of febrile neutropenia, with the ideal being an  
13 individualised, negotiated approach within clear, safe, guidance, consistently used across all centres.  
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18 The expertise and prior relationships in the group members of similar situations may have enhanced  
19 the easy flow of ideas and conversations in this event. All members knew at least one other  
20 participant through in-person interactions, in similar group settings or clinical interactions. Ice-  
21 breaking activities were extremely brief, as there was little ice to be broken. None of the participants  
22 were paid for their time undertaking this work. The INVOLVE guidelines suggest involvement should  
23 come with re-imburement, the group all undertook work with charities related to childhood cancer  
24 treatment, research and support and saw this as an extension of their other activities. Future PPI  
25 work with similar groups of people would benefit from considering holding the group conversations  
26 via a video conferencing platform. The ready availability of web-cams and front-facing cameras on  
27 phones, tablet and laptop computers, and the common use of video conversations in work and  
28 home life mean these were acceptable methods to have discussions with this group. There are  
29 limitations with this approach. It requires a familiarity and access to such equipment, and access to a  
30 relatively stable internet connection. This may exclude PPI, particularly young people, from  
31 disadvantages backgrounds. It may also be very difficult to use to work with younger children, or  
32 older family members, perhaps great-grandparents, who are unfamiliar with video conferencing. If  
33 the approach is used, it may be beneficial to have a 'test run' period prior to the meeting to allow  
34 any technical challenges to be met; we would suggest a period of time when 'drop in' connections to  
35 confirm all is working well would be a sensible way forwards. A backup approach, as simple as a  
36 telephone line, is also very helpful.  
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43 We used social media (Twitter) to recruit the participants; as the researchers all had prior experience  
44 of working with PORT, and 'tagged' them into a post, this may be considered a mixture of open and  
45 direct messaging. This type of use has been fairly widely undertaken previously<sup>17</sup> and has  
46 advantages and disadvantages. It carries little direct risk, as it doesn't ask for people to engage in  
47 discussion in a forum (such as Facebook or Blog comments), but its reach is limited to those who  
48 already follow one of the accounts which post, or re-tweet, the invitations. It provided an excellent  
49 opportunity to draw in active PPI parent volunteers, but did not attract a large number of young  
50 people. Direct advertising of the chance to be involved in the work to young people via other groups,  
51 such as Young People's Advisory Groups hosted by organisations such as the National Cancer  
52 Research Institute or Clic-Sergant, or advertising through the Teenage Cancer Trust, may have meant  
53 more than one young person was involved.  
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58 The findings of this study have immediately influenced an application for a feasibility study of  
59 procalcitonin guided management of febrile neutropenia. They will also influence the ongoing  
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3 development of clinical practice through dissemination through the children's and young people's  
4 professional network groups. The participants in this group have expressed a wish to be part of the  
5 steering committee of a trial addressing this issue, and the ongoing study development will also seek  
6 further young people to be involved, following INVOLVE guidelines<sup>17 18</sup>. One of the group members  
7 has joined the study as a co-applicant, developing the grant, and plans to be involved as a co-  
8 investigator..  
9  
10

## 11 12 13 14 **Figure legend**

15 Interaction of themes and sub-themes  
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## 20 **Funding statement**

21 This research received no specific grant from any funding agency in the public, commercial or not-  
22 for-profit sectors. BP was supported by an NIHR Post-doctoral fellowship: grant number PDF2014-  
23 10872.  
24  
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## 28 **Competing Interests**

29 There are no competing interests to declare.  
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## 34 **Contributorship**

35 This study was conceived by BP and SD, and developed with the assistance of JM. The audio was  
36 transcribed and analysed by BP initially with input from JM and SD. BP drafted the paper, and was  
37 critically revised and developed by JM and SD. The PPI group read and agreed with the content of  
38 the paper. The authors very gratefully acknowledge their input into this specific work.  
39  
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## 43 **Box 1: Original trial design**

44 Site-randomised trial (randomising by hospital) using cluster or step-wedge approach  
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47 Use of single quality of life questionnaire at discharge  
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49 Patient contact for trial purposes only to occur while in-patient – not after discharge  
50

51 Antibiotic decision making on procalcitonin measurements and clinical judgement without family  
52 involvement  
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## 56 **Box 2: Changes following consultation**

57 Individual patient randomised trial (randomising by patient, not by episode)  
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60 Consent permissible at any point during the cancer journey while still 'at risk'

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3 Richer patient experience measures – not just patient QoL but family experience and their costs to  
4 be captured  
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6 Active follow-up after discharge  
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8 Explicitly encouraging shared decision making and sharing of results with families to decide antibiotic  
9 use  
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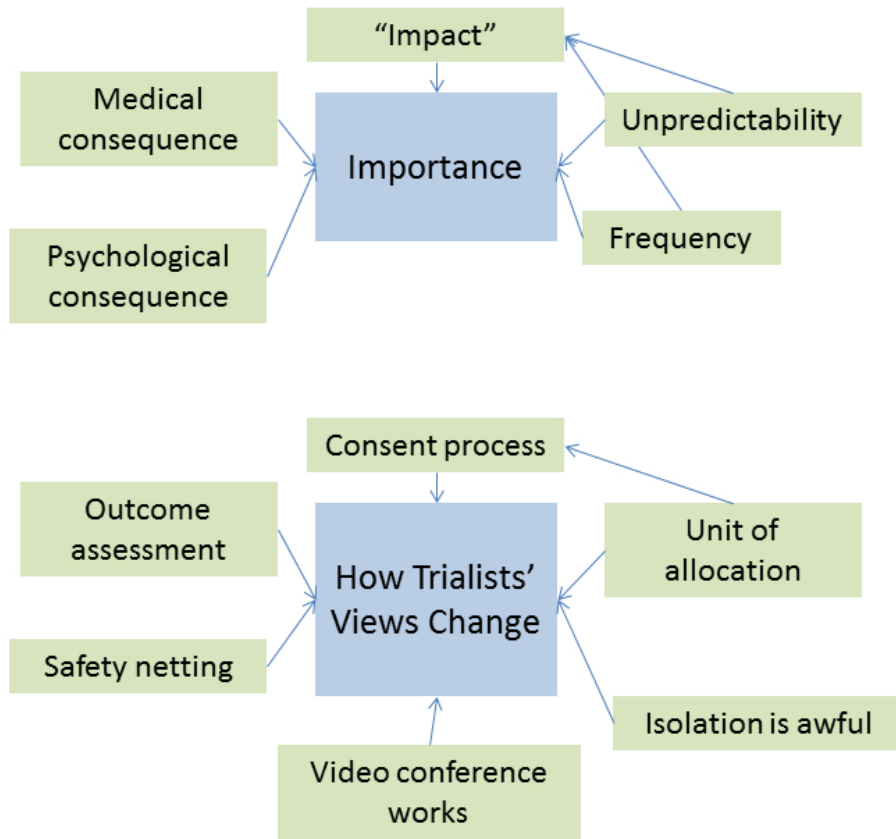
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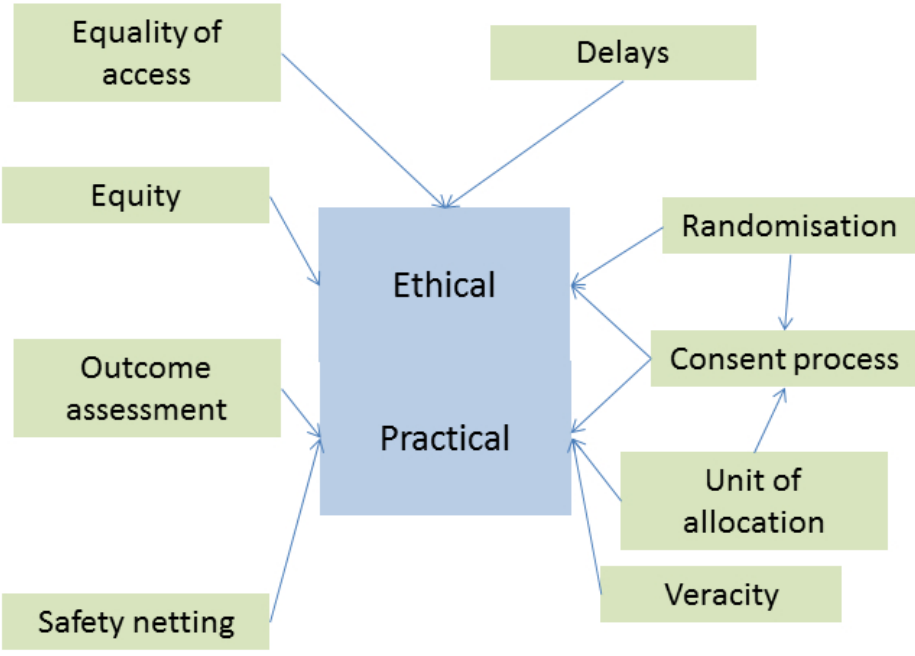
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