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Chronic Illness
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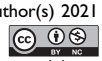

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Burden of cancer trial participation: A qualitative sub-study of the INTERIM feasibility RCT

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Abstract

Objective: A qualitative sub-study was carried out within a larger phase II feasibility trial, to identify and describe the burden experienced by advanced melanoma patients participating in a clinical trial and the factors affecting their capacity to cope with the burden.

Methods: Semi-structured interviews were conducted with fourteen patients with advanced melanoma recruited from National Health Service hospitals in the United Kingdom. Qualitative analysis was undertaken using a framework analysis approach. Normalisation process theory was applied to the concept of research participation burden in order to interpret and categorise findings.

Results: Burdens of participation were identified as arising from making sense of the trial and treatment; arranging transport, appointment and prescriptions; enacting management strategies and enduring side effects; reflecting on trial documents and treatment efficacy, and emotional and mental effects of randomisation and treatment side effects. Factors reported as influencing capacity include personal attributes and skills, physical and cognitive abilities and support network.

Discussion: This is the first study to highlight the substantial burden faced by patients with

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advanced melanoma in a clinical trial and factors that may lessen or worsen the burden. Consideration of identified burdens during trial design and execution will reduce the burden experienced by research participants.

Keywords
Research burden, patient capacity, treatment burden, qualitative, cancer trial participation

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Introduction

Melanoma is a life-threatening skin cancer with a high incidence rate and accounts for 4% of all new cancer cases.[1,2] Globally, incidence rates of melanoma rose by 44% between 2008 and 2018,[3] with deaths increasing by 32%. Australia, New Zealand and the United Kingdom (UK) are among the countries with the highest incidence rates.[4] Melanoma is an aggressive malignancy that tends to metastasize beyond its primary site. The introduction of oral targeted combination therapies that target the BRAF (v-raf murine sarcoma viral oncogene homolog B1) mutations has improved overall survival rates.[5] These targeted therapies incur significant toxicity and this can limit their efficacy. Moreover, patients assume the responsibility for understanding the medication regimen and determining how to best integrate the treatment and treatment-related side effects into their daily lives.[6,7] Consequently, many patients will experience burden both from their illness and from the demanding treatment regimen. The increased emphasis on self-management in cancer patients, deemed necessary to improve outcomes and reduce costs, shifts the long-term management of ill-health from clinicians to patients;[6–9] yet the treatment burden that patients experience is not well understood.[6,8]

Treatment burden is the healthcare workload (tasks recommended by clinicians to improve health status, e.g., attending medical appointments, managing complex medication, diet and exercise regimens) experienced by patients with chronic conditions and the impact this has on behavioural, cognitive, physical and psychological well-being.[6–10] Patients who struggle with complex and demanding treatment regimens often experience adverse outcomes including poor self-management, adherence to medication therapies and quality of life (QOL), leading to increased hospitalisation rates, healthcare costs and mortality.[11] The medical approach to poor outcomes which is to intensify treatment may inadvertently increase treatment burden as already burdened patients are asked to do more by their clinicians.[11] Treatment burden for people with advanced melanoma on oral therapies remains under-researched.[6] Research participation will exacerbate basic treatment burden as patients face the additional burden of increased travel, completing questionnaires and undergoing supplementary procedures specific to a trial.[12] Evidently, research participants in clinical trials experience both treatment and trial burden; underscoring the need to fully explore their experiences.[12,13]

Capacity is the abilities and resources that patients can mobilise to manage and cope with the demands of healthcare and life that if limited, impacts the ability of individuals to self-manage.[7] Patient capacity determines whether the combination of participating in a clinical trial in conjunction with the burden of taking a therapy will be perceived as potentially unmanageable or excessively burdensome. The ability to follow treatment regimens is affected by several factors including social support, financial constraints, personality and cognitive functioning.[7,8] Hence, patients experiencing the same level of

healthcare demands may cope very differently due to variation in capacity.[8,14] Patients with advanced cancer often present with severe ill-health when oral therapy is prescribed,[6] and treatment side effects such as pyrexia and fatigue which impact wellbeing and QOL are common.[15] However, the impact of treatment side effects on QOL is under-estimated by clinicians,[16–18] and although treatment burden and capacity in patients with chronic conditions is gaining recognition,[9,11–14] little is known about the experiences of patients with advanced melanoma taking part in a clinical trial.

Despite improving outcomes, continuous daily dosing is associated with several challenges including treatment resistance with a median progression-free survival of 12 months, treatment compliance and QOL. Hence, intermittent dosing may help delay onset of disease progression, manage drug-induced toxicity and improve tolerability. INTERIM (INTERmittent vs. continuous dosing of oral targeted combination therapy in patients with BRAFV600 mutant stage 3 unresectable or stage 4 metastatic melanoma) was the first randomised phase II feasibility trial to deliver intermittent dosing of the oral targeted combination therapy alongside standard care (continuous dosing), and examine QOL, clinical efficacy, safety, time to treatment failure, overall survival and toxicity. In addition to trial outcomes, patient experiences were explored to gain perspectives about the intervention and trial participation that were not otherwise evaluable through quantitative measures. Qualitative research provides insight into areas of enquiry with little baseline understanding, explores experiences of subgroups, enhances trial findings and allows more complex phenomena to be explored in detail.[19] Therefore, the aim of this qualitative sub-study was to identify and describe the burden of participating in a clinical trial whilst living with advanced melanoma, and the factors affecting capacity to cope with this burden.

Methods

A qualitative sub-study exploring the views and experiences of patients with advanced melanoma was undertaken as part of a phase II randomised controlled trial (RCT) (trial registration number: 2016-005228-27).[20] Briefly, between December 2017 and March 2020, 79 patients with BRAFV600 mutant stage 3 unresectable or stage 4 metastatic melanoma, due to start a course of targeted oral combination therapy (dabrafenib and trametinib treatment) were recruited from 25 participating UK National Health Service (NHS) hospitals and enrolled in the parent RCT (intervention = 40; standard care = 39). Three participants were lost to follow-up and 24 died during the study. This article, prepared using the consolidated criteria for reporting qualitative research (COREQ),[21] reports solely on qualitative study findings. Favourable ethical opinion was obtained from Cambridge South Research Ethics Committee [17/EE/0340].

Intervention

Intervention participants received intermittent dosing of the oral targeted combination therapy and standard care participants, continuous dosing (Online Appendix 1).

Sampling, recruitment, and consent

Study personnel at each site invited participants (face-to-face or via telephone) who had been in the RCT for 6 months, to take part in a semi-structured interview. Convenience sampling was used to recruit intervention and standard care participants in order to understand the perspectives of patients in both arms of the trial. Participants met the following inclusion criteria: age $\geq$ 18 years; histologically or cytologically confirmed mutant stage 3 or stage 4 melanoma; predicted life expectancy >12 weeks; adequate renal, liver and bone marrow function; willingness to comply with scheduled visits, treatment, lab tests and completion of

trial procedures described in the protocol. Of the 16 participants who agreed to be interviewed, two could not be contacted despite several attempts and 14 were interviewed.

Data collection

Participants received postal study information sheets, explaining the research, and consent forms along with a pre-paid envelope (for returning signed consent forms). Prior to data collection, the researcher [CN] also contacted participants to introduce herself, clarify the reasons for the study and answer questions. Written consent was obtained prior to data collection. Telephone interviews, guided by an interview schedule informed by the literature[13,22,23] and developed by the multi-disciplinary study team, were conducted by one researcher [CN]. The interview schedule was piloted with two non-participating cancer patients and revised (Online Appendix 2). The average time for interviews ($n = 14$) was 36 min, with a range between 17 and 60 min. Data collection took place between July 2019 and June 2020.

Table 1. Components of NPT.

Component	Definition
Sense-making work	Learning about disease diagnosis, treatments, and their consequences as well as reading trial paperwork and seeking information on trial processes.
Relationship work	Engaging with others for help and support, arranging medical care and mobilising resources to arrange support or help with transportation, prescriptions, and other essential services.
Enacting work	Implementing the self-management tasks and adapting daily activities to accommodate the illness; completing trial questionnaires and attending hospital appointments.
Appraisal work	Refining and adjusting the treatment regimen as necessary and assessing whether to continue or change current management plans. Reflecting on trial documents including questionnaires and decision to take part in trial.

Data analysis

The framework method was used.[24] All interviews were audio-recorded, transcribed, anonymised, checked for accuracy and imported into NVivo 12 software to aid analysis. Themes were constructed deductively using pre-defined themes within the Normalisation Process Theory (NPT), patient capacity literature[8,13] and inductively by identifying additional themes within the data. The procedure for analysis included: transcription, familiarisation with the interview, coding, developing and applying analytical framework, charting data into the framework matrix and interpreting the data. Two members of the research team [CN, RF] independently coded and analysed the transcripts to identify themes and ensure inter-rater reliability; variations in coding were discussed and agreement reached on designated themes. Thereafter, themes were discussed and agreed with co-authors [CJ and RM]. Themes from all interviews were categorised into those that described burden (facilitated by NPT) and patient capacity.

Conceptual framework. Normalisation Process Theory (NPT) is an analytic framework for understanding the organisation and implementation of tasks such that they become routine and incorporated into everyday practice.[25] Although NPT has often been used to understand complex and technological interventions, it is also being increasingly used to conceptualise the tasks or work carried out by patients to manage chronic illnesses.[11,13,26] NPT encompasses four distinct components (Table 1) which have been used previously to describe

Table 2. Demographic detail of study participants.

No	Identifier	Gender	Geographical location	Age (years)	Intervention arm
1.	P1	Male	England	78	Continuous
2.	P2	Female	England	50	Continuous
3.	P3	Male	England	70	Intermittent
4.	P4	Female	England	70	Intermittent
5.	P5	Male	Scotland	49	Continuous
6.	P6	Male	England	57	Continuous
7.	P7	Male	England	47	Continuous
8.	P8	Female	England	Not available	Intermittent
9.	P9	Female	England	57	Intermittent
10.	P10	Male	England	67	Continuous
11.	P11	Male	England	80	Intermittent
12.	P12	Female	England	81	Intermittent
13.	P13	Female	England	62	Continuous
14.	P14	Female	England	49	Intermittent

the burden experienced by patients managing a chronic illness.[11,25] NPT was applied to the data in order to conceptualise the work undertaken by patients with advanced melanoma taking part in a clinical trial.

Findings

Demographics. Demographic characteristics of the 14 participants (intermittent, $n = 7$ and continuous, $n = 7$) are shown in Table 2.

Table 3. Themes and sub-themes.

Main themes	Sub-themes
Burden of being a research participant in a clinical trial	Sense-making work
	Relationship work
	Enacting work
	Appraisal work
	Psychological burden
Factors affecting patient capacity	Altruistic motivation
	Emotion-focused coping
	Personal attributes and skills
	Physical and cognitive abilities
	Positive reinforcement and feedback
	Financial status
	Support network

Themes. Two major themes and a number of sub-themes emerged from the interview data (Table 3). These themes and their sub-themes are described below, along with representative quotes [with additional quotes appearing in supplementary data file 1]. Excerpts from the transcripts are referenced using P, followed by a number for each participant and the treatment arm, that is, standard care (SC) or intervention (I).

Burden of being a research participant in a clinical trial

The tasks carried out by patients to manage their illness (e.g., taking medications, reading information leaflets, arranging transportation to attend hospital appointments, making lifestyle changes) and the personal impacts of trial participation, were discussed by participants.

Sense-making work. All participants described their diagnosis as life-changing and previous cancer treatments as torturous. However, despite undergoing and experiencing adverse effects of several procedures including surgery, radiotherapy and immunotherapy, they learned that their disease had become advanced

following unfavourable scan results. The combined targeted oral therapy was subsequently prescribed to reduce the likelihood of further disease progression. They reported that clinicians explained the challenges associated with continuous administration of the drug (standard care), however, it was unclear whether equipoise was sufficiently explained.

Participants reported that they were provided with verbal and written information which they described as informative, and noted being given sufficient time to make an informed decision. Many participants acknowledged not having a good understanding of melanoma treatment and management at the outset but invested time and effort into understanding the treatment and trial by reading trial documents and asking questions.

> I basically asked how it would work … just to have the whole process explained to me because it is quite complicated … It did take getting my head round it … what to expect and all that sort of thing … initially, I knew nothing about it. [P8, I]

Some routinely used the internet to look up health information and through personal research, enhanced their understanding of the treatment.

Despite the reported level of written and oral information provided beforehand, some participants acknowledged that they did not fully understand the information provided which subsequently led to misconceptions; for example, erroneously perceiving the treatment as curative rather than life-extending. Important RCT concepts such as randomisation were also difficult for some to understand and/or accept.

> [Randomisation] was quite an unusual aspect to deal with certainly in terms of the fact that we were dealing with such an important treatment for myself … I was keen to try and understand … was every patient treated completely randomly? Or was every second patient treated conversely to the first patient? [P5, SC]

Additionally, participants felt that they had not received comprehensive information regarding treatment side effects.

Relationship work

Participants engaged with clinicians, friends and family with regard to the disease and its management to enable them to provide support. They reported good relationships with the trial clinicians who they consulted frequently during the trial. Those who contacted clinicians by phone either received advice over the phone or organised a clinic appointment. Participants spoke highly of the trial clinicians and mentioned the exceptional care received and the approachability of the research nurses.

> Dr [name] at [city], he organised everything extremely quickly in conjunction with [hospital], and the service and the care I've got was fantastic … well, I couldn't have got any better if I'd have gone private, to be quite honest; it was excellent. [P7, SC]

Participants felt that seeing the same clinicians at each consultation was important and invaluable to their experience. They highlighted that whereas continuity of care was often lacking in secondary care, being in the trial made it possible for participants to be looked after by the same nurse(s), with whom they had developed a relationship.

Participants were also involved in arranging hospital appointments, transportation and prescriptions. Most patients relied on others, mostly family members, to help out with transport to appointments. Some also spent time liaising with and arranging help from social services and cancer charities. There were very few reports of unsatisfactory encounters during the trial that fell below participants' expectations although several participants

complained about the delay with the prescription service that resulted in more time being spent in hospital than necessary.

Enacting work

Participants described the logistic and practical day-to-day activities they had to undertake in order to adhere to treatments and maintain their health. They highlighted the considerable amount of work and time involved in attending multiple hospital appointments, including consultations, questionnaire completion, blood tests and scans.

> The main problem is all the hospital appointments. It's getting there all the time that they want you there … that's the only thing that gets me down a bit. [P1, SC]

However, some felt that this level of monitoring was essential given the advanced stage of the disease and potency of the oral therapy.

Adhering to treatment consumed an immense amount of time, and working out the strict timing of the medication proved particularly difficult for participants. Hence, medication non-compliance occurred despite strategies to prevent it, that is, using alarm clocks and log books/diaries. Additionally, enduring and managing treatment side effects consumed the largest proportion of participant's time and energy. All participants experienced a number of treatment side effects that affected their physical and mental wellbeing, including pyrexia, flu-like symptoms, vomiting, syncope and pustular eruptions.

> One morning I collapsed and then I got the shakes… My blood pressure went very low. I got out of bed and then I fell in the bathroom … and my wife couldn't get me out and then they took me into [hospital] and they kept me in for about five days. [P12, I]

Most participants were taking a variety of medications to control treatment side effects including proton pump inhibitors, morphine and steroids, which also had side effects which they endured, for example, insomnia. Participants stressed that they were solely responsible for self-managing their disease(s) and treatment, and felt that the onus was on patients to follow clinicians' directives. Most reported initially relying on clinicians for advice but had since developed confidence to self-manage their side effects.

Appraisal work

Much effort was also expended on trying to incorporate the treatment and side effects into daily lives, and participants independently altered medication regimens to fit in with their daily activities. In addition, participants spent time assessing management plans either with the help of clinicians or independently, hence, those who suffered severe adverse effects were advised to either introduce a break in the medication regimen or continue on a reduced dose indefinitely. Participants on the reduced dose experienced improved QOL.

> I've noticed a difference now on a lower dose that I'm not that tired … As for the [side effects], they've really kind of dissipated … at the moment the medication's suiting me and keeping the cancer at bay, and my quality of life isn't being affected. [P3, I]

Participants also reported reflecting on self-management practices and treatment efficacy. Participants were motivated to persevere with current treatment despite experiencing side effects as they saw noticeable improvements in the extent of their disease.

Overall, participants were satisfied with the efficacy of the targeted therapy. Participants also attended monthly follow-up visits, self-completed questionnaires every 3 months, and reported all other side effects as they arose by completing questionnaires. Participants felt that the questionnaires were useful because they assessed both physical

and psychological effects, and enabled participants to reflect on their progress and wellbeing. However, some felt that it did not fully capture the psychological issues participants experienced during the trial.

Participants also reflected on and reported being satisfied with the overall conduct of the trial. However, they suggested that in future, due to the potency of the drug, the current dosage should be more closely monitored or reduced in order to prevent severe adverse reactions.

Psychological burden

The emotional and mental effects of trial and treatment featured prominently and were frequently mentioned by participants. For example, some reported feeling fearful and anxious at the possibility of not meeting the trial eligibility criteria. They also reported experiencing low mood, sadness and anxiety during the trial. In addition, they ascribed the strong negative emotions they felt to the targeted therapy.

> The first few weeks it made me feel really aggressive and really quite angry … I've never really experienced that amount of aggression and anger before. [P7, SC]

Given the severity of side effects, many participants reported spending time gauging their physical and mental limitations and adjusting their day accordingly. They found carrying out daily activities very difficult as it demanded more energy than they could muster, leading to feelings of frustration.

Preference for the intermittent arm led to dissatisfaction. Despite progress made during the trial, risk of further disease progression caused distress and anxiety.

Factors affecting patient capacity

Factors that could enhance or reduce patient capacity to manage health problems were described by participants.

Altruistic motivation

Taking part in research in order to benefit future patients and medical science helped to create the feel-good factor and made enduring the burden and workload of participating in the trial worthwhile. Participants were hopeful that lessons learned from their experiences of the treatment, particularly adverse treatment effects, would be applied to future research and improve understanding of the effects of the targeted therapy.

> They're very keen, the clinical trial nurse, to record things that have affected you during this trial. And I think that's obviously a good thing … for the fact that it's going to be reported and looked at and used in the future for other people. [P3, I]

Personal attributes and skills

Personality impacted on how patients managed their health and perceived their care. Characteristics such as resilience, self-efficacy and self-determination enabled participants to find the motivation and inner strength to keep taking prescribed medication, enduring side effects and undertaking research activities.

> I just dealt with it … I'm a pretty robust person in the form of whatever comes my way I just deal with it … I'm quite resilient and able to cope with a lot of things. [P7, SC]

Some participants also used social comparison, that is, comparing themselves to other people, to convince themselves that their burden was not so much that it could not be managed.

Emotion-focused coping

Participants reported several strategies used to manage the negative emotions associated with treatment and trial burden, for example, focusing on other life priorities and carrying on with their everyday life.

> I get fatigue and breathlessness, but … I've not changed my lifestyle … I go out with my friends every weekend; I still go dancing … well, I'm going to do that until I can't do it … it's the only way to be. I'm not going to sit here and shrivel up. [P9, I]

Some focused their energy on work, family interactions, outdoor and leisure activities such as exercising and socialising to keep their spirits up and to avoid ruminating on their disease. Participants also reported using the favourable response to treatment as motivation to persevere.

Positive reinforcement and feedback

Participants felt that receiving frequent progress reports and/or feedback whilst the study was ongoing, would generate enthusiasm, boost morale and encourage active participation in the study. Highlighting and discussing the progress participants have made was deemed crucial for patients with advanced disease, as this would encourage adherence to treatment and endurance of the adverse effects.

> Information is all one way from us to the trial … I need information back … feedback … motivates people slightly more; it's a very good thing to do. [P4, I]

Physical and cognitive abilities

Most participants reported losing physical abilities due to melanoma treatment. They reported that this loss of mobility led to inability to effectively carry out self-care and access health services on their own. They reported being unable to leave the house, walk or carry out tasks.

Those with visual, hearing or cognitive difficulties struggled with logistical work such as organising and remembering to take their medication, and often relied on others, for example, family members, to remind them. Several participants reported having problems with their memory which caused them to either forget to take their medication or to take the same medication twice.

> I can forget things, or I'll repeat things … I've taken my tablets twice thinking, 'Oh, I've not taken my tablets.' … And I've just taken them again quarter of an hour later. So, I have to be quite aware or else I just might repeat [medication]. [P9, I]

Financial status

All participants were receiving treatments under the NHS and most of their care was free at the point of delivery. Those who were able to work, reported suffering a reduction in income due to treatment side effects and were only able to work part time. Some consequently struggled financially.

> I'm a single woman with a mortgage, and when something like this happens it's … you've got to try and get yourself sorted out … it's all right when you're working full-time, but when you have to go part-time. [P9, I]

Support network

Participants reported gaining emotional and companionship support, reassurance and help with decision-making from family, and were able to share information with clinicians openly and comfortably.

> I have to say I've been helped a lot by both my consultant and the clinical nurse, who've been very good and very, helpful to me and encouraging. [P3, I]

Having understanding colleagues and employers was reported to be important as participants had to take time off work to attend multiple hospital appointments and recover from severe side effects. Furthermore, participants mentioned experiencing loneliness and felt that they would benefit from emotional support and interacting with other people with advanced melanoma.

Participants stressed the need to encourage people living with cancer, taking part in a trial, to seek mental health support and be provided with or signposted to information sources and support groups.

Discussion

To our knowledge, this is the first study to provide a detailed description of the burdensome impacts of trial participation and elements of patient capacity that could influence the burden experienced by patients with advanced melanoma taking oral targeted combination therapy. This study reveals the extensive effort afforded by patients entering a clinical trial including understanding their illness, the treatments, trial documents and processes. Findings show that participants received adequate amount of verbal and written information, and had easy access to clinicians; however, knowledge gaps and misconceptions still existed. In addition, the rationale for randomisation were poorly understood. These findings are in line with the literature[12] which also found therapeutic misconceptions, and insufficient health and research literacy in patients with chronic illness. The rationale for these findings include information overload at an emotional time and failure to remember, understand or fully engage with trial information prior to consenting to participate.[12] Similar to our findings, evidence shows that treatment side effects, for example, fatigue, contribute to emotional distress and mental health problems among patients with cancer, potentially leading to inability to work.[27] Furthermore, up to 70% of patients with cancer stop working or experience a reduction in work hours after being diagnosed or treated for cancer, with negative implications for their income.[27]

Participants in this study lived a considerable distance from hospitals, attended multiple appointments for treatment and trial-related activities, and endured an enormous burden associated with travel to attend appointments. This has cost implications as out-of-pocket expenses for travel are not covered or reimbursed.[28] The high burden of trial participation in clinical trials has been identified as a barrier to recruitment, retention and active engagement in interventions.[29] A recent systematic review[12] found that the most common reasons cited by people with cancer for declining participation, missing hospital appointments and withdrawing from an ongoing trial, were complexity and stringency of the study protocol, additional research procedures, appointments and travel time to hospitals. These are important points of consideration because the success of RCTs depend on their ability to recruit sufficient patients and to ensure that as few patients as possible withdraw from the trial or become lost to follow-up. Similar to our findings, the literature[12] shows that aspects of the trial process such as recruitment, randomisation and treatment allocation often impose a psychological burden on research participants including disappointment, anger and depression.

Patients with advanced melanoma in this study experienced demanding treatment workload with debilitating side effects. Participants obtained and administered oral medication, monitored symptoms and self-managed side effects. In line with other studies,[26,28] several participants in this study also took several medications to control treatment side effects. Thus, the daily work that patients do to manage their cancer is exacerbated by the additional effort to manage drug interactions and side effects, all of which have to be integrated into their social, work and family lives.[28] Self-management practices represent a significant burden for patients despite being seen as a solution to the long-term management of chronic illness by healthcare

professionals and policy makers,[7,11,26] as the resources to achieve these ends may not be available to the patient.[7] Participants in this study highlighted several factors that they felt affected the burdens they experienced including altruistic motivation, emotion-focused coping, personal attributes and skills, physical and cognitive abilities and support network. These are resources that may counteract the negative impact of excessive demand of healthcare, lessen the treatment burden and influence adherence and engagement with clinicians.[7,30] Hence, it is vital that clinicians assess and assist with areas in which patients may need extra support and guidance, and consider patients' capacity to undertake healthcare workload.[13,28] It is also vital that trials consider patient burden and capacity as study variables.

The findings also show that participants drew upon a range of personal and social resources to help them manage and cope with the demands of research participation. For example, in line with the literature, emotion-focused coping such as focussing on other life priorities, could help to manage negative emotions arising from the burdensome work of self-care.[30] Also, altruistic motivation, maintaining a positive attitude and support from social network, employers and clinicians could bolster a sense of positive psychological wellbeing and adherence to self-care regimens.[12,13,30,31] The literature supports the use of social comparison as a means of adapting to stressful circumstances.[30] Participants also identified positive reinforcement and feedback in research studies as enabling factors, in line with the literature.[12] These findings underscore the need to encourage patients to acknowledge their burdens and communicate what could be done to better support them.[32]

Considerations for future trials to minimise participant burden

Patients and members of the public should be involved at the planning stage of a trial. Drawing on their experiential knowledge and ideas will ensure that burdens are identified early and either eliminated or strategies are put in place to minimise their effect.

Clinicians and researchers should assess and carefully consider the difficulties and challenges that patients will experience from therapeutic commitments and trial participation. Consideration should also be given to capacity to manage burden. The standard care clinical burden that patients already face need to be determined and balanced against the demands of the trial in order to determine whether they can realistically participate.[29]

Education, guidance and support should be provided on how patients can effectively integrate taking medications into their daily lives, simplify the regimen, increase adherence and manage side effects of treatment. The reliance of patients on clinicians for advice and support creates an opportunity for clinicians and patients to co-create a feasible and actionable plan that would help maximise patient capacity. These discussions could elicit a more open dialogue with patients about how they are coping with their illness, treatment and research participation, and how they can be assisted in areas where they may need extra support and guidance. Toolkits to aid discussion include goal elicitation, instrument for patient capacity assessment, workload assessments and medication therapy management tools.[8] Patients should also be signposted to financial and mental health support resources.

The process of seeking informed consent in trials contributes to psychological burden, particularly where patients are told about the potential benefits of a new treatment and then informed that their treatment allocation would be determined by randomisation.[6,33] A clear explanation of true equipoise and the rationale for randomisation could reduce this burden. Furthermore, research burden is not sufficiently considered by regulatory agencies which focus more on the risks of the intervention and data collection.[8] Shifting the focus to ensure protocols meet ethical standards whilst imposing the smallest possible burden to effectively answer research questions is paramount.

One study showed that the median number of items collected per participant in a sample of cancer RCTs was 599, but only 18% of the collected data was used and reported.[24] Researchers are urged to include only essential items.[34] Furthermore, using electronic questionnaires and scheduling several activities for the same day, for example, consenting patients in clinic during wait times and collecting data at the same visit, could minimise number of patient visits to hospitals, interruptions to daily routine and work, as well as minimising parking issues and other burdens.[35]

Strengths and limitations of the study

This study examined the burden of research participation experienced by patients with advanced melanoma taking part in a clinical trial, and factors that may affect their capacity to cope with these burdens. Although the sample size is small, the study obtained rich information about participants' experiences. However, this study used a convenient sample of patients who volunteered their time and provided self-reports of their experiences and it is possible that the most burdened patients declined to be interviewed due to time constraints or severity of illness. The factors affecting patient capacity discussed here were based on participants' account and further research is needed to examine their possible role in influencing capacity to manage burden of research participation. In addition, NPT appears to offer a robust conceptual framework for understanding overall burden of research participation, although in line with another qualitative study,[11] psychological burden fell outside the NPT framework. Nevertheless, by combining inductive and deductive analyses, the emotional aspects of participants' experiences were captured.

Conclusion

This study provides a detailed description of burdens experienced by patients with advanced melanoma in a clinical trial and elucidates factors that may lessen or worsen the burden. Clearly, the burden of research participation for chronically ill patients is a significant issue and will become even more pronounced with the projected rise of cancer survivors in the UK and around the world. The consideration of burdens during the planning and design of RCTs could help improve their conduct, recruitment and retention as many of the burdens can be anticipated and avoided in a move towards minimally disruptive research.

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Authorship

PC, MM, CJ, RF, AG and RM conceived the study, developed the study protocol and obtained ethical approval. CN researched the literature and was responsible for patient recruitment. RF and CN were involved in data analysis. CN wrote the first draft of the manuscript. All authors reviewed and edited the manuscript and approved the final version of the manuscript.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical approval (*include full name of committee approving the research and if available mention reference number of that approval*)

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Informed consent

Written informed consent was obtained from all subjects before the study.

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Supplemental material

Supplemental material for this article is available online.

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